Health Evidence Review Commission's

Value-based Benefits Subcommittee

August 09, 2012

Meridian Park Hospital
Community Health Education Center, Room 117B&C
19300 SW 65th Avenue, Tualatin, OR 97062

AGENDA
VALUE-BASED BENEFITS SUBCOMMITTEE
August 9, 2012
8:30am - 1:30pm
Meridian Park Hospital
Community Health Education Center, Room 117B&C
19300 SW 65th Avenue, Tualatin, OR 97062
A working lunch will be served at approximately 12:00 PM
All times are approximate

I. Call to Order, Roll Call, Approval of Minutes – Lisa Dodson 8:30 AM

II. Staff report –Ariel Smits, Cat Livingston, Darren Coffman 8:35 AM

III. Coverage Guidances for Prioritized List– HERC Staff 8:45 AM

A. HERC Coverage Guidances

A. Planned cesarean delivery
B. Elective induction of labor
C. Routine ultrasound in pregnancy
D. MRI for breast cancer screening
E. Low back pain—pharmacologic interventions
F. Low-back pain—non-pharmacologic interventions
G. Knee arthroscopy for osteoarthritis

B. HTAS Coverage Guidances

A. Artificial disc replacement
B. Lumbar discography
C. Hip resurfacing

V. New Discussion Items – Cat Livingston 10:00 AM

A. Enzyme replacement therapies
   i. Summary
   ii. Fabry's Disease
   iii. Gaucher's Disease
   iv. Hunter's Disease
   v. PKU
   vi. Pompe's Disease
   vii. Enzyme Replacement Therapy Guideline

VI. ICD 10 – HERC Staff 10:30 AM

A. Pancreas/kidney transplants for Type 2 diabetics
B. Orthopedics
C. Sleep conditions
D. Hyperbaric oxygen
E. Dysfunction lines
F. Lactose intolerance
G. Hematology
H. General Surgery
   i. Hernia lines
   ii. Cholelithiasis lines
I. Ophthamology follow up issues
   i. Albinism
   ii. Chelation

J. Foreign body in GI tract
K. Dermatology follow up issue
L. Prevention for breast cancer follow up issue

VII. Biennial Review – Darren Coffman **12:30 PM**

C. New Prioritized List, October 1, 2014

VIII. Follow Up Discussion Items – HERC Staff **1:00 PM**

D. Gender identity disorder

Guests: Bruce Boston, Karin Selva, Jenn Burleton

IX. Public Comment **1:25 PM**

X. Adjournment – Lisa Dodson **1:30 PM**

Value-based Benefits Subcommittee Recommendations Summary

For Presentation to:

Health Evidence Review Commission on June 14, 2012.

For specific coding recommendations and guideline wording, please see the text of the 6/14/12 VbBS minutes.

CODE MOVEMENT

- A number of straightforward coding changes were approved
- Abnormal chromosomal markers in normal individuals were moved to the maternity care line (Line 1) and the new lower prevention line
- Percuteneous allergy testing for drug allergies was added to the poisoning line (Line 113)
- 349.9, Unspecified disorders of the nervous system, was removed from the dysfunction lines and excluded from the List
- Amputation codes were added to the a burn line (Line 64)
- The code for the screening portion of SBIRT (Screening, Brief Intervention & Referral to Treatment) for alcohol & drug use was recommended to be added to the Diagnostic List and removed from medical lines, and related HCPCS treatment codes were added to the medical lines

ITEMS CONSIDERED BUT NO CHANGES MADE

- Balloon dilatation for transient cerebral ischemia was considered for addition to Line 440, but was rejected

GUIDELINE CHANGES

- GUIDELINE NOTE 6, Rehabilitative Therapies, was modified with “medical necessity” replaced by “medical appropriateness”. No changes were made regarding the coverage for a new diagnosis of a chronic condition.
- GUIDELINE NOTE 41, Spinal Stenosis, Clinically Significant, was modifed to clarify central and foraminal stenosis are included
- DIAGNOSTIC GUIDELINE D1, Non-Prenatal Genetic Testing Guideline, was modified to expand genetic testing for cystic fibrosis, to clarify microarray codes, and to modify coverage of gene testing for inherited clot disorders
- GUIDELINE NOTE 47, Urinary Incontinence, was modified with regard to physical therapy

CHANGES FOR THE OCTOBER 1, 2014 (TENTATIVE DATE) PRIORITIZED LIST AS PART OF THE ICD-10 CONVERSION PROCESS

- Specialty group recommendations for pediatric metabolics were reviewed
  - Multiple lines were created, renamed, deleted/merged, and rescored
- Vitrectomy was added to the glaucoma line with a coding specification
- Coverage of treatment of neonatal lacrimal duct obstruction was added to Line 452 with a guideline note
- A guideline note for the new Severe Inflammatory Skin Disease line was finalized

MEETING MINUTES

VALUE-BASED BENEFITS SUBCOMMITTEE
Wilsonville Training Cetner
June 14, 2012
9:30 AM – 1:30 PM

Members Present: Lisa Dodson, MD, Chair; Kevin Olson, MD, Vice-chair; Chris Kirk, MD; David Pollack MD; Irene Croswell RPh; Laura Ocker, LAc.

Members Absent: James Tyack, DMD; Mark Gibson.

Staff Present: Darren Coffman; Cat Livingston, MD, MPH; Dave Lenar.

Also Attending: Denise Taray, DMAP; Kate Skoglund and Paul Lewis, MD, OHA volunteers; Tracy Oman, Oregon Optometric Physicians Association.

Call to Order, Roll Call, Approval of Minutes
Lisa Dodson called the Value-based Benefits Subcommittee (VbBS) to order, and called role. The minutes were approved with no modifications.

Director's report
Darren Coffman discussed the delayed implementation of ICD-10-CM and DMAP's decision to hold off implementation of a new List until October 1, 2014, which would encompass the ICD-10-CM conversion, rather than implementing a new ICD-9-CM code version for 9 months. Coffman provided an update on the outstanding ICD-10-CM issues, including the need to rank the lower Prevention Line.

Coffman discussed that for the August meeting, some of the coverage guidances would be brought simultaneously to the VbBS and the HERC, in order to facilitate implementation for the October 1, 2012 List. However, if HERC requested revisions of the proposed coverage guidances, the topic would need to be re-reviewed by both VbBS and its originating subcommittee.

Topic: ICD-10 Review—Pediatric Metabolic

Discussion: Livingston presented a summary of the ICD-10-CM recommendations of the pediatric metabolic experts. There was discussion about the proposed reranking of Line 329, DISORDERS OF AMINO-ACID TRANSPORT AND METABOLISM (NON PKU), to approximately line 110, given the magnitude of the difference in the new proposed line number. After some discussion, it was agreed a chronic disease management category made more sense, and given the impact of education and strict dietary adherence, both line rescoring recommendations were accepted. Hereditary fructose intolerance was considered of the same severity of the former Line 329 conditions, and after clarification, members agreed it was okay to combine these lines. There was clarification about the genetic counseling codes; they did not need to be placed on the pediatric metabolid lines because they are in the Diagnostic File. It was

also clarified the related HCPCS code S0265 was not usable and should be removed from the List.

There was a discussion raised about enzyme replacement therapies, specifically in the contest of the treatment of Fabry's disease. Coffman discussed how current Guideline Note 67 refers to enzyme replacement therapies but only specifically calls out Hunter's disease; however, other ICD-9 codes (including Fabry's disease) were included on this line, with the intent that future applications of enzyme replacement therapy would automatically map to Line 684 and need to be reviewed individually to be prioritized higher based on evidence. It was agreed the guideline needed to be clarified further at the August meeting to better demonstrate HERC intent.

Actions:

1) Rescore lines
    a. Line 264 GLYCOGENOSIS
        i. Category - Change to category 3 – chronic disease management
        ii. Healthy Life Years – change to 9, not universally fatal in childhood
        iii. Score 1950, Approximate New Line 158
    b. Line 329 DISORDERS OF AMINO-ACID TRANSPORT AND METABOLISM (NON PKU)
        i. Change to category 3 – chronic disease management
        ii. Change healthy life years to 10
        iii. Change pain and suffering to 2
        iv. Tertiary prevention is not considered due to chronic disease category
        v. Effectiveness of treatment – change to 2, no treatment results in death. Treatment is effectective at reducing hospitalization but very few have normal neurologic status. Now doing liver transplant < age 1 with goal to prevent neurologic compromise.
        vi. Net cost of 1
        vii. New score 2250, Approximate New line 110

2) Rename lines
    a. 370 ~~HEREDITARY FRUCTOSE INTOLERANCE,~~ INTESTINAL DISACCHARIDASE AND OTHER DEFICIENCIES
    b. 329 DISORDERS OF AMINO-ACID TRANSPORT AND METABOLISM (NON PKU); HEREDITARY FRUCTOSE INTOLERANCE
        i. Move the following codes to Line 329
            1. E74.12 Hereditary fructose intolerance
            2. E74.8 Other specified disorders of carbohydrate metabolism
            3. E74.19 Other disorder of fructose metabolism
            4. E74.4 Disorder of pyruvate

3) Code movement
    a. Do not accept recommendation to add genetic counseling codes to pediatric metabolic lines, as these are on the Diagnostic File.
    b. Remove S0265 from the List from Lines 1 and 1104 (new higher prevention line), this is not a currently viable code (not open for payment)
    c. Add medical nutrition therapy codes to Line 264 GLYCOGENOSIS

97802	Medical nutrition therapy; initial assessment and intervention, individual, face-to-face with the patient, each 15 minutes
97803	Medical nutrition therapy; re-assessment and intervention, individual, face-to-face with the patient, each 15 minutes
97804	Medical nutrition therapy; group (2 or more individual(s)), each 30 minutes

4) Guidelines – Guideline Note 67 needs to be clarified with regard to placement intent of other types of enzyme replacement therapy. Staff will bring this back at the August meeting.

Topic: ICD-10 Review—Genetics – Chromosomal markers in normal individuals

Discussion: Livingston presented a summary document. There was minimal discussion. It was decided these should go on the lower prevention line rather than the higher.

Actions:

1) Place the following codes on Line 1 PREGNANCY and 1105 (lower prevention line)

Q92.61 Marker chromosomes in normal individual
Q95.0 Balanced translocation and insertion in normal individual
Q95.1 Chromosome inversion in normal individual

Topic: ICD-10 Review—Ophthamology follow up issues

Discussion: Livingston presented a summary document. For vitrectomy and laser surgery, there was minimal discussion. For neonatal lacrimal duct obstruction there was a limited discussion about the evidence, the input, and the guideline. The decision was made to cover surgical treatment with a guideline.

Actions:

1) Approve recommendation for vitrectomy code addition to the glaucoma line
    a) Add vitrectomy code CPT 67036 to line 149
    b) Add coding specification to line 149
        - "Vitrectomy (CPT 67036) is only included on this line for the treatment of conditions related to ICD-10 codes H40.831 to H40.839."
2) Approve line descriptions with "laser surgery"
    - Line 106 DIABETIC AND OTHER RETINOPATHY, Treatment: ~~LASER SURGERY~~ Medical, Surgical, and Laser Treatment
        (i) add 67028 to this line

- Line 149 GLAUCOMA, OTHER THAN PRIMARY ANGLE-CLOSURE, Treatment: ~~MEDICAL AND SURGICAL TREATMENT~~ Medical, Surgical, and Laser Treatment
- Line 258 PRIMARY ANGLE-CLOSURE GLAUCOMA, Treatment: ~~IRIDECTOMY, LASER SURGERY~~ Medical, Surgical, and Laser Treatment
- Line 473 DEGENERATION OF MACULA AND POSTERIOR POLE, Treatment: Medical, Surgical And Laser Treatment ~~VITRECTOMY, LASER SURGERY~~

3) Allow limited coverage of treatment of neonatal lacrimal duct obstruction
   a) Add neonatal lacrimal duct obstruction (ICD-10 H04.531-9) to line 452 STRABISMUS; CONGENITAL ANOMALIES OF EYE; keep on line 537 DYSFUNCTION OF NASOLACRIMAL SYSTEM; LACRIMAL SYSTEM LACERATION for adult patients
   b) Congenital lacrimal duct obstruction (ICD-9 743.65) is already present on line 452
   c) Change name of line 537 to DYSFUNCTION OF NASOLACRIMAL SYSTEM IN ADULTS; LACRIMAL SYSTEM LACERATION
   d) Change name of Line 452 to STRABISMUS WITHOUT AMBLYOPIA AND OTHER DISORDERS OF BINOCULAR EYE MOVEMENTS; CONGENITAL ANOMALIES OF EYE; LACRIMAL DUCT OBSTRUCTION IN CHILDREN
   e) Add 68810-68840 (probing of nasolacrimal duct) to line 452 to pair with congenital lacrimal duct occlusion
   f) Add a guideline to lines 452 and 537, See Appendix A.

Topic: ICD-10 Review— Dermatology – severe psoriasis treatment guideline

Discussion: Livingston presented a summary document. There was discussion on appropriate first and second line agents, and recommendations from evidence-based sources. There was a suggestion that the SIGN guideline presented an evidence-based algorithm on page 6 that could be used for operationalization.

Actions:

1) Modify new SEVERE INFLAMMATORY SKIN DISEASE Line Guideline Note. See Appendix A.

Topic: Percutaneous testing for drug allergies

Discussion: Livingston presented a summary document. There was discussion about the potential overuse of some of these codes. One option suggested was to institute a prior authorization process for all drug allergy testing. It was decided if these codes appear to be overused, a future guideline could be written.

Actions:

1) Add 95010, 95015 and 95075 (drug allery testing) to line 113 POISONING BY INGESTION, INJECTION, AND NON-MEDICINAL AGENTS

Topic: Unspecified disorders of the nervous system

Discussion: Livingston presented a summary document about ICD-9 code 349.9, Unspecified disorders of nervous system. There was minimal discussion. The code is considered too vague to be able to determine appropriate pairing or prioritize it on the List. There was a separate discussion about sensory processing disorder, and it was determined this might be a reasonable topic in the future for staff to look into.

Actions:

1) Remove 349.9 from lines 78, 318, 375, 407 (Dysfunction Lines)
2) Advise DMAP to remove 349.9 from the Diagnostic Work Up file and place 349.9 on the Excluded List
3) Staff to review evidence on sensory processing/integration disorder and bring back to a future meeting

Topic: Amputation for burns resulting in deep tissue necrosis

Discussion: Livingston presented a summary document. There was no discussion.

Actions:

1) Add the following codes to Line 64 BURN FULL THICKNESS GREATER THAN 10% OF BODY SURFACE

CPT code	Code Description
25900	Amputation, forearm, through radius and ulna;
25905	Amputation, forearm, through radius and ulna; open, circular (guillotine)
25907	Amputation, forearm, through radius and ulna; secondary closure or scar revision
25909	Amputation, forearm, through radius and ulna; re-amputation
25915	Krukenberg procedure
25920	Disarticulation through wrist
25922	Disarticulation through wrist; secondary closure or scar revision
25924	Disarticulation through wrist; re-amputation
25927	Transmetacarpal amputation;
25929	Transmetacarpal amputation; secondary closure or scar revision
25931	Transmetacarpal amputation; re-amputation
26910	Amputation, metacarpal, with finger or thumb (ray amputation), single, with or without interosseous transfer
26951	Amputation, finger or thumb, primary or secondary, any joint or phalanx, single, including neurectomies; with direct closure
26952	Amputation, finger or thumb, primary or secondary, any joint or phalanx, single, including neurectomies; with local advancement flaps (V-Y, hood)
27888	Amputation, ankle, through malleoli of tibia and fibula (eg, Syme, Pirogoff type procedures), with plastic closure and resection of nerves

28800	Amputation, foot; midtarsal (eg, Chopart type procedure)
28805	Amputation, foot; transmetatarsal
28810	Amputation, metatarsal, with toe, single
28820	Amputation, toe; metatarsophalangeal joint
28825	Amputation, toe; interphalangeal joint

Topic: Balloon dilation for transient cerebral ischemia

Discussion: Livingston presented a summary document. There was minimal discussion. Balloon dilatation for transient cerebral ischemia (Line 440) is experimental.

Actions:

1) Make no change, do not cover balloon dilatation for this indication

Topic: SBIRT

Discussion: Coffman introduced a summary document. There was minimal discussion.

Actions:

1) Recommend DMAP add the screening only code, 99420, to the Diagnostic List and remove it from the Prioritized List medical therapy lines where it is currently located
2) Place G0396 and G0397 on the other medical therapy lines that the SBIRT intervention CPT codes appear on (beyond Lines 3 and 4 where they already appear)

Topic: **Urinary Incontinence and Physical Therapy Requirement**

Discussion: Livingston presented a summary document. There is a concern about fulfilling the trial of physical therapy requirement in the urinary incontence guideline when physical therapy coverage is limited (OHP Plus) or absent (OHPR Standard). There were questions about the relative effectiveness of physical therapy and surgery. The subcommittee decided to adopt the proposed guideline change.

Actions:

1) Modify Guideline Note 47. See Appendix B.

Topic: Physical Therapy Guideline

Discussion: Livingston presented a summary document that addressed the issue of a new diagnosis of a chronic condition and the physical therapy benefit. Many of the plans are interpreting the guideline to mean a new diagnosis is actually considered an acute event. It was agreed there is variation in implementation and that a revision to the guideline may result in inappropriate restriction. This is a complex issue and the question was raised about the efficacy and supporting evidence of physical therapy for a number of these conditions, and exacerbation of these conditions. They thought case

management was appropriate, but nothing in the guideline prevents a CCO or plan from using case management and oversight.

Actions:

1) In the future, a more comprehensive revision of the rehabilitative therapy guideline needs to be undertaken, perhaps with a task force
2) Obtain expenditures on physical therapy, speech and occupational therapy to assist in that discussion
3) Make no change to the rehabilitative therapy guideline except to replace all reference to "medical necessity" with "medical appropriateness". See Appendix B for modified Guideline Note 6.

Topic: Spinal stenosis

Discussion: Dr. Paul Lewis presented a summary of the issue for spinal stenosis, clarifying any difference between foraminal and central stenosis. There was minimal discussion.

Actions:

1) Approve modification to Guideline Note 41 to clarify central and foraminal stenosis are included. See Appendix B for the modified guideline note.

Topic: Hereditary thrombophilia genetic testing draft guideline

Discussion: Kerry Silvey, Chair to the former Genetics Advisory Committee to the Health Services Commission, presented a summary of recommendations for modifying the genetic testing guideline with regard to the placement of the new genetics CPT codes. Since the time of the HSC review, there has been subsequent input that some of the guidelines are difficult to interpret. There are recommendations related to 3 sets of these guidelines**.** Two genetic tests represented by CPT 81240 F2 (prothrombin, coagulation factor II) and CPT 81241 F5 (coagulation Factor V) were discussed. The specialists who knew about this wanted to change the wording of the recommendation, with one minor content change. There is a third condition for which the evidence does not support the usefulness of the testing, for recurrent fetal loss or placental abruption. There is no evidence supporting these tests for idiopathic venous thromboembolism, for asymptomatic family members of patients with venous thromboemmbolism, or for determining etiology of recurrent fetal loss or placental abruption. There was a decision made about whether or not to include rationale in decision making embedded within the guideline itself. The guideline was modified per the proposed recommendation, without rationale. There was a last minute suggestion that maybe this should be covered after all, but the response was that this indicates there at least is conflicting data, and so would be unlikely to arise to the level of coverage.

Actions:

1) Modify the non-prenatal genetic testing guideline regarding CPT 81240 and 81241, see Appendix B for modified Guideline.

Topic: Microarray genetic testing guideline

Discussion: Silvey presented a summary of the issues with the current microarray genetic testing guideline. There is a need to clarify confusing language in the guideline and clarify which CPT codes are indicated for microarray analysis. There was a question about needing to reference the 2012 codes, because they may no longer be in existence in January 2013.

Action:

1) Modify the microarray genetic testing portion of the non-prenatal genetic testing guideline, see Appendix B for modified Guideline.
2) Remove reference to "in 2012"

Topic: Cystic fibrosis testing guideline

Discussion: Kerry Silvey presented a summary of the issues related to the current cystic fibrosis guideline. There is some confusion in the language. Several alternatives were proposed. Cost information was provided on performing the mutation panel on all people with cystic fibrosis in the state to see if they are eligible for kayldelco (there are currently 40 untested adults in the state on OHP). There was a proposal to delay the decision based on consideration by the P&T Committee. The pharmacist on the former GAC recommended testing be covered because patients may be able to get pharmaceutical sponsored free therapy. The overall costs of sequencing Oregon Medicaid patients for whom it is indicated is relatively low.

Action:

1) Approve Alternative 2 as proposed and open up genetic testing for cystic fibrosis. See Appendix B for modified Guideline.

Topic: Straightorward items May 2012

Discussion: There was no discussion.

Action:

1) Adopt staff recommendations per meeting materials.

Topic: Straigforward items June 2012

Discussion: There was no discussion.

Action:

1) Adopt staff recommendations per meeting materials.

Topic: Ancillary codes

Discussion: There was no discussion.

Action:

1) Adopt staff recommendations per meeting materials.

Topic: Ranking of lower prevention line

Discussion: The subcommittee decided to address the outstanding issue of where the new lower prevention line should be ranked. It was clarified the higher prevention line would remain at its currently location, Line 3. There was a discussion of highly evidence-based, evidence-informed, and non-evidence based preventive services. The heterogenous conditions on this line make for difficulty in deciding ranking. There was clarification made about the role of carrier status.

Line containes 6 categories of preventive services:

1) Encounters for screening for cancerous conditions with insufficient evidence
2) Carrier of certain infectious diseases
3) Prophylactic breast cancer removal
4) Counseling for patients with family members who abuse or are addicted to psychoactive sustances
5) Dietary counseling
6) History of falls

The breast cancer screening in those at high risk was decided to go onto the breast cancer line. Historically, cancer treatments were separated from these prevention codes, but it now appears the ICD-9 codes do not allow clarity. It was decided it made sense to move these prevention codes to the breast cancer line given that treatments may be similar (e.g. prophylactic mastectomy). There was a discussion about the drug counseling, as there is insufficient evidence to support its use and it was clarified other codes would be used in cases of treatment or for SBIRT type of interventions. It was clarified while fall risk used to be an "I" level recommendation, it is now a "B" level recommendation and this code was moved to Line 3. The remaining conditions have insufficient evidence and it was decided these should be in the nonfunded region, along with similar lines without evidence of effective treatment or none necessary.

New scoring
Category: 1
Healthy Life Years: 1
Pain and suffering: 1
Population effects: 0
Impact on vulnerable populations: 2
Tertiary prevention: N/A
Effectiveness: 0
Net cost: 4
Need for service: 0.05
New Score: 0
Approximate Line: 680

Action:

1) Create New lower prevention line: PREVENTIVE SERVICES WITH LIMITED OR NO EVIDENCE OF EFFECTIVENESS. Place around Line 680 with other similar lines
2) Place high risk of breast cancer codes on Line 197
3) Move history of falls to higher prevention line (Line 3)

Public Comment

There was no public comment

Issues for next meeting:

1) ICD-10-CM review topics:
    - Hyperbaric oxygen
    - Orthopedics
    - Hematology
    - Dysfunction Lines
2) Lactose intolerance
3) Albinism
4) Review of seven coverage guidances pending approval at June HERC meeting and as many as ten additional ones to be considered at August HERC meeting
5) Final line structure of biennial list

Next meeting:

The next meeting will be held on Thursday, August 9, 2012 in Conference Room 117B&C at the Meridian Park Hospital Community Health Education Center in Tualatin, OR. It was recognized that the number of agenda items may necessitate a earlier starting time.

The meeting was adjourned at 1:25 pm.

Appendix A

Guideline Changes Recommended as Part of the ICD-10-CM Conversion/Biennial Review of List

Note: These would tentatively be scheduled to take effect on October 1, 2014

GUIDELINE NOTE XXX NEONATAL NASOLACRIMAL DUCT OBSTRUCTION

Lines 452, 537

Probing of nasolacrimal duct (CPT 68810-68840) is included on line 452 only for children 12 months of age and older who have failed conservative management (e.g. topical antibiotics, Crigler massage) and for children younger than 12 months of age with multiple episodes of purulent infections.

Guideline Note XX SEVERE INFLAMMATORY SKIN DISEASE

Line XX

For severe psoriasis, first line agents include topical agents, phototherapy and methotrexate. Second line agents include other systemic agents and oral retinoids and should be limited to those who fail, or have contraindications to, or do not have access to first line agents.

Biologics are only covered on this line for the indication of severe plaque psoriasis; after documented failure of first line agents and failure of (or contraindications to) a second line agent.

Appendix B

Guideline Changes Recommended to be Implemented October 1, 2012

GUIDELINE NOTE 6, REHABILITATIVE THERAPIES

Lines 12,50-52,64,74-76,78,80,85,89,90,94,95,98-101,108,109,115,116,122,129,139,141-143,145,146,158,161,167,179,184,185,189,190,192,194,195,201,202,208,209,216,226,237,239,270,271,273,274,279,288,289,293,297,30204,307-309,318,336,342,349,350,363,367,369,375,376,378,382,384,385,387,400,406,407,434,441,443,448,455,467,478,489,507,516,549,562,58097,619,638

Physical, occupational and speech therapy, and cardiac and vascular rehabilitation, are covered for diagnoses paired with the respective CPT codes, depending on medical ~~necessity~~ appropriateness, for up to 3 months immediately following stabilization from an acute event.
Following the 3 month stabilization after an acute event, or, in the absence of an acute event, the following number of combined physical and occupational therapy visits are allowed per year, depending on medical ~~necessity~~ appropriateness:

- Age < 8: 24
- Age 8-12: 12
- Age > 12: 2

And the following number of speech therapy visits are allowed per year, depending on medical ~~necessity~~ appropriateness (with the exception of swallowing disorders, for which limits do not apply):

- Age < 8: 24
- Age 8-12: 12
- Age > 12: 2

Whenever there is a change in status, regardless of age, such as surgery, botox injection, rapid growth, an acute exacerbation, or for evaluation/training for an assistive communication device, the following additional visits are allowed:

- 6 visits of speech therapy and/or
- 6 visits of physical or occupational therapy

No limits apply while in a skilled nursing facility for the primary purpose of rehabilitation, an inpatient hospital or an inpatient rehabilitation unit.
If the admission/encounter is for rehabilitation, a V code from V57.1-V57.3,V57.8 should be listed as the principle/first diagnosis. The underlying diagnosis for which rehab is needed should be listed as an additional diagnosis and this diagnosis must appear in the funded region of the Prioritized List for the admission/encounter to be covered.

GUIDELINE NOTE 41, SPINAL DEFORMITY, CLINICALLY SIGNIFICANT

Line 434

Clinically significant scoliosis is defined as curvature greater than or equal to 25 degrees or curvature with a documented rapid progression. Clinically significant spinal stenosis is defined as having MRI evidence of moderate to severe central or foraminal spinal stenosis in addition to a history of neurogenic claudication, or objective evidence of neurological impairment consistent with MRI findings (see Guideline Note 37).

GUIDELINE NOTE 47, URINARY INCONTINENCE

Line 478

Surgery for genuine stress urinary incontinence may be indicated when all of the following are documented (A-G):

A) Patient history of (1, 2, and 3):
   1) Involuntary loss of urine with exertion
   2) Identification and treatment of transient causes of urinary incontinence, if present (e.g., delirium, infection, pharmaceutical causes, psychological causes, excessive urine production, restricted mobility, and stool impaction)
   3) Involuntary loss of urine on examination during stress (provocative test with direct visualization of urine loss) and low or absent post void residual

B) Patient's voiding habits

C) Physical or laboratory examination evidence of either (1 or 2):
   1) Urethral hypermobility
   2) Intrinsic sphincter deficiency

D) Diagnostic workup to rule out urgency incontinence

E) Negative preoperative pregnancy test result unless patient is postmenopausal or has been previously sterilized

F) Nonmalignant cervical cytology, if cervix is present

G) Patient required to have 3 months of alternative therapy (e.g., pessaries or physical therapy, including bladder training, pelvic floor exercises, biofeedback, and/or electrical stimulation, as available). If limited coverage of physical therapy is available, patients should be taught pelvic floor exercises by their treating provider, physical therapist or trained staff, and have documented consistent practice of these techniques over the 3 month period.

DIAGNOSTIC GUIDELINE D1, NON-PRENATAL GENETIC TESTING GUIDELINE

Coverage of genetic testing in a non-prenatal setting shall be determined the algorithm shown in Figure C.1 unless otherwise specified below.

A) Related to genetic testing for patients with breast/ovarian and colon/endometrial cancer suspected to be hereditary, or patients at increased risk to due to family history.
   1) Services are provided according to the Comprehensive Cancer Network Guidelines.
      a) Lynch syndrome (hereditary colorectal and endometrial cancer) services (CPT 81292-81300, 81317-81319) should be provided as defined by the NCCN Clinical Practice Guidelines in Oncology. Colorectal Cancer Screening. V.2.2011 (10/22/10). ***www.nccn.org***
      b) BRCA1/BRCA2 testing services (CPT 81211-81217) for women without a personal history of breast and/or ovarian cancer should be provided to high risk women as defined in Guideline Note 3 or as otherwise defined by the US Preventive Services Task Force.

c) BRCA1/BRCA2 testing services (CPT 81211-81217) for women with a personal history of breast and/or ovarian cancer and for men with breast cancer should be provided according to the NCCN Clinical Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Breast and Ovarian. V.1.2011 (4/7/11). ***www.nccn.org***

2) Genetic counseling should precede genetic testing for hereditary cancer. Very rarely, it may be appropriate for a genetic test to be performed prior to genetic counseling for a patient with cancer. If this is done, genetic counseling should be provided as soon as practical.
   a) Pre and post-test genetic counseling by the following providers should be covered.
      i) Medical Geneticist (M.D.) - Board Certified or Active Candidate Status from the American Board of Medical Genetics
      ii) Clinical Geneticist (Ph.D.) - Board Certified or Active Candidate Status from the American Board of Medical Genetics.
      iii) Genetic Counselor - Board Certified or Active Candidate Status from the American Board of Genetic Counseling, or Board Certified by the American Board of Medical Genetics.
      iv) Advance Practice Nurse in Genetics - Credential from the Genetic Nursing Credentialing Commission.
3) If the mutation in the family is known, only the test for that mutation is covered. For example, if a mutation for BRCA 1 has been identified in a family, a single site mutation analysis for that mutation is covered (CPT 81215), while a full sequence BRCA 1 and 2 (CPT 81211) analyses is not. There is one exception, for individuals of Ashkenazi Jewish ancestry with a known mutation in the family, the panel for Ashkenazi Jewish BRCA mutations is covered (CPT 81212).
4) Costs for rush genetic testing for hereditary breast/ovarian and colon/endometrial cancer is not covered.

B) Related to diagnostic evaluation of individuals with intellectual disability (defined as a full scale or verbal IQ < 70 in an individual > age 5), developmental delay (defined as a cognitive index <70 on a standardized test appropriate for children < 5 years of age), Autism Spectrum Disorder, or multiple congenital anomalies:
CPT 81228, Cytogenomic constitutional microarray analysis ~~interrogation of genomic regions for copy number variants (eg, Bacterial Artificial Chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis):~~ for copy number variants for chromosomal abnormalities: Cover for diagnostic evaluation of individuals with intellectual disability/developmental delay; multiple congenital anomalies; or, Autism Spectrum Disorder accompanied by at least one of the following: dysmorphic features including macro or microcephaly, congenital anomalies, or intellectual disability/developmental delay in addition to those required to diagnose Autism Spectrum Disorder. This test may also be billed using one of CPT 88384-88386, or stacking CPTs 83890-83915.
CPT 81229, Cytogenomic constitutional ~~(genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities::~~ microarray analysis for copy number variants for chromosomal abnormalities; plus cytogenetic constitutional microarray analysis for single nucleotide polymorphism (SNP) variants for chromosomal abnormalities: Cover for diagnostic evaluation of individuals with intellectual disability/developmental

delay; multiple congenital anomalies; or, Autism Spectrum Disorder accompanied by at least one of the following: dysmorphic features including macro or microcephaly, congenital anomalies, or intellectual disability/developmental delay in addition to those required to diagnose Autism Spectrum Disorder; only if (a) consanguinity and recessive disease is suspected, or (b) uniparental disomy is suspected, or (c) another mechanism is suspected that is not detected by the copy number variant test alone. This test may also be billed using one of CPT 88384-88386, or stacking CPTs 83890-83915. ~~Array-based evaluation of multiple molecular probes (CPT 88384-88386) will be covered for diagnostic evaluation of individuals with intellectual disability/developmental delay; multiple congenital anomalies; or, Autism Spectrum Disorder for 2012~~

1) CPT 81243, 81244, Fragile X genetic testing is covered for individuals with intellectual disability/developmental delay. Although the yield of Fragile X is 3.5-10%, this is included because of additional reproductive implications.
2) A visit with the appropriate specialist (often genetics, developmental pediatrics, or child neurology), including physical exam, medical history, and family history is covered. Physical exam, medical history, and family history by the appropriate specialist, prior to any genetic testing is often the most cost-effective strategy and is encouraged.

C) Related to other tests with specific CPT codes:
1) The following tests are not covered:
   a) CPT 81225, CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *5, *6)
   b) CPT 81226, CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN).
   c) CPT 81227, CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *5, *6)
   d) CPT 81291, MTHFR (5,10-methylenetetrahydrofolate reductase) (eg, hereditary hypercoagulability) gene analysis, common variants (eg, 677T, 1298C)
   e) CPT 81330, SMPD1(sphingomyelin phosphodiesterase 1, acid lysosomal) (eg, Niemann-Pick disease, Type A) gene analysis, common variants (eg, R496L, L302P, fsP330)
   f) CPT 81350, UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (eg, irinotecan metabolism), gene analysis, common variants (eg, *28, *36, *37)
   g) CPT 81355, VKORC1 (vitamin K epoxide reductase complex, subunit 1) (eg, warfarin metabolism), gene analysis, common variants (eg, -1639/3673)
2) The following tests are covered only if they meet the criteria for the Non-Prenatal Genetic Testing Algorithm AND the specified situations:
   a) CPT 81205, BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) (eg, Maple syrup urine disease) gene analysis, common variants (eg, R183P, G278S, E422X): Cover only when the newborn screening test is abnormal and serum amino acids are normal

b) CFTR, cystic fibrosis transmembrane conductance regulator tests. CPT 81220, 81223, 81222: For infants with a positive newborn screen for cystic fibrosis or who are symptomatic for cystic fibrosis, or for clients that have previously been diagnosed with cystic fibrosis but have not had genetic testing, CFTR gene analysis of a panel containing at least the mutations recommended by the American College of Medical Genetics* (CPT 81220) is covered. If two mutations are not identified, CFTR full gene sequencing (CPT 81223) is covered. If two mutations are still not identified, duplication/deletion testing (CPT 81222) is covered. These tests may be ordered as reflex testing on the same specimen.

c) ~~CPT 81223, CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence: covered for patients who are symptomatic or who have positive newborn screening for CF AND genetic testing for common mutations is negative AND if the patients ethnicity has <90% coverage by common mutation panels.~~

d) CPT 81224, CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility): Covered only after genetic counseling.

e) ~~CPT 81240, F2 (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysis, 20210G>A variant: Not covered for routine testing in the following circumstances: (1) adults with idiopathic venous thromboembolism. (2) Asymptomatic adult family members of patients with idiopathic venous thromboembolism and F5 mutation, for the purpose of considering primary prophylactic anticoagulation. Test may have clinical utility in other circumstances, e.g. family history of coagulopathy, deciding short range anticoagulation therapy, problems with anticoagulation therapy management, muliptle pregnancy losses.~~

f) ~~CPT 81241, F5 (coagulation Factor V) (eg, hereditary hypercoagulability) gene analysis, Leiden variant: Not covered for routine testing in the following circumstances: (1) adults with idiopathic venous thromboembolism. (2) Asymptomatic adult family members of patients with idiopathic venous thromboembolism and F5 mutation, for the purpose of considering primary prophylactic anticoagulation. Test may have clinical utility in other circumstances, e.g. family history of coagulopathy, deciding short range anticoagulation therapy, problems with anticoagulation therapy management, muliptle pregnancy losses.~~

g) CPT 81240. F2 (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysis, 20210G>A variant: Factor 2 20210G>A testing should not be covered for adults with idiopathic venous thromoboembolism; for asymptomatic family members of patients with venous thromboembolism and a Factor V Leiden or Prothrombin 20210G>A mutation; or for determining the etiology of recurrent fetal loss or placental abruption.

h) CPT 81241. F5 (coagulation Factor V) (eg, hereditary hypercoagulability) gene analysis, Leiden variant: Factor V Leiden testing should not be covered for: adults with idiopathic venous thromoboembolism; for asymptomatic family members of patients with venous thromboembolism and a Factor V Leiden or Prothrombin 20210G>A mutation; or for determining the etiology of recurrent fetal loss or placental abruption.

i) CPT 81256, HFE (hemochromatosis) (eg, hereditary hemochromatosis) gene analysis, common variants (eg, C282Y, H63D): Covered for diagnostic testing of patients with elevated transferrin saturation or ferritin levels. Covered for predictive testing ONLY when a first degree family member has treatable iron overload from HFE.

j) CPT 81332 SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase, antitrypsin, member 1) (eg, alpha-1-antitrypsin deficiency), gene analysis, common variants (eg, *S and *Z): The alpha-1-antitrypsin protein level should be the first line test ofr a suspected diagnosis of AAT deficiency in symptomatic individuals with unexplained liver disease or obstructive lung disease that is not asthma or in a middle age individual with unexplained dyspnea. Generic testing or the anpha-1 phenotype test is appropriate is the protein test is abnormal or borderline. The genetic test is appropriate for siblings of people with AAT deficiency regardless of the AAT protein test results.

3) Do not cover a more expensive genetic test (generally one with a wider scope or more detailed testing) if a cheaper (smaller scope) test is available and has, in this clinical context, a substantially similar sensitivity. For example, do not cover CFTR gene sequencing as the first test in a person of Northern European Caucasian ancestry because the gene panels are less expensive and provide substantially similar sensitivity in that context.

CG - Indications for Planned Cesarean Section

Question: CG - Indications for Planned Cesarean Section

Question source: Health Evidence Review Commission

Issue: Evaluate Line 1, condition of pregnancy with treatment of maternity care, to evaluate if the Prioritized List aligns with the HERC Coverage Guidance "Indications for Planned Cesarean Section." If there is misalignment, determine how to bring the two into alignment.

Review indicated that all HERC Coverage Guidance conditions recommended for planned cesarean section (CS) are included on Line 1.

An issue identified is that there are maternal conditions for which planned CS is not to be covered but these ICD-9 codes are on Line 1 and can potentially pair with CS. Guideline Note 22 specifies that CS on maternal request is not a covered service but the note does not specify these other Line 1 ICD-9 codes which are not to be covered for planned CS. The Coverage Guidance states not to cover for planned CS the following conditions: small for gestational age; suspected cephalopelvic disproportion; maternal hepatitis B infection; and maternal hepatitis C infection.

Recommendations:

1) Change the title of Guideline Note 22 and expand it to include conditions that the Coverage Guidance does not recommend for planned cesarean; this includes small for gestational age; suspected cephalopelvic disproportion; maternal Hepatitis B infection; or maternal Hepatitis C infection.

GUIDELINE NOTE 22, PLANNED CESAREAN DELIVERY
Line 1
Cesarean delivery on maternal request without medical or obstetrical indication is not a covered service. Planned cesarean delivery is also not covered for: small for gestational age; suspected cephalopelvic disproportion; maternal Hepatitis B infection; or maternal Hepatitis C infection.

CG - Induction of Labor

Question: CG - Induction of Labor

Question source: Health Evidence Review Commission

Issue: Evaluate Line 1, Pregnancy, to evaluate if the Prioritized List aligns with the HERC Coverage Guidance "Induction of Labor." If there is misalignment, determine how to bring the two into alignment.

Review indicated that all HERC Coverage Guidance conditions recommended for induction of labor are included on Line 1.

An issue identified is that there are maternal conditions for which elective induction of labor is not to be covered but these ICD-9 codes are on Line 1 and can potentially pair with induction. Guideline Note 85 specifies that elective induction on maternal request is not a covered service. The Coverage Guidance states not to cover induction of labor for the following conditions: macrosomia in the absence of maternal diabetes and breech presentation.

Recommendation:

1) Expand Guideline Note 85 to include conditions that the Coverage Guidance does not recommend for elective induction of labor; this includes macrosomia in the absence of maternal diabetes and breech presentation.

GUIDELINE NOTE 85, ELECTIVE INDUCTION OF LABOR

Line 1

Elective i~~I~~nduction of labor without medical or obstetrical indication prior to 39 weeks of completed gestation is not a covered service. Elective induction of labor is also not covered for fetal macrosomia in the absence of maternal diabetes and for breech presentation.

CG - Routine Ultrasound in Pregnancy

Question: CG - Routine Ultrasound in Pregnancy

Question source: Health Evidence Review Commission

Issue: Evaluate the Prioritized List to determine if coverage of prenatal ultrasound aligns with the HERC Coverage Guidance "Routine Ultrasound in Pregnancy." If there is misalignment, determine how to bring the two into alignment.

Basic prenatal ultrasound CPT codes are located on lines 1 PREGNANCY, 41 TERMINATION OF PREGNANCY, 43 ECTOPIC PREGNANCY, 69 SPONTANEOUS ABORTION COMPLICATED BY INFECTION AND/OR HEMORRHAGE, MISSED ABORTION, and 394 SPONTANEOUS ABORTION. CPT codes for fetal anomaly screens are only located on Line 1. There are currently no limitations on prenatal ultrasounds in the Prioritized List.

The coverage guidance recommended that routine ultrasound for the average risk pregnant woman be covered 1) one in the first trimester for the purpose of identifying fetal aneuploidy or anomaly (between 11 and 13 weeks of gestation) and /or dating confirmation. In some instances, if a patient's LMP is truly unknown, a dating ultrasound may be indicated prior to an aneuploidy screen. 2) once for the purpose of anatomy screening after 18 weeks gestation. 3) only 1 type of routine prenatal ultrasound should be covered in a single day (i.e. transvaginal or abdominal).

Recommendation:

1) Create a new guideline to limit use of prenatal ultrasounds to the indications in the coverage guidance (see below)

GUIDELINE NOTE XXX, ROUTINE PRENATAL ULTRASOUND
Lines 1, 41, 43, 69, 394
Routine ultrasound for the average risk pregnant woman is covered for 1) one ultrasound in the first trimester for the purpose of identifying fetal aneuploidy or anomaly (between 11 and 13 weeks of gestation) and /or dating confirmation. In some instances, if a patient's LMP is truly unknown, a dating ultrasound may be indicated prior to an aneuploidy screen; 2) one ultrasound for the purpose of anatomy screening after 18 weeks gestation; 3) only one type of routine prenatal ultrasound should be covered in a single day (i.e. transvaginal or abdominal).

CG - MRI for Breast Cancer Screening

Question: CG - MRI for Breast Cancer Screening

Question source: Health Evidence Review Commission

Issue: Lines 4 and 197 are the only two lines which contain the diagnosis of screening for breast cancer. Check to see if the HERC Coverage Guidance for use of MRI for breast cancer screening aligns with these two lines on the Prioritized List. If there is misalignment, determine how to bring the two into alignment.

The Coverage Guideline states that breast MRI should not be covered for breast cancer screening. Currently, there are no restrictions on the use of breast MRI for breast cancer screening on the Prioritized List. MRI of the breast CPT codes are located on the DMAP Diagnostic File.

Recommendation:

1) Create a Diagnostic Guideline to establish that breast MRI is not covered for screening for breast cancer.

Diagnostic Guideline DXXX, MRI for Breast Cancer Screening
Breast MRI is not covered for screening for breast cancer.

CG - Low Back Pain - Pharmacologic Interventions

Question: Does the Prioritized List align with the HERC coverage guidance "Low Back Pain - Pharmacologic Interventions?"

Question source: Health Evidence Review Commission

Issue: Evaluate the Prioritized List to determine if it aligns with the HERC Coverage Guidance "Low back pain – pharmacologic interventions." If there is misalignment, determine how to bring the two into alignment.

Musculoskeletal low back pain and other types of back pain with ICD-9 codes listed in the coverage guidance are located on a variety of lines: 52 RHEUMATOID ARTHRITIS AND OTHER INFLAMMATORY POLYARTHROPATHIES, 208 CANCER OF BONES, 400 DISORDERS OF SPINE WITH NEUROLOGIC IMPAIRMENT, 434 SPINAL DEFORMITY, CLINICALLY SIGNIFICANT, 562 ACUTE AND CHRONIC DISORDERS OF SPINE WITHOUT NEUROLOGIC IMPAIRMENT, 607 SPINAL DEFORMITY, NOT CLINICALLY SIGNIFICANT. Of note, pain caused by cancer (such as diagnoses on line 208 CANCER OF BONES) are generally covered with much more liberal pain medication guidelines. Also, the diagnoses on line 52 are generally not considered routine low back pain.

There is no limitation or control of medications that are not considered procedures (i.e. are given by infusion, have an accompanying CPT code for administration, etc.) on the Prioritized List. Medication usage is generally limited by prior authorization (PA) process as DMAP or the health plans.

Recommendation:

1) No changes required to the Prioritized List, as medications are not generally regulated by Prioritized List methods
2) If the VbBS/HERC determine that some type of regulation for medications for low back pain be added to the List, then the following guideline should be considered:

GUIDELINE NOTE XXX, PHARMACOLOGIC INTERVENTIONS FOR LOW BACK PAIN

Lines 400, 434, 562, 607

Pharmacologic interventions for low back pain should be covered as follows:

a. Acute low back pain: Initial pharmacologic therapy should be acetaminophen or non-steroidal anti-inflammatory medications (NSAIDS) and/or skeletal muscle relaxants. Benzodiabepines and opiods should be second line agents.
b. Chronic low back pain (>1 month): First line therapy should be acetaminophen or NSAIDs, triyclic antidepressants. Second line therapy should be benzodiabepines and opioids. Skeletal muscle relaxants should not be covered for chronic low back pain.
c. Systemic steroids should not be covered for low back pain
d. Herbal therapies which may be covered for acute exacerbations of chronic low back pain include devil's caw, willow bark, and capsicum.
e. If opiates or benzodiazepines are used, there should be a risk assessment prior to initiating therapy, and clear documentation of functional benefit should be required for ongoing prescription coverage.

CG - Non-pharmacologic management of low back pain

Question: How should the coverage guidance on non-pharmacologic treatments of low back pain be incorporated into the Prioritized List?

Question Source: HERC Staff, Evidence Based Guidelines Subcommittee

Issue: Evaluate the Prioritized List to determine if it aligns with the HERC Coverage Guidance "Low back pain – non-pharmacologic/non-invasive interventions." If there is misalignment, determine how to bring the two into alignment.

Musculoskeletal low back pain and other types of back pain with ICD-9 codes listed in the coverage guidance are located on a variety of lines: 52 RHEUMATOID ARTHRITIS AND OTHER INFLAMMATORY POLYARTHROPATHIES, 208 CANCER OF BONES, 400 DISORDERS OF SPINE WITH NEUROLOGIC IMPAIRMENT, 434 SPINAL DEFORMITY, CLINICALLY SIGNIFICANT, 562 ACUTE AND CHRONIC DISORDERS OF SPINE WITHOUT NEUROLOGIC IMPAIRMENT, 607 SPINAL DEFORMITY, NOT CLINICALLY SIGNIFICANT. Of note, back pain caused by cancer or by specific rheumatologic conditions are generally not considered routine low back pain. The lines which need to be considered for alignment with this coverage guidance are lines 400, 434, 562 and 607.

The coverage guidance recommends self care for pain of 4 weeks or less duration, and spinal manipulation for those who do not improve with self care.

For pain of greater than 4 weeks duration, the treatments recommended in this coverage guidance include

1) Osteopathic manipulation (98925-9) and chiropractic manipulative treatment (98940-3) which are located on lines 400, 562 and 607, but not line 434.
2) Acupuncture (97810-4) which is not found on lines 400, 434, 562 or 607.
3) Cognitive behavioral therapy (90804-15) which are not found on lines 400, 434, 562 or 607.
4) Physical therapy modalities (97001-97002, 97110-97150, 97530) which are located on lines 400, 434, 562 and 607 (includes massage therapy, exercise therapy)
5) Yoga (no CPT code)

Treatments which are recommended for exclusion from coverage include

1) Traction (97012) which is located on lines 400, 434, 562 and 607, as well as 41 other lines.
2) Electrical stimulation (97014) is not covered on the Prioritized List (on DMAP Excluded List)

CG - Non-pharmacologic management of low back pain

Recommendations:

1) Add osteopathic manipulation (98925-9) and chiropractic manipulative treatment (98940-3) to line 434
2) Add acupuncture (97810-4) to lines 400, 434, 562 and 607.
3) Add cognitive behavioral therapy (90804-15) to lines 400, 434, 562 and 607.
4) Adopt the guideline below to allow limitation of use of modalities other than spinal manipulation for pain of 4 weeks duration or less and to prohibit use of traction for low back pain

GUIDELINE XXX, NON-PHARMACOLOGIC MANAGEMENT OF LOW BACK PAIN

Lines 400, 434, 562, 607

For low back pain of 4 weeks or less duration, only spinal manipulation (CPT codes 98925-98929, 98940-98943) is covered for treatment. For low back pain of greater than 4 weeks duration, the following are covered for treatment: acupuncture, cognitive-behavioral therapy, exercise therapy, physical therapy, massage therapy, spinal manipulation, and yoga (CPT codes 90804-90815, 97001-97002, 97110-97150, 97530, 97810-97814, 98925-98929, 98940-98943). Spinal traction (CPT code 97012) is not covered for treatment of low back pain.

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

COVERAGE GUIDANCE: LOW BACK PAIN: NON-PHARMACOLOGIC/NON-INVASIVE INTERVENTIONS*

DATE: 06/14/2012

HERC COVERAGE GUIDANCE

For pain ≤ 4 weeks, self-care is recommended, and for those who do not improve with self-care, spinal manipulation should be covered.

For pain > 4 weeks duration, the following treatments may be covered:

- Acupuncture
- Cognitive-behavioral therapy
- Exercise therapy
- Intensive interdisciplinary rehabilitation
- Massage therapy
- Progressive relaxation
- Spinal manipulation
- Yoga (viniyoga)

The following should not be covered for low back pain:

- Continuous or intermittent traction
- Transcutaneous electrical nerve stimulation

*Coverage guidance for pharmacologic interventions, imaging, percutaneous interventions and surgery for low back pain will be addressed in subsequent documents.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Heath Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

EVIDENCE SOURCES

Livingston, C., King, V., Little, A., Pettinari, C., Thielke, A., & Gordon, C. (2011). *State of Oregon Evidence-based Clinical Guidelines Project. Evaluation and management of low back pain: A clinical practice guideline based on the joint practice guideline of the American College of Physicians and the American Pain Society (Diagnosis and treatment of low back pain).* Salem: Office for Oregon Health Policy and Research. Available at: http://www.oregon.gov/OHA/OHPR/HERC/Evidence-Based-Guidelines.shtml

Chou, R., Huffman, L. *Nonpharmacologic Therapies for Acute and Chronic Low Back Pain:A Review of the Evidence for an American Pain Society/American College of Physicians Clinical Practice Guideline.* Ann Intern Med. 2007; 147; 492-504. Available at: http://www.annals.org/content/147/7/492.full.pdf+html

Chou R., Qaseem, A., Snow, V., Casey, D., Cross, J.T., Jr., Shekelle, P., Owens, D.K.; Clinical Efficacy Assessment Subcommittee of the American College of Physicians; American College of Physicians; American Pain Society Low Back Pain Guidelines Panel. *Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society.* Annals of Internal Med. 2007; 147(7); 478-491. Available at: http://www.annals.org/content/147/7/478.long

The summary of evidence in this document is derived directly from these evidence sources, and portions are extracted verbatim.

SUMMARY OF EVIDENCE

Clinical Background

Low back pain is the fifth most common reason for all physician visits in the United States. Approximately one quarter of U.S. adults reported having low back pain lasting at least 1 whole day in the past 3 months, and 7.6% reported at least 1 episode of severe acute low back pain within a 1-year period. Low back pain is also very costly: Total incremental direct health care costs attributable to low back pain in the U.S. were estimated at $26.3 billion in 1998. In addition, indirect costs related to days lost from work are substantial, with approximately 2% of the U.S. work force compensated for back injuries each year.

Many patients have self-limited episodes of acute low back pain and do not seek medical care. Among those who do seek medical care, pain, disability, and return to work typically improve rapidly in the first month. However, up to one third of patients report persistent back pain of at least moderate intensity 1 year after an acute episode, and 1 in 5 report substantial limitations in activity. Approximately 5% of the people with back pain disability account for 75% of the costs associated with low back pain.

Many options are available for evaluation and management of low back pain. However, there has been little consensus, either within or between specialties, on appropriate clinical evaluation and management of low back pain. Numerous studies show unexplained, large variations in use of diagnostic tests and treatments. Despite wide variations in practice, patients seem to experience broadly similar outcomes, although costs of care can differ substantially among and within specialties.

Evidence Review

Recommendation 1: *Clinicians should provide patients with evidence-based information on low back pain with regard to their expected course, advise patients to remain active, and provide information about effective self-care options (strong recommendation, moderate-quality evidence).*

Clinicians should inform all patients of the generally favorable prognosis of acute low back pain with or without sciatica, including a high likelihood for substantial improvement in the first month. General advice on self-management for nonspecific low back pain should include recommendations to remain active, which is more effective than resting in bed for patients with acute or subacute low back pain. Self-care education books based on evidence-based guidelines, such as *The Back Book* are recommended because they are an inexpensive and efficient method for supplementing clinician-provided back information and advice and are similar or only slightly inferior in effectiveness to such costlier interventions as supervised exercise therapy, acupuncture, massage, and spinal manipulation.

[Evidence source]

Recommendation 2: *For patients who do not improve with self-care options, clinicians should consider the addition of nonpharmacologic therapy with proven benefits—for acute low back pain, spinal manipulation; for chronic or subacute low back pain, intensive interdisciplinary rehabilitation, exercise therapy, acupuncture, massage therapy, spinal manipulation, yoga, cognitive-behavioral therapy, or progressive relaxation (weak recommendation, moderate-quality evidence).*

For acute low back pain (duration <4 weeks), spinal manipulation administered by providers with appropriate training is associated with small to moderate short-term benefits. Supervised exercise therapy and home exercise regimens are not effective for acute low back pain, and the optimal time to start exercise therapy after the onset of symptoms is unclear. For subacute (duration >4 to 8 weeks) low back pain, intensive interdisciplinary rehabilitation (defined as an intervention that includes a physician consultation coordinated with a psychological, physical therapy, social, or vocational intervention) is moderately effective, and functional restoration with a cognitive-behavioral component reduces work absenteeism due to low back pain in occupational settings. For chronic low back pain, moderately effective nonpharmacologic therapies include acupuncture, exercise therapy, massage therapy, Viniyoga-style yoga, cognitive-behavioral therapy or progressive relaxation, spinal manipulation, and intensive interdisciplinary rehabilitation. Transcutaneous electrical nerve stimulation and intermittent or continuous traction (in patients with or without sciatica) have not been proven effective for chronic low back pain.

[Evidence source]

Overall Summary

Non-pharmacologic treatments that have been shown to be effective for LBP include spinal manipulation, intensive interdisciplinary rehabilitation, exercise therapy, acupuncture, massage therapy, yoga, cognitive-behavioral therapy and progressive relaxation. Transcutaneous electrical nerve stimulation and intermittent or continuous traction have not been proven effective in the treatment of chronic LBP.

PROCEDURES

Acupuncture
Cognitive-behavioral therapy
Continuous or intermittent traction
Exercise therapy
Intensive interdisciplinary rehabilitation
Massage therapy
Progressive relaxation
Spinal manipulation
Transcutaneous electrical nerve stimulation
Viniyoga-style yoga

DIAGNOSES

Low back pain

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
170.2	Tumor lumbosacral region primary
198.5	Tumor lumbosacral region secondary
344.60	Cauda equine syndrome
720.1	Spinal enthesopathy
720.2	Sacroiliitis, not elsewhere classified
721.3	Lumbosacral spondylosis without myelopathy
721.42	Spondylosis with myelopathy, lumbar region
721.5	Kissing spine
721.6	Ankylosing vertebral hyperostosis
721.7	Traumatic spondylopathy
721.8	Other allied disorders of spine
721.9	Spondylosis of unspecified site
722.1	Displacement of thoracic or lumbar intervertebral disc without myelopathy
722.2	Displacement of intervertebral disc, site unspecified, without myelopathy
722.32	Schmorl's nodes, lumbar region
722.39	Schmorl's nodes, other region
722.5	Degeneration of thoracic or lumbar intervertebral disc
722.6	Degeneration of intervertebral disc, site unspecified
722.70	Intervertebral disc disorder with myelopathy, unspecified region
722.72	Intervertebral disc disorder with myelopathy, thoracic region
722.73	Intervertebral disc disorder with myelopathy, lumbar region
722.80	Postlaminectomy syndrome, unspecified region
722.82	Postlaminectomy syndrome, thoracic region
722.83	Postlaminectomy syndrome, lumbar region
722.90	Other and unspecified disc disorder, unspecified region
722.92	Other and unspecified disc disorder, thoracic region
722.93	Other and unspecified disc disorder, lumbar region
724	Other and unspecified disorders of back
724.0	Spinal stenosis other than cervical
724.00	Spinal stenosis, unspecified region
724.01	Spinal stenosis, thoracic region
724.02	Spinal stenosis, lumbar region, without neurogenic claudication
724.03	Spinal stenosis, lumbar region, with neurogenic claudication
724.09	Spinal stenosis, other region
724.1	Pain in thoracic spine
724.2	Lumbago
724.3	Sciatica
724.4	Thoracic or lumbosacral neuritis or radiculitis, unspecified
724.5	Backache, unspecified
724.6	Disorders of sacrum
724.7	Disorders of coccyx
724.70	Unspecified disorder of coccyx
724.71	Hypermobility of coccyx
724.79	Other disorders of coccyx
724.8	Other symptoms referable to back

CODES	DESCRIPTION
724.9	Other unspecified back disorders
730.2	Unspecified osteomyelitis
732.0	Juvenile osteochondrosis of spine
733.0	Osteoporosis
737.2	Lordosis (acquired)
737.30	Scoliosis [and kyphoscoliosis], idiopathic
737.39	Other kyphoscoliosis and scoliosis
737.4	Curvature of spine associated with other conditions
737.8	Other curvatures of spine
737.9	Unspecified curvature of spine
738.4	Acquired spondylolisthesis
738.5	Other acquired deformity of back or spine
739.2	Nonallopathic lesions, thoracic region
739.3	Nonallopathic lesions, lumbar region
739.4	Nonallopathic lesions, sacral region
754.2	Congenital musculoskeletal deformities of spine
756.1	Congenital anomalies of spine
846	Sprains and strains of sacroiliac region
847.1	Sprain of thoracic
847.2	Sprain of lumbar
847.3	Sprain of sacrum
847.4	Sprain of coccyx
847.9	Sprain of unspecified site of back
ICD-9 Volume 3 (procedure codes)	
None	
CPT	
Spinal Manipulation	
98925	Osteopathic manipulative treatment (OMT); 1-2 body regions involved
98926	3-4 body regions involved
98927	5-6 body regions involved
98928	7-8 body regions involved
98929	9-10 body regions involved
98940	Chiropractic manipulative treatment (CMT); spinal, 1-2 regions
98941	spinal, 3-4 regions
98942	spinal, 5 regions
98943	extraspinal, 1 or more regions
Acupuncture	
97810	Acupuncture, 1 or more needles; without electrical stimulation, initial 15 minutes of personal one-on-one contact with the patient
+97811	without electrical stimulation, each additional 15 minutes of personal one-on-one contact with the patient, with re-insertion of needle(s)
97813	with electrical stimulation, initial 15 minutes of personal one-on-one contact with the patient
+97814	with electrical stimulation, each additional 15 minutes of personal one-on-one contact with the patient, with re-insertion of needle(s)
Cognitive Behavioral Therapy	
90804	Individual psychotherapy, insight oriented, behavior modifying and/or supportive, in

CODES	DESCRIPTION
	an office or outpatient facility, approximately 20 to 30 minutes face-to-face with the patient
90805	with medical evaluation and management services
90806	Individual psychotherapy, insight oriented, behavior modifying and/or supportive, in an office or outpatient facility, approximately 45 to 50 minutes face-to-face with the patient
90807	with medical evaluation and management services
90808	Individual psychotherapy, insight oriented, behavior modifying and/or supportive, in an office or outpatient facility, approximately 75 to 80 minutes face-to-face with the patient
90809	with medical evaluation and management services
90810	Individual psychotherapy, interactive, using play equipment, physical devices, language interpreter, or other mechanisms of non-verbal communication, in an office or outpatient facility, approximately 20 to 30 minutes face-to-face with the patient
90811	with medical evaluation and management services
90812	Individual psychotherapy, interactive, using play equipment, physical devices, language interpreter, or other mechanisms of non-verbal communication, in an office or outpatient facility, approximately 45 to 50 minutes face-to-face with the patient
90813	with medical evaluation and management services
90814	Individual psychotherapy, interactive, using play equipment, physical devices, language interpreter, or other mechanisms of non-verbal communication, in an office or outpatient facility, approximately 75 to 80 minutes face-to-face with the patient
90815	with medical evaluation and management services
90875	Individual psychophysiological therapy incorporating biofeedback training by any modality (face-to-face with the patient), with psychotherapy (eg, insight oriented, behavior modifying or supportive psychotherapy)
97001	Physical therapy evaluation
97002	Physical therapy re-evaluation
97012	Traction, mechanical
97014	Electrical stimulation (unattended)
97110	Therapeutic procedure, 1 or more areas, each 15 minutes; therapeutic exercises to develop strength and endurance, range of motion and flexibility
97112	neuromuscular reeducation of movement, balance, coordination, kinesthetic sense, posture, and/or proprioception for sitting and/or standing activities
97116	gait training (includes stair climbing)
97124	massage, including effleurage, petrissage and/or tapotement (stroking, compression, percussion)
97140	Manual therapy techniques (eg, mobilization/manipulation, manual lymphatic drainage, manual traction), 1 or more regions, each 15 minutes
97150	Therapeutic procedures(s), group (2 or more individuals) (Group therapy procedures involve constant attendance of the physician or therapist, but by definition do not require one-on-one patient contact by the physician or therapist)
97530	Therapeutic activities, direct (one-on-one) patient contact by the provider (use of dynamic activities to improve functional performance), each 15 minutes
HCPCS Level II Codes	
E0830	Ambulatory traction device, all types, each
E0941	Gravity assisted traction device, any type
H0002	Behavioral health screening to determine eligibility for admission to treatment

CODES	DESCRIPTION
	program
H0004	Behavioral health counseling and therapy, per 15 minutes
H0031	Mental health assessment, by nonphysician
H0032	Mental health service plan development by nonphysician
H2000	Comprehensive multidisciplinary evaluation
H2001	Rehabilitation program, per ½ day
S9451	Exercise classes, nonphysician provider, per session

Note: Inclusion on this list does not guarantee coverage

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

CG - Knee Arthroscopy for Osteoarthritis

Question: How should the HERC approved Coverage Guidance – Knee Arthroscopy for Osteoarthritis—be incorporated into the Prioritized List?

Question source: Health Evidence Review Commission

Issue: Evaluate Line 384, Rheumatoid Arthritis, Osteoarthritis, Oseochondritis Dissecans, and Aseptic Necrosis of Bone, to evaluate if the Prioritized List aligns with the newly approved HERC Coverage Guidance "Knee Arthroscopy for Osteoarthritis".

Currently on Line 384 pairing between knee arthroscopy CPT codes and osteoarthritis ICD-9 codes exists.. No other lines contained pairings of these procedure and diagnosis codes. The Coverage Guidance states that knee arthroscopy should not be covered for osteoarthritis, so a solution must be made in order to prevent these procedure and diagnosis codes from being claimed together.

Recommendations:

1. Create a coding specification that prevents the knee arthroscopy CPT codes and the osteoarthritis ICD-9 codes from being paired together (see below).

Line: 384
Condition: RHEUMATOID ARTHRITIS, OSTEOARTHRITIS, OSTEOCHONDRITIS DISSECANS, AND ASEPTIC NECROSIS OF BONE (See Guideline Notes 6,15,64,65,71,76,83)
Treatment: ARTHROPLASTY/RECONSTRUCTION
ICD-9: 714.0,714.30-714.33,715.10-715.38,715.90-715.98,716.10-716.19,719.10-719.19,732.7,733.40-733.49,V54.81-V54.82,V57.1,V57.21-V57.3,V57.81-V57.89
CPT: 20610,20690-20694,23120,23470,23472,23800,23802,24000,24006,24101,24102,24130,24160,24164,24360-24366,24800,24802,25000,25101-25109,25115-25119,25240,25270,25320,25337,25390-25393,25441-25492,25800,25810-25830,26320,26516-26536,26820-26863,26990-26992,27036,27090,27091,27122-27132,27187,27284,27286,27358,27437-27454,27457,27580,27620-27626,27641,27700-27704,27870,27871,28090,28104,28114,28116,28122,28725,28740,28750,29819-29826,29834-29838,29843-29848,29861-29863,29871-29876,29884-29887,29891,29892,29894-29899,29904-29907,77014,77261-77295,77300,77305-77315,77331-77336,77401-77423,77427,77470,97001-97004,97012,97022,97110-97124,97140-97530,97535,97542,97760-97762,98966-98969,99051,99060,99070,99078,99201-99360,99366,99374,99375,99379-99444,99468-99480,99605-99607
HCPCS: G0157-G0161,G0406-G0408,G0425-G0427,S0270-S0274,S2118,S2325

Knee arthroscopy (29871, 29873- 29876, 29884-29887) is not included on this line for coverage when paired with osteoarthritis/osteoarthrosis of the knee (715.16, 715.26, 715.36, and 715.96).

CG – Artificial Disc Replacement

Question: Does the Prioritized List align with the HERC coverage guidance "Artificial Disc Replacement?"

Question source: Health Evidence Review Commission

Issue: Artificial disc replacement (CPT 22856-22865) was discussed at the April, 2005 HOSC meeting, and the recommendation at that time was to obtain cost information comparing artificial disc use and spinal fusion and to review the full NICE guidance on the topic prior to adopting coverage of artificial disc replacement procedures. Further discussion in July, 2005 led to this procedure being added to the Excluded List. The July, 2005 minutes note that "contraindications to use include lumbar stenosis and isolated radicular compression syndromes, thus excluding this technology from a currently covered line. The NICE guidance was reviewed. Eric noted questionable safety data (re-op rate of 3-24%, 16-45% complication rate) and lack of long-term outcomes."

Currently, artificial disc replacement (CPT 22856-22865) is on the Excluded List.

The diagnoses recommended for limited coverage in the HERC coverage guidance are located on lines 400 DISORDERS OF SPINE WITH NEUROLOGIC IMPAIRMENT and 562 ACUTE AND CHRONIC DISORDERS OF SPINE WITHOUT NEUROLOGIC IMPAIRMENT.

ICD-9 Code	Code Description	Line 400	Line 562
722.0	Displacement of cervical intervertebral disc without myelopathy	X	X
722.1	Displacement of thoracic or lumbar intervertebral disc without myelopathy	X	X
722.4	Degeneration of cervical intervertebral disc		X
722.5	Degeneration of thoracic or lumbar intervertebral disc		X
722.6	Degeneration of intervertebral disc, site unspecified		X
722.7	Intervertebral disc disorder with myelopathy	X	
722.9	Other and unspecified disc disorder		X

The HERC coverage guidance on artificial disc replacement recommends inclusion of this service with specific limitations, as outlined below:

Artificial disc replacement should be a covered service only when all of the following criteria are met:

Lumbar artificial disc replacement

1) Patients must first complete a structured, intensive, multi-disciplinary program for management of pain, if covered by the agency;
2) Patients must be 60 years or under;
3) Patients must meet FDA approved indications for use and not have any contra-indications. FDA approval is device specific but includes:
   - Failure of at least six months of conservative treatment
   - Skeletally mature patient
   - Replacement of a single disc for degenerative disc disease at one level confirmed by patient history and imaging

Cervical artificial disc replacement

1) Patients must meet FDA approved indications for use and not have any contra-indications. FDA approval is device specific but includes:
   - Skeletally mature patient

• Reconstruction of a single disc following single level discectomy for intractable symptomatic cervical disc disease (radiculopathy or myelopathy) confirmed by patient findings and imaging.

Recommendation:

1) Either
    a. Add artificial disc replacement (CPT 22856-22865) to both line 400 DISORDERS OF SPINE WITH NEUROLOGIC IMPAIRMENT and line 562 ACUTE AND CHRONIC DISORDERS OF SPINE WITHOUT NEUROLOGIC IMPAIRMENT
        i. Diagnoses on both these lines are included in the coverage guidance

    OR

    b. Add artificial disc replacement (CPT 22856-22865) to only line 562
        i. Adding to a non-covered line is in greater agreement with former HSC decision to not cover this procedure
2) Adopt the following guideline:

GUIDELINE NOTE XXX ARTIFICIAL DISC REPLACEMENT

Line 400, 562

Artificial disc replacement (CPT 22856-22865) should be a covered service only when all of the following criteria are met:

Lumbar artificial disc replacement

1) Patients must first complete a structured, intensive, multi-disciplinary program for management of pain, if covered by the agency;
2) Patients must be 60 years or under;
3) Patients must meet FDA approved indications for use and not have any contra-indications. FDA approval is device specific but includes:
    • Failure of at least six months of conservative treatment
    • Skeletally mature patient
    • Replacement of a single disc for degenerative disc disease at one level confirmed by patient history and imaging

Cervical artificial disc replacement

1) Patients must meet FDA approved indications for use and not have any contra-indications. FDA approval is device specific but includes:
    • Skeletally mature patient
    • Reconstruction of a single disc following single level discectomy for intractable symptomatic cervical disc disease (radiculopathy or myelopathy) confirmed by patient findings and imaging.

CG – Lumbar Discography

Question: Does the Prioritized List align with the HERC coverage guidance "Lumbar Discography?"

Question source: Health Evidence Review Commission

Issue: Lumbar discography (CPT 62290, 62291, 72295) was discussed at the August 2007 HOSC meeting, and placed on the Excluded List. There was minimal discussion at that time.

The HERC coverage guidance states: "Lumbar discography should not be a covered service for patients with low back pain."

Recommendation:

1) No change required to current lack of coverage on the Prioritized List

CG – Hip Resurfacing

Question: Does the Prioritized List align with the HERC coverage guidance "Hip Resurfacing?"

Question source: Health Evidence Review Commission

Issue: Hip resurfacing (HCPCS S2118) was discussed at the December 2008 HOSC meeting as part of the new code placement determination. This procedure was added to the Prioritized List on what is now line 384 RHEUMATOID ARTHRITIS, OSTEOARTHRITIS, OSTEOCHONDRITIS DISSECANS, AND ASEPTIC NECROSIS OF BONE, with a guideline (Guideline Note 71).

From the December 2008 HOSC minutes:
The group felt that the evidence supported coverage of hip resurfacing. Discussion centered around the guideline proposed to specify when hip resurfacing should be a covered benefit. The statement referring to the FDA contraindications was considered to not be specific enough. The actual contraindications were added to the guideline.

The HERC coverage guidance on hip resurfacing recommends inclusion of this service with specific limitations, as outlined below:

> Hip resurfacing should be a covered service for patients who are likely to outlive a traditional prosthesis and who would otherwise require a total hip replacement, and should only be done by surgeons with specific training in this technique. The following criteria should be required:
> • Diagnosis of osteoarthritis or inflammatory arthritis;
> • Individual has failed nonsurgical management; and
> • The device is FDA approved
>
> Patients who are candidates for hip resurfacing must not have FDA contraindications including:
> • Patients with active or suspected infection in or around the hip joint, or sepsis
> • Patients who are skeletally immature
> • Patients with any vascular insufficiency, muscular atrophy, or neuromuscular disease severe enough to compromise implant stability or postoperative recovery
> • Patients with bone stock inadequate to support the device, including severe osteopenia or a family history of severe osteoporosis or osteopenia
> • Patients with osteonecrosis or avascular necrosis with >50% involvement of the femoral head
> • Patients with multiple cysts of the femoral head
> • Females of childbearing age
> • Patients with known moderate-to-severe renal insufficiency
> • Patients who are immunosuppressed with diseases such as AIDS or persons receiving high doses of corticosteroids
> • Patients who are severely overweight
> • Patients with known or suspected metal sensitivity

Recommendation:

1) Amend the current Guideline Note 71 to conform with the HERC coverage guidance

GUIDELINE NOTE 71 HIP RESURFACING

Line 384

Hip resurfacing is a covered service for patients who are likely to outlive a traditional prosthesis, who would otherwise require a total hip replacement, and should only be done by surgeons with specific training in this technique.

The following criteria are required to be met for coverage of this procedure: the diagnosis of osteoarthritis or inflammatory arthritis; failure of nonsurgical management; and the device my be FDA approved.

Patients who are candidates for hip resurfacing must not be:

i. Patients with active or suspected infection in or around the hip joint, or sepsis
ii. Patients who are skeletally immature
iii. Patients with any vascular insufficiency, muscular atrophy, or neuromuscular disease severe enough to compromise implant stability or postoperative recovery
iv. Patients with bone stock inadequate to support the device, including severe osteopenia or a family history of severe osteoporosis or osteopenia
v. Patients with osteonecrosis or avascular necrosis with >50% involvement of the femoral head
vi. Patients with multiple cysts of the femoral head
vii. Females of childbearing age
viii. Patients with known moderate-to-severe renal insufficiency
ix. Patients who are immunosuppressed with diseases such as AIDS or persons receiving high doses of corticosteroids
x. Patients who are severely overweight
xi. Patients with known or suspected metal sensitivity

Revised 8/7/12

Summary of enzyme replacement therapy recommendations

Condition	**Treatment**	**Staff Recommendation**
Fabry's disease	Agalsidase-alpha (Replagal) Agalsidase-beta (Fabrazyme)	Include on Line 684
Hunter's disease	Idursulfase	Include on Line 684
Pompe's disease	Alglucosidase alfa	Include on Line 264 – for children with infantile onset Include on Line 684 – for adults
Gaucher's disease	Imiglucerase Velaglucerase Alglucerase	Include on Line 684

Author	Journal	Publication Year	Article Type	Included in Review	Explanation
Eng	NEJM	2001	Double Blind RCT	Yes	
Desnick	Ann Intern Med	2003	Review	No	Review Article and Outdated
Banikazemi	Ann Intern Med	2007	RCT	Indirect	Included in the Cochrane Review used for the evidence review
Germain	J Am Soc Nephrol	2007	Phase III Extension Trial	No	Excluded from the Cochrane Review as it is in non-randomized extension trial
Germain	Orphanet J Rare Dis	2010	Review	No	Review Article of the Disease
Eng	Genet Med	2006	Review	No	Review Article and Outdated
Wraith	J Pediatr	2008	Open Label Study	No	Reviewed for the Cochrane, excluded due to lack of randomization. Also manufacturer-sponsored.
Warnock	Clin J Am Soc Nephrol	2010	Review	No	Review Article written by the Manufacturer
Watt	Genet Med	2010	Registry Review	No	Registry looking at Quality of Life in Patients on ERT
Motwani	Mol Gen and Met	2012	Registry Review	No	Registry from a single institution of patients on ERT

Enzyme replacement therapy for Anderson-Fabry disease (Review)

El Dib RP, Pastores GM

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2012, Issue 4

http://www.thecochranelibrary.com

[Intervention Review]

Enzyme replacement therapy for Anderson-Fabry disease

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Editorial group: Cochrane Cystic Fibrosis and Genetic Disorders Group.
Publication status and date: Edited (no change to conclusions), published in Issue 4, 2012.
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Citation: El Dib RP, Pastores GM. Enzyme replacement therapy for Anderson-Fabry disease. *Cochrane Database of Systematic Reviews* 2010, Issue 5. Art. No.: CD006663. DOI: 10.1002/14651858.CD006663.pub2.

ABSTRACT

Background

Anderson-Fabry disease is an X-linked defect of glycosphingolipid metabolism. Progressive renal insufficiency is a major source of morbidity, additional complications result from cardio- and cerebro-vascular involvement. Survival is reduced among affected males and symptomatic female carriers.

Objectives

To evaluate the effectiveness and safety of enzyme replacement therapy compared to other interventions, placebo or no interventions, for treating Anderson-Fabry disease.

Search methods

We searched 'Clinical Trials' on *The Cochrane Library*, MEDLINE, EMBASE, LILACS and the Cystic Fibrosis and Genetic Disorders Group's Inborn Errors of Metabolism Trials Register (date of the most recent search: 07 April 2010).

Selection criteria

Randomized controlled trials of agalsidase alfa or beta in participants diagnosed with Anderson-Fabry disease.

Data collection and analysis

Two authors selected relevant trials, assessed methodological quality and extracted data.

Main results

Five studies comparing either agalsidase alfa or beta in 187 participants fulfilled the selection criteria.

Both trials comparing agalsidase alfa to placebo reported on globotriaosylceramide concentration in plasma and tissue; aggregate results were non-significant. One study reported pain scores, there was a statistically significant improvement for participants receiving treatment at up to three months, mean difference -2.10 (95% confidence interval (CI) -3.79 to -0.41); at up to five months, mean difference -1.90 (95% CI -3.65 to -0.15); and at up to six months, mean difference -2.00 (95% CI -3.66 to -0.34). There was a significant difference in pain-related quality of life at over five months and up to six months, mean difference -2.10 (95% CI -3.92 to -0.28) but not at other time-points. Neither study reported deaths.

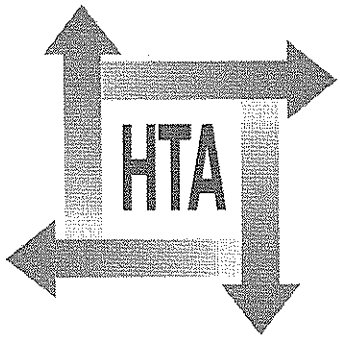
Health Technology Assessment 2006; Vol. 10: No. 20

A systematic review of the clinical effectiveness and cost-effectiveness of enzyme replacement therapies for Fabry's disease and mucopolysaccharidosis type I

M Connock, A Juarez-Garcia, E Frew, A Mans, J Dretzke, A Fry-Smith and D Moore

June 2006

Health Technology Assessment
NHS R&D HTA Programme



A systematic review of the clinical effectiveness and cost-effectiveness of enzyme replacement therapies for Fabry's disease and mucopolysaccharidosis type I

M Connock,[1] A Juarez-Garcia,[2] E Frew,[2] A Mans,[3] J Dretzke,[1] A Fry-Smith[1] and D Moore[1*]

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Declared competing interests of authors: none

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Abstract

A systematic review of the clinical effectiveness and cost-effectiveness of enzyme replacement therapies for Fabry's disease and mucopolysaccharidosis type I

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* Corresponding author

Objectives: To determine the clinical effectiveness and cost-effectiveness of the administration of intravenous enzyme replacement therapy (ERT) to symptomatic patients for the prevention of long-term damage and symptoms in Fabry's disease and in mucopolysaccharidosis type I (MPSI).
Data sources: Electronic databases from inception up to mid-2004. Contact with clinical experts.
Review methods: Relevant studies were identified and assessed using recommended quality criteria.
Results: The results suggested beneficial effects of ERT for Fabry's disease on measures of pain, cardiovascular function and some end-points reflecting neurosensory function. Renal function appeared to be stabilised by ERT. At present there are no utility-related health-related quality of life data on which to assess the relative health gain of ERT in MPSI. In order to be able to demonstrate the full extent of health gain from treatment, it was necessary to review the natural history of untreated patients in each disease in order to try to estimate the health loss prevented. The published information for Fabry's disease tallied with descriptions of a multi-system, life-threatening disorder particularly involving kidney, heart and brain with individual patients exhibiting many manifestations. The fragmentary information reviewed in 16 studies relevant to the natural history of MPSI did not generate a coherent picture of disease progression and could provide little added value to published narrative reviews. For Fabry's disease, the mean cost per patient (50 kg) treated is around £85,000 per annum in England and Wales. The cost per patient varies considerably by dose. No published evidence reporting an economic evaluation of ERT for Fabry's disease was identified by this review. A dynamic decision model was constructed based on a birth cohort of male patients who are followed up until death. Owing to lack of information reported in the literature, many assumptions had to be applied. The key assumptions were that ERT returns patients to full health and a normal life expectancy. As far as possible, all assumptions favoured rather than detracted from the value of ERT. ERT was assumed to restore patients to full health in the base case. The estimated incremental cost-effectiveness ratio (ICER) in the base case was £252,000 per QALY (agalsidase beta). Univariate sensitivity analysis around the key assumptions produced ICERs ranging from £602,000 to £241,000. The base case unit cost of ERT was taken as £65.1/mg based on the cost of agalsidase beta. The unit cost would have had to be reduced to £9 to obtain an ICER of £30,000 per QALY. For MPSI, the mean cost per child patient (20 kg) treated is approximately £95,000 and an adult (70 kg) around £335,000 per annum in England and Wales. The cost per patient varies considerably by dose. There is no published evidence reporting an economic evaluation of ERT for MPSI and no study was identified that reported the quality of life of MPSI patients within a utility format. Furthermore, no or minimal information of the severity and rate of change of clinical manifestations of disease or the impact of ERT on these factors was identified. Information on the effect of ERT on mortality is also lacking owing to the relatively short time that the treatment has been available. Given this lack of data, it was not possible to develop a cost-effectiveness model of ERT treatment for MPSI as the model would consist almost completely of assumptions based on no published evidence, leading to an incremental cost per QALY result that would be meaningless.

Conclusions: Although ERT for treating the 'average' patient with Fabry's disease exceeds the normal upper threshold for cost-effectiveness seen in NHS policy decisions by over sixfold, and the value for MPS I is likely to be of a similar order of magnitude, clinicians and the manufacturers argue that, as the disease is classified as an orphan disease under European Union legislation, it has special status, and the NHS has no option but to provide ERT. More information is required before the generalisability of the findings can be determined. Although data from the UK have been used wherever possible, this was very thin indeed. Nonetheless, even large errors in assumptions made will not reduce the ICER to anywhere near the upper level of treatments usually considered cost-effective. In order to overcome limited evidence on the natural history of the disease and the clinical effectiveness of the intervention, the establishment of disease-specific data registries is suggested to facilitate the process of technology assessment and improving patient care. These registries should attempt to include all affected patients in the UK, and collect longitudinal patient level data on clinically relevant problems, interventions received and quality of life in a utility format.

Author	Journal	Publication Year	Article Type	Included in Review
Eng	NEJM	2001	Double Blind RCT	Yes (in El Dib 2010)
Desnick	Ann Intern Med	2003	Review	No
Banikazemi	Ann Intern Med	2007	RCT	Yes (in El Dib 2010)
Germain	J Am Soc Nephrol	2007	Phase III Extension Trial	No
Germain	Orphanet J Rare Dis	2010	Review	No
Eng	Genet Med	2006	Review	No
Wraith	J Pediatr	2008	Open Label Study	No
Warnock	Clin J Am Soc Nephrol	2010	Review	No
Watt	Genet Med	2010	Registry Review	No
Motwani	Mol Gen and Met	2012	Registry Review	No

Revised 8/7/12

Explanation

Included in the Cochrane Review used for the evidence review

Review Article and Outdated

Included in the Cochrane Review used for the evidence review

Excluded from the Cochrane Review as it is in non-randomized extension trial

Review Article of the Disease

Review Article and Outdated

Reviewed for the Cochrane, excluded due to lack of randomization. Also manufacturer-sponsored.

Review Article written by the Manufacturer

Registry looking at Quality of Life in Patients on ERT

Registry from a single institution of patients on ERT

All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan

Final Appraisal Report

Agalsidase alfa (Replagal®)
Shire Human Genetic Therapies

Advice No: 1107 – October 2007

Recommendation of AWMSG

Agalsidase alfa (Replagal®) should be recommended for use within NHS Wales as a long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease.

Patients receiving agalsidase alfa (Replagal®) will be entered into the Fabry Outcomes Survey. AWMSG urge the manufacturers of agalsidase alfa and agalsidase beta to develop a combined outcomes database.

Treatment will be administered under the supervision of a physician experienced in the management of Fabry disease or other inherited metabolic diseases.

Treatment will be administered according to agreed guidelines at appropriate designated centres.

AWMSG will review this and other enzyme replacement therapies within three years.

This report should be cited as:

1.0 RECOMMENDATION OF AWMSG:

Date: 18th October 2007

The recommendation of AWMSG is:

Agalsidase alfa (Replagal®) should be recommended for use within NHS Wales as a long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease.

Patients receiving agalsidase alfa (Replagal®) will be entered into the Fabry Outcomes Survey. AWMSG urge the manufacturers of agalsidase alfa and agalsidase beta to develop a combined outcomes database.

Treatment will be administered under the supervision of a physician experienced in the management of Fabry disease or other inherited metabolic diseases.

Treatment will be administered according to agreed guidelines at appropriate designated centres.

AWMSG will review this and other enzyme replacement therapies within three years.

4.0 EXECUTIVE SUMMARY:

4.1 Review of the evidence on clinical effectiveness

In the clinical trials reviewed, agalsidase alfa when compared to placebo showed improvement in all the parameters assessed, and demonstrated that there is some benefit to treatment. Data is currently limited, in particular for children, patients with more advanced disease and patients with variant forms of the disease. It should be noted ERT, for any patient, is life long. AWMSG are of the opinion that further longer term data that focuses on clinical outcomes, including survival, are required in order to provide clearer evidence of the efficacy of agalsidase alfa in treating and preventing manifestations of Fabry disease in patients.

4.2 Review of the evidence on cost effectiveness

The economic model presented for agalsidase alfa compares the drug against usual symptomatic care. Agalsidase beta was not considered as a comparator, but may be relevant if patients that are treated with agalsidase beta switch to agalsidase alfa (as is specified implicitly in the budget impact analysis). Several assumptions are made relating to the efficacy of agalsidase alfa, which are overoptimistic and significantly bias the model in its favour; however, the incremental cost per QALY still exceeds £250,000. When tested in plausible but limited sensitivity analysis, the estimated incremental cost per QALY gained was significantly higher than in the base-case analysis, indicating that the outputs of the model are sensitive to the assumptions made around the efficacy of the drug. In addition, there appears to be errors in the calculation of the results of this sensitivity analysis, which adds to the uncertainty of the estimated cost-effectiveness.

AWMSG is mindful of the ultra-orphan drug status of agalsidase alfa. However, there is no evidence presented to suggest that agalsidase alfa serves to bridge a gap to a "definitive" therapy, or that this "definitive" therapy is currently in development. The case for agalsidase alfa representing an innovative advance on existing therapy has not been demonstrated, and AWMSG is aware of the opinion that agalsidase alfa may not represent efficient use of healthcare resources.

5.0 LIMITATIONS OF DECISION CONTEXT:

- Studies are extremely limited in children and have not been performed in patients over the age of 65 years. Therefore safety and efficacy in these patient populations have not yet been established[1].
- Limited data are available in patients on dialysis or post kidney transplantation[1].
- No studies have been performed in patients with hepatic impairment[1].
- A head to head trial comparing agalsidase alfa to the alternative ERT agalsidase beta would be required to provide clear evidence of their relative efficacy in preventing and treating meaningful manifestations of Fabry disease.
- There is currently a lack of detailed information regarding the advantages and disadvantages of receiving agalsidase alfa in the home setting.

6.0 SUMMARY OF THE EVIDENCE ON EFFICACY AND SAFETY

6.1 Clinical efficacy:

The company submission[13] includes a pivotal Phase II randomised, double blind, placebo controlled study (TKT003) and its open-label extension study (TKT006). These studies were designed to evaluate the efficacy and safety of agalsidase alfa in male patients with confirmed Fabry disease[14-16]. The pivotal trial and also two papers reporting on results from the extension study are outlined and discussed together

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June 27, 2012

Mr. Darren Coffman, Director
Health Economic Review Commission
1225 Ferry Street, SE, Suite C
Salem, OR 97301

Dear Mr. Coffman:

Genzyme requests the opportunity to meet directly with members of the HERC to address the clinical aspects of Fabrazyme and to answer any questions the committee may have.

I am pleased to submit the enclosed Information Packet which provides background information for Fabry Disease and evidence of the safety and efficacy/effectiveness of Fabrazyme. In addition we have provided a brief review of the other Enzyme Replacement Therapies (ERT) manufactured by Genzyme as a reference since these disease states and therapies are different. Covered are the following:

Disease	Genzyme Brand Name	Chemical Name
Fabry	Fabrazyme®	Agalsidase beta
Gaucher (Type I)	Cerezyme®	Imiglucerase
Pompe	Myozyme®, Lumizyme®	Alglucosidase alfa
Mucopolysaccharidosis I	Aldurazyme®	Laronidase

All comments made in this document are supported by product labeling and/or citations from the published literature. Given the rare nature of Lysosomal Storage Disease (LSD), we have included references not only to randomized controlled trials (RCTs) and pivotal studies but also observational studies and other published research. The appendix contains copies of the labeling for all Genzyme ERT products mentioned.

Over the past 30 years, Genzyme has chosen to focus on developing innovative recombinant protein therapies for LSDs. During the last decade, there has been a dramatic increase in our understanding of LSDs and their treatment. The development of treatments for rare diseases was boosted in large part by the Orphan Drug Act of 1983. Prior to the introduction of legislation, patients with rare diseases were underserved, as there were insufficient incentives to risk research and development costs for these diseases. These laws and regulations have been successful in initiating the development of many new therapies to attempt to meet the unmet medical needs of patients with rare diseases. Furthermore, the reauthorization of the Prescription Drug User Fee Act (PDUFA) recently enacted by Congress builds on the strong federal commitment to advance patient access to orphan drugs. The PDUFA reauthorization includes provisions to expedite the review of drugs for serious and life-threatening diseases through the accelerated approval provisions of the Food, Drug and Cosmetic Act. The new law will also advance the FDA's capabilities for validation of surrogate biomarkers and enhances the agency's Rare Disease Program by providing additional funding for guidance on clinical design, the training of reviewers on the unique challenges of orphan drug applications, and the need for flexible scientific judgment.

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Even with appropriate incentives to conduct research in rare diseases, drug development and generation of clinical evidence remains challenging. Despite the fact that RCTs are considered the gold standard because inherent in their design is the minimization of bias, optimal trial design in rare diseases presents multiple challenges.

Rare diseases such as LSDs are often heterogeneous groups of disorders with poorly understood natural histories, and their diverse impact on multiple body systems makes targeted measurement of treatment effectiveness challenging. The number of patients available for evaluation is small, and many rare diseases are serious and progressive conditions. Therefore, trial designs for rare diseases often necessitate study designs that are different than those performed on larger populations, including use of external or historical controls.

In addition to the clinical review for Fabrazyme, and Genzyme's other ERT's, we have included in appendix I the diagnostic code and billing table based on disease state, indication and product for your reference.

We hope that you find the information contained within instructive and look forward to speaking with you in person at the August 9 HERC meeting.

If you have any questions regarding this information, please contact Cecilia Fairley, MSL, Medical Affairs at 415-385-4890 and Cecilia.Fairley@genzyme.com or Daniel Gruskin, M.D., Medical Affairs, at 617-768-6188 and Daniel.Gruskin@genzyme.com.

Sincerely,

Daniel J. Gruskin, MD
Senior Director, Medical Affairs

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OVERVIEW OF SUBMISSION

This package contains in-depth information on Fabry disease, one of the lysosomal storage disorders (LSDs), and Fabrazyme, an enzyme replacement therapy (ERT) used to treat Fabry disease. Fabrazyme received European approval in August 2001 and subsequently received FDA approval in April 2003. We have also included some background information on LSDs in general, with a minor focus on Gaucher disease, MPS I disease, and Pompe disease, and their ERTS, which are also manufactured by Genzyme, a Sanofi Company. The appendices contain information from the PI for each of the treatments discussed. We have also included a diagnostic code and billing table for your information.

TABLE OF CONTENTS

INTRODUCTION TO LYSOSOMAL STORAGE DISORDERS

Lysosomes are membrane-bound organelles that contain numerous acid hydrolases whose function is to catabolize a wide range of macromolecules. They play a critical role in the normal cellular metabolism, protein localization, membrane transport, development, and cell intercommunication (Wilcox et al., 2004). If there is absence or defective function of one of these enzymes, there is a bottleneck in the catabolic pathway leading to progressive accumulation of specific macromolecules. This leads to proliferation and distension of lysosomes in specific tissues, eventually causing disruption of cellular function or cell death and ultimately may cause organ dysfunction. Lysosomal storage disorders (LSDs) include over 40 monogenic inherited disorders that are a consequence of a deficiency of a single enzyme or protein. The genetic causes of most have been identified and most are inherited in an autosomal recessive manner. However, a few are X-linked, such as Fabry disease. Currently, no definitive genotype-phenotype correlation has been demonstrated in most LSDs, and therefore genotype often does not predict the clinical course of the disease.

LSDs are a part of a larger category called “orphan diseases”. Orphan diseases are defined as conditions affecting fewer than 200,000 patients in the United States and fewer than 5 in 10,000 in Europe. Each of the LSDs discussed in this document, Fabry, Gaucher, MPS I and Pompe disease, affect fewer than 3,000 patients in the United States and fewer than 1,000 patients in the United Kingdom (Dear et al., 2006). LSDs differ from each other by a number of variables including: the underling genetic defect, the associated enzyme deficiency, the substrate stored, and the cell types affected. Because of this, LSDs encompass a remarkable heterogeneity of symptoms, organ systems affected and severity of clinical outcomes. For example, signs and symptoms can range from osteopenia to hepatomegaly to severe neurodegeneration, and differing rates of progression and severity can result in a range of lifespans from a few months to almost a normal life span. Unfortunately, the pathophysiology underlying the progression from accumulation of partially degraded material to cellular and organ

dysfunction is not well understood for many, if not most, LSDs. Longitudinal data collection in disease registries of the four disorders covered in this submission have helped to more clearly delineate the natural history of these disorders, but many questions still remain. We will be highlighting some of this disease heterogeneity and natural history data when we further describe Fabry disease, Gaucher disease, MPS I disease, and Pompe disease in the next sections.

FABRY DISEASE

OVERVIEW

Fabry disease is a progressive, multisystemic, X-linked lysosomal storage disorder caused by a mutation in the gene encoding for the enzyme α-galactosidase A (α-GAL A) (Desnick et al., 2001). The resultant partial or complete deficiency in α-GAL A activity leads to an inability to break down certain glycosphingolipids that cause the underlying pathology of the disease: intralysosomal accumulation of globotriaosylceramide (GL-3) and related substrates in numerous tissue types throughout the body. The accumulation of GL-3 is particularly prominent in the vascular endothelium (vascular smooth muscle cells). Over time, progressive accumulation of GL-3 manifests clinically as renal, cardiac, and/or cerebrovascular complications that significantly increase patient morbidity and ultimately result in premature mortality (Wanner, 2007).

Historically, treatment of Fabry disease consisted primarily of symptom-based interventions that failed to address the underlying cause of the disease (Eng et al., 2006). However, Fabrazyme® (agalsidase beta), a recombinant form of human α-GAL A, was approved by the European Medicines Agency (EMA) in 2001 and the Food and Drug Administration (FDA) in 2003 to correct the enzyme deficiency in Fabry patients. By providing an exogenous source of α-GAL A, Fabrazyme is able to stabilize or reverse the organ-specific progression experienced by untreated patients and to

improve clinical outcomes and quality of life (Eng et al., 2006; Banikazemi et al., 2007; Germain et al., 2007; Watt et al., 2010; Hilz et al., 2004).

EPIDEMIOLOGY

Fabry disease is an extremely rare disorder that begins early in life and affects both males and females. Published estimates of disease prevalence range from 1 in 40,000–60,000 males to 1 in 117,000 in the general population (both genders) (Meikle et al., 1999; Desnick et al., 2001)

PATHOPHYSIOLOGY

- Fabry disease is an X-linked inborn error of the glycosphingolipid metabolic pathway. The metabolic defect in FD is deficiency of the lysosomal hydrolase alpha-galactosidase A (alpha-Gal A). Alpha-Gal A is encoded for by the GLA gene, with more than 400 mutations linked to the onset of Fabry disease (Stenson et al., 2003; Guce et al., 2010). A mutation of the GLA gene impacts the production or enzymatic activity of α-GAL A and leads to the underlying pathology of Fabry disease: accumulation of glycosphingolipids in numerous cell and tissue types (Desnick et al., 2001). Storage of GL-3 begins before birth; however patients are typically asymptomatic in the first few years of life (Tsutsumi et al., 1985; Vedder et al., 2006; Zarate and Hopkin, 2008).
- While GL-3 is a naturally occurring substance, lack of its efficient degradation in the lysosome leads to the primary pathology and secondary pathology seen in Fabry disease. The progressive organ damage caused by these primary and secondary disease processes contributes to the onset of life-affecting symptoms and, ultimately, organ dysfunction and/or failure and premature death (Waldek et al., 2009).
    - Primary pathology: In patients with Fabry disease, deficiency of lysosomal α-GAL A activity leads to the buildup of GL-3 and related substrates within

vascular endothelium, cardiac, renal, and smooth muscle cells, and neurons (Desnick et al., 2001).

- Secondary pathology: Ongoing accumulation of GL-3 and resultant dysfunction of affected cells and tissues may trigger an insidious cascade of organ-specific pathological processes in patients with Fabry disease. These processes, including ischemia and inflammatory or neurohormonal mechanisms (e.g., release of cytokines, growth factors, and stress-signaling molecules) may manifest as a number of different damaging changes in the tissues (Eng et al., 2006; Wanner, 2007). These may include tissue remodeling, hypertrophy, fibrosis, inflammation, and sclerosis. While affected organ systems do not differ much in the time of onset of such cascades (i.e., all begin early in life), they do differ in the speed with which the progression of pathology results in clinical manifestations.

- Organ specific accumulation of GL3 occurs predominately in three systems: renal, cardiac, and cerebrovascular.
  - In the kidneys, renal biopsy studies have demonstrated deposition of large amounts of GL-3 in the mesangial cells, glomerular endothelial cells, distal tubular cells, arterial and arteriolar smooth muscle cells, vascular endothelial cells, interstitial cells, and podocytes (Gubler et al., 1978; Pabst and Sterzel, 1983; Desnick et al., 2001; Sessa et al., 2001; Thurberg et al., 2002; Eng et al., 2006). Age-dependent and progressive accumulation of GL-3 inclusions in podocytes has been reported in young patients with normal GFR and low to absent proteinuria (Najafian et al., 2011).
  - In the heart, GL-3 accumulates in vascular endothelial cells, cardiomyocytes, smooth muscle cells, conduction system cells, and valvular fibrocytes (Desnick et al., 2001; Kampmann et al., 2002b; Linhart et al., 2002).

GL3 accumulation in vascular endothelial cells, smooth muscle cells, and neurons of the autonomic system leads to vascular dysfunction, tissue ischemia, and vessel occlusion. Accumulation also occurs in specific neuronal populations in the central nervous system, particularly in the brainstem, hypothalamus, amygdala, hippocampus, and entorhinal cortex. These areas of the brain associated with regulation of the autonomic nervous system (Kaye et al., 1988; deVeber et al., 1992). Storage of GL3 in the vessel walls of the central nervous system results in dilatations and increased vessel tortuosity resulting in abnormal blood flow (Bersano et al., 2012)

INHERITANCE AND DISEASE MANIFESTATIONS

The GLA gene mutated in Fabry disease is found on the X chromosome and the inheritance of Fabry disease follows a typical X-linked pattern. However, contrary to many X-linked diseases, both male and female patients can be affected with the disease. The risk of inheriting the mutation therefore depends on the gender of the affected parent.

- Fathers (hemizygotes) affected with Fabry disease pass along the defective gene to 100% of their daughters. There is no male-to-male transmission.
- Mothers (heterozygotes) affected with Fabry disease have a 50% risk in each conception of passing along the defective *GLA* gene to their children, regardless of gender

- The majority of male hemizygotes demonstrate a severe “classical” Fabry phenotype, whereas female heterozygotes may display a broad spectrum of clinical presentations. This spectrum ranges from a lack of symptoms to the more classical and severe phenotype typically observed in males (Wilcox et al., 2008).

- The more variable presentation of Fabry disease in female patients may be partly attributed to the phenomenon of X chromosome inactivation – the permanent epigenetic silencing of one X chromosome – also known as Lyonization (Lyon, 1961). However, other yet unidentified epigenetic and genetic (i.e. promoting) factors may play an important role in the phenotypic variability observed in women with Fabry disease (Belmont, 1996).
- Although the symptoms of Fabry disease were previously thought to be rare or mild in female patients, current knowledge indicates that this is not actually the case (Deegan et al., 2006; Eng et al., 2006; Wang et al., 2007; Wilcox et al., 2008). While the phenotypic presentation is more variable in females than in males, the majority of female heterozygotes suffer from significant morbidity and premature mortality, with most demonstrating histological evidence of GL-3 storage indicating the presence of Fabry disease (MacDermot et al., 2001a; Eng et al., 2006; Wang et al., 2007; Warnock et al., 2010).

CLINICAL PRESENTATION

NATURAL HISTORY

The natural history of each patient with Fabry disease is unique in terms of age of presentation, cluster of presenting symptoms, disease progression, and co-morbidities. To further delineate the natural history of the Fabry population as a whole, the Fabry Registry was established in 2001. As of 2012, more than 4,200 patients have been enrolled under more than 300 participating physicians. More than sixteen papers have been published demonstrating the full range of symptoms and severity. For example, classically-affected males typically experience an earlier and more severe onset and progression of disease than females with Fabry disease, who tend to present with a more variable and sometimes less severe clinical presentation. However, despite this phenotypic variability, virtually all males and most female patients develop symptoms in early childhood that progress to considerable morbidity and early mortality as a result of

ongoing storage of GL-3 and other substrates (Hopkin et al., 2008; Schiffmann et al., 2009; Waldek et al., 2009).

While the onset of GL-3 accumulation occurs prenatally in the majority of Fabry patients, affected infants are asymptomatic, and often remain so for the first years of life. Data from a Fabry registry study that included 352 pediatric patients found that on average, male patients experienced the onset of all symptoms at an earlier age and often with greater severity than female patients. The median age of onset was 6 years of age for the 77% of males who had symptoms at enrollment and 9 years of age for the 51% of females with symptoms at enrollment (Hopkin et al., 2008).

Disease manifestation can be differentiated between those symptoms that are life-affecting versus those symptoms that are life-threatening. Life-affecting signs and symptoms include painful peripheral neuropathy, autonomic dysfunction resulting in hypohydrosis, and gastrointestinal disturbances. Life-threatening manifestations include renal insufficiency or failure, cardiomyopathy, and transient ischemic attacks or strokes.

LIFE-AFFECTING FABRY DISEASE MANIFESTATIONS- CHILDHOOD

- The earliest life-affecting symptoms of Fabry disease reflect involvement of the peripheral and autonomic nervous systems and manifest clinically as episodic pain crises, peripheral neuropathy, gastrointestinal disturbances, and anhidrosis (i.e., inability to sweat), and hot/cold intolerance (Eng et al., 2007; Hopkin et al., 2008; Burlina et al., 2011).
- Pain in the extremities is common in all patients with Fabry disease and is associated with damage of the peripheral nerve fibers that transmit pain (Moller and Jensen, 2007). Episodes may be triggered by illness, exercise, fever, stress, or weather changes and are usually accompanied by fever, joint pain, and sometimes elevated erythrocyte sedimentation rates (Morgan et al., 1990;

MacDermot et al., 2001b; Ramaswami et al., 2006; Bodensteiner et al., 2008). The duration of these episodes may last from minutes to weeks.

- Patients with Fabry disease also frequently exhibit symptoms and signs indicative of autonomic dysfunction. These symptoms, including anhydrosis/hypohydrosis and gastrointestinal disturbances, are also thought to result from damage of the peripheral nerve fibers (Germain, 2010). Gastrointestinal disturbance may manifest as acute abdominal pain and diarrhea. In male patients, GI symptoms are associated with early satiety, postprandial bloating, nausea, vomiting, and difficulty gaining weight (MacDermot et al., 2001b; Mehta et al., 2009; Whybra et al., 2004; Eng et al., 2006; Ramaswami et al., 2006; Hoffmann and Keshav, 2007; Bodensteiner et al., 2008). Females may also experience GI symptoms, usually beginning in adolescence or early adulthood (MacDermot et al., 2001a; Eng et al., 2006). In all Fabry patients, symptoms appear to worsen with age.
- Importantly, Fabry-related peripheral pain has a significant negative impact on patient quality of life (QoL) and, in some instances, have been linked with depression (Grewal, 1993; Cole et al., 2007).
- It's also important to note that some patients have shown more serious manifestations of Fabry disease in childhood: as early as 16 years for microalbuminuria and glomerulosclerosis (Tondel et al., 2008), 12 years for arrhythmias (Hopkin et al., 2008), 12 years for transient ischemic attacks (Mehta et al., 2004), 18 years for strokes (Rolfs et al., 2005). Of note, white matter lesions visible on brain MRIs have been reported in children as young as an 8-year old male (Cabrera-Salazer et al., 2005) and a 13-year old female (Bouwman et al., 2011).

LIFE-THREATENING FABRY DISEASE MANIFESTATIONS- ADULT PATIENTS

- At about 20 years of age, the life-affecting symptoms of Fabry disease begin to progress to life-threatening complications. While peripheral neurological

symptoms may decrease in intensity (a finding reflective of neuron loss) (Burlina et al. 2011), the pathological progression of GL-3 accumulation and tissue damage in the kidneys, heart, and cerebrovascular system becomes clinically symptomatic over time. Patients demonstrate chronic kidney disease, cardiomyopathy, and central nervous system complications including premature stroke, all of which contribute significantly to the early mortality observed in patients with Fabry disease (Eng et al., 2007; Kampmann et al., 2008; Ortiz et al., 2008; Wilcox et al., 2008; Schiffmann et al., 2009; Sims et al., 2009; Waldek et al., 2009; Patel et al., 2011).

- Renal disease: onset typically begins early in life, but signs may not manifest until the second or third decade as microalbuminuria and proteinuria (Sessa et al., 2001). Because of compensatory mechanisms and the vast functional reserve of the kidneys (i.e., extra excretory capacity), patients often remain relatively asymptomatic despite significant nephron loss. However, once a critical number of nephrons are damaged, adequate glomerular filtration cannot be maintained and rapid onset of kidney failure ensues (Desnick and Brady, 2004). Progressive renal dysfunction in the form of chronic kidney disease (CKD) results from renal tissue remodeling fibrosis, tubular atrophy, and glomerulosclerosis, possibly similar to the pathophysiological mechanisms in diabetic nephropathy. However, potentially due to GL3 storage, which begins before birth, many of the Fabry related renal complications appear as early as the second decade and generally become apparent in the third or fourth decade of life (Branton et al., 2002a; Desnick et al., 2003; Eng et al., 2006; Germain, 2010).
    - Historically, CKD is the most frequent cause of death among classically affected males, who commonly progress to ESRD leading to premature mortality (Branton et al., 2002b; Desnick et al., 2003). Although this manifestation can be more attenuated and generally occurs at a later age in female patients, females who do progress to advanced CKD typically do so at a similar mean age as men (Deegan et al., 2006; Ortiz et al., 2008;

Reisin et al., 2011). The incidence of CKD 4/5 (previously known as ESRD) was assessed in a series of 1,262 Fabry Registry patients. Thirteen percent of males and 3% of females had CKD 4/5 by mean age of 43.8 (range 21-79) and 46.6 (range 20-74) respectively (Ortiz et al., 2008).

- The degree of proteinuria is a major prognostic determinant for more rapidly progressive Fabry nephropathy, as its prevalence and degree of severity increases with decreasing renal function in all patients with Fabry disease (Banikazemi et al., 2007; Germain et al., 2007; Ortiz et al., 2008).
- Data from the Fabry Registry has also indicated that a considerable number of patients with mild to moderate impairment of renal function (i.e., CKD stages 2 or 3) do not have proteinuria but have clearly experienced early, extensive renal damage in the form of GL-3 deposits in podocytes and renal vasculature (Wang et al., 2007). Podocyte GL-3 accumulation has also been seen to increase with age (Najfian et al., 2011). Further, severe GL-3 accumulation in podocytes has been observed in children and adolescents aged 7 to 18 years, along with morphological changes in the glomerular, tubulointerstitial, and vascular compartments (Tondel et al., 2008). Damage and subsequent loss of podocytes is associated with progression and severity of kidney dysfunction in Fabry disease (Eng et al., 2006; Feldt-Rasmussen, 2011).
- Patients who demonstrate renal progression share a common clinical profile including certain risk factors: age greater than 40 years, significant baseline proteinuria (>2 g/24 hr), and greater than 50% glomerular sclerosis at pre-treatment (Germain et al., 2007). These irreversible changes—particularly significant glomerular scarring—mark the end stage of renal disease, which generally occurs between the third to fifth decades of life but has been reported in patients as young as 16 years. (Sheth et al., 1983; Desnick et al., 2001; MacDermot et al.b, 2001; Branton et al., 2002b).

- Cardiac: complications include left ventricular hypertrophy (LVH), arrhythmia, angina, and dyspnea. Progressive damage can lead to death due to myocardial fibrosis and congestive heart failure, or a malignant arrhythmia (Germain, 2010). Cardiac events are the major cause of mortality in all patients, and especially in females with Fabry disease (Waldek et al., 2009).
    - A recent analysis of 2869 patients enrolled in the Fabry Registry studied the incidence of major cardiovascular (CV) events and the natural history of CV complications in patients with Fabry disease: 5.8% of men and 3.7% of women experienced a major CV event with an increasing incidence seen with age (Patel et al., 2011). The mean age at first CV event was significantly younger in men (45.2 years) than in women (53.6 years; $P < 0.0001$), with men most likely (72%) to experience their first event between the ages of 35 and 55 years, whereas most women (72%) experienced their first CV event between the ages of 45 and 65.). Six percent of men and 1.9% of women experienced a CV event before the age of 25. Prior to their first CV event, the majority of patients in Patel and colleagues' Registry study had experienced LVH (93% of men, 78% of women) and hypertension (56% of men, 58% of women) (Patel et al., 2011). Both of these conditions are well-established risk factors for CV complications.
    - Arrhythmias are also a common cause of cardiac death for Fabry patients (Zarate and Hopkin, 2008). Kaplan–Meier estimates have been calculated for the time to first arrhythmia in a retrospective study of men and women with Fabry disease: arrhythmias first appeared in adolescence in males, whereas in female patients they first appeared in their early twenties (Schiffmann et al., 2009). By the age of 45 years, 50% of males in the study had a documented cardiac rhythm disturbance.
    - Cardiac fibrosis was also found in 23% of female Fabry patients prior to the onset of left ventricular hypertrophy (Niemann et al., 2011). As fibrosis is not commonly assessed during routine cardiac evaluations, cardiac

disease in females may have earlier onset than previously described, and further studies are underway.

- Cerebrovascular: events most commonly include transient ischemic attacks, strokes, and brain imaging abnormalities.
    - Strokes and transient ischemic attacks: Fabry patients of both genders are vulnerable to the development of life-threatening strokes (e.g., ischemic or hemorrhagic) and TIAs from a relatively young age. Recent analysis of natural history data from the Fabry Registry (N = 2,446) revealed a stroke incidence of approximately 5.6% (7% of men and 4% of women) in patients with Fabry disease. This rate was markedly higher for both men and women when compared with the incidence of stroke in the general US population. As expected, the incidence of stroke increased with age, with a stroke frequency of >22% in males 55 years and older (Sims et al., 2009). The mean age at first stroke among Fabry patients was also considerably younger, 39.8 years for males and 45.7 years for females, than that among the general population (76 and 81 years, respectively). In addition, the majority of first strokes were ischemic (86.8%) rather than hemorrhagic (13.2%). In a separate screening study of young patients with cryptogenic stroke (i.e., stroke of unknown origin) 4.9% of men and 2.4% of women were diagnosed with Fabry disease (Rolfs et al., 2005).
    - Brain imaging abnormalities: The most prominent structural brain imaging findings in patients with Fabry disease are the presence of white-matter lesions, which may appear as early as 13 years of age (Cabrera-Salazer et al., 2005; Reisin et al., 2011). In adults, two studies have reported comparable frequency and severity of white-matter lesions in men and women with Fabry disease (males: 31% and 34%; females: 36% and 27%, respectively) (Fellgiebel et al., 2005; Fellgiebel et al., 2006; Ginsberg et al., 2006). In a study of 50 patients with Fabry disease, approximately half had white-matter lesions (increasing to 100% if ≥ 50 years of age). In general, the burden of cerebral lesions tends to increase with age, but

sometimes precedes the onset of TIAs or strokes, making diagnosis of Fabry disease difficult (Crutchfield et al., 1998).

- Vessel abnormality, with dilatations and aneurysms as well as vessel tortuosity, also are significant pathological findings in Fabry disease, leading to aneurysms or vascular bleeds and strokes (Bersano et al., 2012).
- The appearance of cerebral events tends to correlate with the presence of other pathology common to Fabry disease. As seen in the Fabry Registry, 67.4% of patients who experienced a stroke had also experienced a cardiac or renal event. Interestingly, more than 70% of these patients experienced a stroke before a cardiac or renal event, or they experienced stroke only (i.e., not other events) (Sims et al., 2009).

LIFE E□PECTANCY

- The degenerative natural history and life-threatening complications experienced by patients with Fabry disease lead to a life expectancy that is markedly lower than that observed in the general population. Results from a recent analysis of the Fabry Registry indicated that cardiovascular complications are the most common cause of death among both genders, of which 57% had had previously received renal replacement therapy (Waldek et al, 2009).
    - Males: prior to the advent of renal dialysis and kidney transplantation, the average age at death for males with classical Fabry disease was 41 years (Colombi et al., 1967). More recently, the survival curve for untreated male patients shows a steep increase in mortality after the age of 35, but the average life expectancy has extended by approximately 10 years, to an average survival of 50 years (MacDermot et al., 2001b; Branton et al., 2002b; Schiffmann et al., 2009). This lifespan represents an approximate reduction of 20 years from that of the general male population (MacDermot et al., 2001b).

These findings are supported by newer data from patients in the Fabry Registry. In this study of patient life expectancy, the average age at death was 53.7 years in males, with 81% of deceased patients having received ERT for a median duration of only 12 months (Waldek et al., 2009).

- Similar to untreated males, a gradual decline is observed in the survival of untreated females with Fabry disease after the age of 35. In one study, the median cumulative survival in female patients was approximately 70 years, which represents an approximate reduction of 15 years from that of females in the general population (MacDermot et al., 2001a). The more recent Registry analysis by Waldek and colleagues showed similar results, reporting a median age at death of 62 years (Waldek et al., 2009). Approximately 41% of the deceased patients in this study had received ERT for a median duration of only four months.

DIAGNOSIS

- The rarity and non-specific symptoms associated with Fabry disease contribute significantly to a high rate of misdiagnosis in this population. As a result, correct diagnosis of affected patients is frequently delayed for several years. In a study from the Fabry Registry, there was a mean time delay of diagnosis after symptom onset of 14.2 years for males and 15.7 years in females (Wilcox et al., 2008). Such delays in recognition and treatment permit progression of the disease, increasing the probability of symptom onset and the appearance of severe complications.
- A family history suggestive of the disorder is of obvious assistance in diagnosis.
- In the setting of clearly established family history and classic phenotype, the diagnosis is usually confirmed if there is low alpha-Gal A activity in leukocytes or plasma in males. For females, DNA analysis of the alpha-Gal A gene is required to make the diagnosis.

TREATMENT

Prior to the availability of ERT, the treatment of Fabry disease was limited to symptomatic care and non-specific treatments to address pain, renal disease, and cardiac complications. These treatments fail to address the enzyme deficiency that underlies the onset and progression of the disease (Ortiz et al., 2008). In contrast, enzyme replacement therapy (ERT) (Fabrazyme) was developed to provide an exogenous source of α-GAL A in Fabry patients, thereby enabling the breakdown of accumulating glycosphingolipids that give rise to the pathology of the disease.

The endpoints included in clinical studies of Fabrazyme can be categorized as those demonstrating significant reduction of "surrogate markers" (also know as "subclinical paramenters"). For example, low-density lipoprotein levels, a surrogate marker of heart disease, are commonly measured as they are now recognized to predict the risk of heart attack, an overall infrequent event (Genest et al., 2009). Accelerated FDA approval of Fabrazyme in 2003 was granted based on the randomized placebo controlled phase III trail which demonstrated significant clearance of substrate in cell types of the heart, skin and kidney, which are most affected in Fabry disease. Accelerated approval of a therapy is typically used when a disease is so rare or the desired clinical endpoint (e.g. survival) is likely to be so far in the future that the length of a clinical trial would have to be unreasonably long in order to obtain a sufficient number of outcomes (Alfadhel and Sirrs, 2011).

In order to establish the correlation between modification of surrogate markers and a clinical benefit to the patients, an additional 82 patient confirmatory, double–blind, randomized, placebo-controlled study was conducted. It demonstrated a significant 53% (intent-to-treat population) or 61% (per-protocol population) risk reduction of patients experiencing a clinical outcome of renal , cardiac or cerebrovascular event or

death in patients receiving Fabrazyme compared to the placebo group (Banikazemi et al., 2007). In the hierarchy of published evidence, clinical outcomes are generally of higher quality or importance, as they clearly demonstrate the value of therapy to the patient in terms of morbidity and/or mortality.

Overall, the safety and efficacy of Fabrazyme has been demonstrated in six major clinical trials (N>190) (Eng et al., 2001a; Eng et al., 2001b, Germain et al., 2007; Banikazemi et al., 2007; Wraith et al., 2008; Lubanda et al., 2009), and numerous supporting studies. These studies demonstrate that Fabrazyme 1.0 mg/kg biweekly effectively reverses the accumulation of vascular endothelial GL-3 in kidneys, heart and skin, seen in long-term follow-up of at least 4.5 years (Germain et al., 2007). In the majority of patients in these trials, median estimated eGFR, proteinuria, and serum creatinine remained stable while receiving Fabrazyme. Fabrazyme also provides significant reductions in cardiac size, improves heart function, and increases exercise tolerance. In addition, Fabrazyme significantly reduces the risk of major clinical events, such as kidney failure and heart failure. Fabrazyme is also associated with reductions in pain and gastrointestinal symptoms, as well as improvements in energy and QOL. Several studies are detailed below:

PLACEBO-CONTROLLED DOUBLE-BLIND STUDIES

- Phase III 20 week trial that included 58 patients (56 males and 2 females) with Fabry disease and designed to assess the efficacy, safety, and Quality of Life (QOL) outcomes in Fabry patients treated with Fabrazyme versus placebo (1:1 randomization) (Eng et al., 2001b):
    - Primary endpoint: 20/29 (69%) Fabrazyme treated patients were free of microvascular endothelial GL-3 deposits on renal biopsies versus 0% of placebo patients at 20 weeks

- Secondary endpoints: Fabrazyme treatment decreased GL-3 deposits in endothelium of skin and heart ($p<0.001$) compared to placebo group, as well as in plasma
- Mild to moderate infusion associated reactions (IARs) in the Fabrazyme group, with rigors and fevers occurring more frequently than in the placebo group ($p = 0.004$)
- Demonstrated that Fabrazyme cleared microvascular endothelial deposits of GL-3 from kidneys, skin, heart, and plasma

- Phase IV study that included 72 males and 10 females with Fabry disease and designed to determine if Fabrazyme delays the onset of clinical events in Fabry patients with advanced disease (2 Fabrazyme : 1 placebo randomization) (Banikazemi et al., 2007):
  - 27% of Fabrazyme versus 42% of placebo treated patients experienced clinical events in the intent-to-treat population (53% risk reduction); risk reduction 61% was seen in the per-protocol population
    - Greater treatment effect was seen observed in patients with higher eGFR
  - Mild to moderate treatment IARs observed in 55% of Fabrazyme group versus 23% of placebo group
  - Demonstrated that Fabrazyme slowed progression to composite clinical outcome of renal, cardiac, and cerebrovascular complications and death versus placebo

OPEN-LABEL E□TENSION STUDY

- Phase III extension study up to 54 months (original 20 week study published as Eng et al., 2001) (Germain et al., 2007)
  - All patients maintained complete GL-3 clearance in renal capillary endothelial cells, in addition to other renal cell types.

    - Median creatinine and eGFR remained stable and normal for the overall population
    - 6/58 (10%) patients had renal progression: 4 had risk factors for progression such as proteinuria, age, and glomerulosclerosis
- Complete clearance of skin and heart capillary endothelium in the patients assessed
- Mean plasma GL3 remained decreased and in the normal range
- IARs were most common treatment-related event but decreased over time
- Demonstrated that long-term ERT with Fabrazyme stabilized renal function in patients without renal involvement at baseline.

REGISTRY STUDIES

- Long-term progression of impaired kidney function in adults (151 males, 62 females) enrolled in the Fabry Registry and treated for at least 24 months at Fabrazyme 1.0 mg/kg every two weeks (Warnock et al., 2012)
    - Patients were group into quartiles according to eGFR slope observed during the treatment period (i.e., stable eGFR in Q1 and most rapid decline in Q4)
    - Males: Q1 mean eGFR slope -0.1 mL/min/1.73 m^2/year *versus* Q4 mean eGFR slope of -6.7 mL/min/1.73 m^2/year
    - Females: Q1 mean eGFR slope 2.7 mL/min/1.73 m^2/year *versus* Q4 mean eGFR slope of -4.4 mL/min/1.73 m^2/year
    - Concluded that risk factor most strongly associated with renal progression was baseline urinary protein:creatinine ratio (Ur Pr:Cr) > 1 g/g in both genders (odds ratio 112, 95% confidence interval (95% CI) 4-3109, P = 0.0054). Longer time from symptom onset to treatment was also associated (odds ratio 19, 95% CI 2-184, P = 0.0098) for males.

- Incidence of clinical events after the initiation of Fabrazyme in 1013 males enrolled in the Fabry Registry who had been receiving treatment with 1.0 mg/kg Fabrazyme biweekly for up to 5 ± 2.4 years (mean ± SD) (Hopkin et al., 2012)
    - 783 (77%) had no renal, cerebrovascular, or cardiovascular event during 4 ± 2.5 years of treatment
    - Patients who had events were more likely to have experienced events before initiation of treatment versus those who remained event free (48% versus 18%)
    - Men who started treatment with Fabrazyme after age 40 years were more likely to experience clinical events than those <30 years of age (rate ratio 3.5, 95% CI 1.46-7.42, p = 0.001)
    - Concluded that early initiation of Fabrazyme is associated with fewer clinical events
- Impact of Fabrazyme 1.0 mg/kg biweekly treatment for median of 3 years (2-5 year range) on cardiac function in a single-center registry study of 66 Fabry patients (44 males, 22 females) (Motwani et al., 2012)
    - Fabrazyme improves left ventricular morphology and function in majority of patients who had left ventricular hypertrophy at baseline ($p < 0.01$)
    - Fabrazyme normalized majority of patients with documented long QTc intervals, short PR intervals, and short PV waves at baseline ($p < 0.001$)
- Comparison of the effect of Fabrazyme 1.0 mg/kg biweekly treatment (n=115) compared to natural history cohort on left ventricular mass (LVM) on adult males enrolled in the Fabry Registry with a baseline and at least 1 additional measurement ≥ 2 years later (Germain et al., 2012).
    - Baseline demographic and clinical characteristics were very similar in treated and untreated men.

    - LVM decreased or remained stable in men treated with agalsidase beta for ≥ 2 years and who began treatment before the age of 50 years.
    - The greatest improvement in LVM was seen with treatment initiation before 30 years of age versus the natural history cohort: difference in mean estimated slope for those 18-29 years was -13 g/year ± 2.72 (standard error of the mean), p <0.0001
- Effect of 2-3 years of Fabrazyme treatment on longitudinal self-reported health-related quality of life (HRQL) via SF-36 short-form questionnaires for 71 males and 59 females enrolled in the Fabry Registry (Watt et al., 2010)
    - Males reported largest improvements in the impact of physical and mental health on performance of work and daily activities ($p < 0.05$)
    - Women reported largest improvements in impact of physical health on performance, general health perception, and social function ($p < 0.05$)

TIMING OF INITIATION OF FABRA□YME

In 2006, an international panel of experts proposed guidelines for the evaluation and management of patients with Fabry disease (Eng et al., 2006). Evidence-based recommendations were presented regarding the recognition, evaluation, and surveillance of morbidities associated with the condition, along with treatment strategies for both preventative and symptomatic care. For patients with Fabry disease, the key therapeutic goals of ERT are symptom reduction and the prevention of late complications such as renal failure, cardiac failure, and stroke (Eng et al., 2006; Mehta et al., 2010). In young patients, the aim of ERT is to prevent onset of the clinical signs and symptoms of the condition; in older patients with more advanced disease, the goal is to stabilize progression, reverse underlying pathological abnormalities, and improve organ dysfunction (Desnick et al., 2003). In addition to ERT, supportive or adjunctive

treatment is recommended for successful management of Fabry disease; they may act as prophylaxis for outcomes anticipated by the natural history of the disorder (e.g., control of blood pressure, lipids, and proteinuria) or may include interventions that target the complications observed in patients with more advanced disease (e.g., kidney failure, CVD) who were initiated on ERT later in life.

Guidelines for the initiation of ERT in patients with Fabry disease vary among countries and in particular concerning the timing of treatment in heterozygous females and children (Germain, 2010). Recommendations from an international panel of physicians state that every male Fabry patient should be offered ERT, irrespective of the stage of CKD. Female patients should be offered ERT if they present significant symptoms or show evidence of progressive end organ Fabry involvement (e.g., chronic acroparesthesia (peripheral neuropathy), persistent proteinuria, low eGFR, etc. (Eng et al., 2006). Current recommendations for the initiation of ERT in subpopulations of Fabry disease patients are presented in Table 1.

TABLE 1: CURRENT GUIDELINES FOR THE INITIATION OF ERT IN PATIENTS WITH FABRY DISEASE

Fabry Subpopulation	Guidelines for Initiating ERT
Adult males (≥16 years)	At the time of diagnosis of Fabry disease
Boys (<16 years)	At the time of development of significant symptoms *or* if symptomatic, consider at 10–13 yrs
Females (all ages)	Monitor and institute if significant symptoms present or evidence of progression of organ involvement

Source: Eng et al., (2006)

Several studies have demonstrated that clinical outcomes are influenced by the extent of organ damage due to a delay in the onset of treatment. As detailed in the previous section, time to treatment initiation affected renal outcomes (Warnock et al., 2012), cardiac outcomes (Motwani et al., 2012; Germain et al., 2012), or the likelihood of the

occurrence of a clinical event, such as renal, cardiac, cerebrovascular events or death (Hopkin et al., 2012). Still, stabilization of progression remains an important achievement of therapy in Fabry patients who, without treatment, would progress to a more severe stage of the disease.

The Fabrazyme PI is included in Appendix A. Further information will be available upon request.

SUMMARY OF FABRY DISEASE AND FABRAZYME

- Fabry disease is a rare, progressive, multisystemic genetic disorder caused by the deficiency of a lysosomal enzyme, alpha-galactosidase A resulting in accumulation of GL-3 and other substrates.
- This deficiency results in progressive accumulation of GL-3, which then triggers secondary, irreversible tissue damage and subsequent organ dysfunction.
- Major manifestations of Fabry disease are pain, GI, hypohidrosis, and heat intolerance early in life, and serious renal, cardiovascular, and cerebrovascular complications later in life.
- Early diagnosis and prompt initiation of enzyme replacement therapy are required for optimal management of patients with Fabry disease.
- Enzyme replacement with Fabrazyme may provide clinical benefit across organ systems to help change the future for people living with Fabry disease.
- Fabrazyme restores enzyme activity sufficient to clear the accumulating substrate, providing rapid and durable reductions of GL-3 substrates from multiple cell types.
- Patients treated relatively early in the disease process with Fabrazyme 1.0 mg/kg have demonstrated long-term stabilization of renal function, as measured by glomerular filtration rate and serum creatinine levels, particularly when urine protein is controlled.
- Studies have shown that Fabrazyme:
    - Reduced the risk of life-threatening complications related to Fabry disease

- Improved cardiac morphology and normalized electrical conduction abnormalities
- Improved symptoms related to Fabry disease and increased health-related quality of life

GAUCHER DISEASE AND EN□YME REPLAECMENT THERAPY WITH CERE□YME

Gaucher disease is an autosomal recessive glycolipid storage disorder that results from a deficiency in the activity of glucocerebrosidase (acid □-glucosidase). This leads to accumulation of glucosylceramide (glucocerebroside) in cells derived from the monocyte/ marcrophage system (Grabowski et al., 2010)).

Gaucher disease is the most commonly diagnosed LSD with an estimated incidence of 1 in 59,000-86,000 (Meikle et al., 1999; Poorthuis et al., 1999) and a prevalence in the United States of < 3,000 identified patients. Three subtypes of Gaucher disease are commonly recognized: type 1 (non-neuronopathic), type 2 (acute neuronopathic), and type 3 (subacute/chronic neuronopathic) (Grabowski et al., 2010). Gaucher disease type 1 is differentiated from types 2 and 3 by the absence of primary central nervous system involvement (Grabowski et al., 2010)) and is by far the most common type, accounting for approximately 94% of the total Gaucher disease population (Charrow et al., 2000).

Because of the glucocerebroside accumulation in cells of a macrophages lineage, organ dysfunction occurs in sites where tissue macrophages are prevalent. This primarily includes the liver, spleen, bone and bone marrow, as well as secondarily the lungs and central nervous system (Grabowski et al., 2010)). The presenting features are variable and may occur at almost any age. The most common symptoms are:

- Anemia and thrombocytopenia
- Hepatomegaly and splenomegaly

- Osteonecrosis, osteopenia, bone fracture, bone marrow infiltration and bone remodeling

Gaucher disease has been extensively studied for many years, however clinical questions still remain and others are being discovered. One tool that has helped delineate the natural history has been the Gaucher Registry, an international, observational voluntary database established in 1991. The Gaucher Registry currently has more than 6100 patients enrolled under 700 investigators. Thirty two papers have been published of cohort studies and longitudinal data analysis findings, including treatment outcomes based on data from the Gaucher Registry.

Enzyme replacement therapy is the accepted standard of treatment for symptomatic patients with Type I Gaucher disease. Cerezyme (imiglucerase for injection) has received FDA approval for the treatment of Gaucher disease Type I in May 1994 (see Appendix B for full prescribing information). Cerezyme is indicated for Gaucher-related anemia, thrombocytopenia, bone disease, and hepatomegaly or splenomegaly. Further information will be provided upon request.

MUCOPOLYSACCHARIDOSIS TYPE (MPS 1) AND ENZYME REPLACEMENT THERAPY WITH ALDURAZYME

Mucopolysaccharidosis type I (MPS I) is an autosomal recessive storage disorder that results from a deficiency in the activity of α-L-iduroniadase. This leads to lysosomal accumulation of glycosaminoglycans (GAGs) in cells throughout the body specifically in the extracellular matrix of connective tissues (Clarke, 2008).

MPS I disease has an estimated incidence of 1 in 84,000-111,000 (Meikle et al., 1999; Poorthuis et al., 1999) and a prevalence in the United States of <2,000 identified patients. MPS I disease was first described in its severe form by Gertrud Hurler and in its more mild form by Harold Scheie. It is now recognized to be the same disease

biochemically and molecularly (Muenzer et al., 2011) and is typically described as either severe or attenuated.

MPS I is a multisystemic disease caused by the accumulation of two specific GAGs, dermatan sulfate and heparan sulfate. These two GAGs are distributed throughout the body and thus MPS I displays pathology in most tissue types (Clarke, 2008), including the respiratory, skeletal, nervous system, cardiovascular, and gastrointestinal systems (Martins et al., 2009). Although disease manifestations include a wide spectrum of organ systems and severity, MPS I disease is often characterized into broad categories of severe and attenuated forms. Major disease manifestations span the spectrum in terms of severity and disease systems affected (Martins et al., 2009): They can include:

- Facial dysmorphism
- Mental retardation
- Multiple dysostosis multiplex (characteristic skeletal findings)
- Joint stiffness and contractures
- Short stature
- Corneal clouding
- Hearing loss
- Cardiomyopathy and valvular compromise
- Hepatosplenomegaly
- Respiratory insufficiency and recurrent respiratory infections

Although Hurler syndrome was first described in 1919 and Scheie syndrome was later described in 1962, the natural history of MPS I is still being defined. The MPS I Registry was established in 2003 and currently there are over 1000 patients enrolled under more than 180 participating investigators. It is a voluntary international database designed to collect observational data, with the goal of both further delineating the natural history of both the severe and attenuated forms of the disease as well as treatment outcomes. Seven papers describing data from the MPS I Registry have been published thus far.

Without treatment, patients with the most severe form of the disease have a median survival of 6.8 years (Moore et al., 2008). Patients with the more attenuated form of the disease may live to adolescence or adulthood without treatment, but with significant morbidity (Thomas et al., 2010). Aldurazyme (laronidase) is an enzyme replacement therapy that received FDA approval in 2003 (see Appendix C for full prescribing information). Aldurazyme is indicated for patients with Hurler and and Hurler-Scheie forms of Mucopolysaccharidosis I (MPS I) and for patients with the Scheie form who have moderate to severe symptoms. Further information will be provided upon request.

POMPE DISEASE AND EN□YME REPLACEMENT THERAPY WITH MYO□YME OR LUMI□YME

Pompe disease is an autosomal recessive storage disorder that results from a deficiency in the activity of acid alpha-glucosidase. This leads to lysosomal accumulation of glycogen in multiple cell types, but most predominately in the muscle. The proximal muscles, the paraspinal muscles and the diaphragm are affected in the majority of older patients (Kishani et al., 2006); additionally the cardiac muscle is affected in infants (Hirshhorn et al., 2001; Kishani et al., 2006).

Pompe disease occurs at an estimated incidence of 1 in 40,000- 146,000 (Meikle et al., 1999; Poorthuis et al., 1999 ; Martiniuk et al., 1998; Ausems et al., 1999) and a prevalence in the United States of < 2,000 identified patients. Although the symptoms of Pompe disease may manifest at any age, there are two main sub-types of Pompe disease: the rapidly progressive infantile-onset type and the more slowly progressing late-onset type (Hirschhorn et al., 2001).

- Infantile-onset type: symptoms appear within the first few months of life and include feeding difficulties, poor weight gain, respiratory problems, profound muscle weakness, hearing loss and ‘floppy baby’ appearance (Hirshhorn et al., 2001). The disease progresses rapidly with infants manifesting progressive
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cardiomyopathy that ultimately results in death from cardiorespiratory failure before one year of age (Kishnani et al.; 2004; Kishnani et al.; 2006).

- Late-onset type: symptoms can appear between the first and sixth decade of life and may include difficulty with running, climbing stairs, rising from a chair, breathing problems, and excessive fatigue (Hagemans et al., 2005(a). The late-onset form of the disease progresses at a variable rate but considerably slower than the infantile form. Over time the progressive limb-girdle muscle weakness and respiratory involvement lead to wheelchair and/or ventilator dependence (Hagemans et al., 2006; Winkel et al., 2005; van der Beek et al., 2009). The most common cause of death is respiratory insufficiency (Wokke et al., 2008; Winkel et al., 2005; Hagemans et al., 2005(b)), with the age of death varying from early childhood to late adulthood (Hagemanns et al., 2004).

Although Pompe disease was first described by a Dutch pathologist J.C. Pompe in 1932, the natural history is still being defined. The Pompe Registry, a voluntary international database was established in 2004. Currently there are over 1000 patients enrolled under more than 170 investigators to enter observational data, with the goal of both further delineating the natural history of all types of Pompe disease as well as treatment outcomes. Two registry papers have been published thus far.

Presently two different enzyme replacement therapies are available for Pompe disease: Myozyme (aglucosidase alfa produced at the 160 L scale) and Lumizyme (aglucosidase alfa produced at the 4000 L scale). Myozyme and Lumizyme are two different products and should be prescribed according to their respective indications:

- Myozyme is indicated for use in patients with Pompe disease (GAA deficiency). Myozyme has shown to improve ventilator-free survival in patients with infantile-onset Pompe disease as compared to an untreated historical control. The use of Myozyme in patients with other forms of Pompe disease has not been adequately studied to assure safety and efficacy. FDA approval for this indication was granted on April 28, 2006 (see Appendix D for full prescribing information).

- Lumizyme (alglucosidase alfa) is a lysosomal glycogen-specific enzyme indicated for patients 8 years and older with late (non-infantile) onset Pompe disease (GAA deficiency) who do not have evidence of cardiac hypertrophy. The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients, or in late (non-infantile) onset patients less than 8 years of age. Lumizyme received FDA approval in 2010 (see Appendix E for full prescribing information).

Further information will be provided upon request.

APPENDI

APPENDIX A: PACKAGE INSERT FOR FABRAZYME® (AGALSIDASE BETA)

See separate PDF attachment

APPENDIX B: PACKAGE INSERT FOR CEREZYME® (IMIGLUCERASE)

See separate PDF attachment

APPENDIX C : PACKAGE INSERT FOR ALDURAZYME® (LARONIDASE)

See separate PDF attachment

APPENDIX D : PACKAGE INSERT FOR MYOZYME® (ALGLUCOSIDASE ALFA)

See separate PDF attachment

APPENDIX E : PACKAGE INSERT FOR LUMIZYME® (ALGLUCOSIDASE ALFA)

See separate PDF attachment

APPENDIX F: Billing and ICD-9 Codes

Product	Manufacturer	HCPCS
Cerezyme® (imiglucerase for injection)	Genzyme	J1786 Injection, imiglucerase, 10 units
Fabrazyme® (agalsidase beta)	Genzyme	J0180 Injection agalsidase beta, per 1 mg
Aldurazyme® (laronidase)	Genzyme	J1931 Injection laronidase per .1 mg
Lumizyme® (alglucosidase alfa)	Genzyme	J0221Lumizyme injection per 10 mg
Myozyme® (alglucosidase alfa)	Genzyme	J0220 Alglucosidase alfa Injection per 10 mg
ELELYSO™ (taliglucerase alfa)	Pfizer	J3490 Unclassified Drug or J3590 Unclassified Biologic
Naglazyme® (galsulfase)	BioMarin	J1458 Injection, galsulfase, per 1 mg
ELAPRASE® (idursulfase)	Shire	J1743 Idursulfase Injection 1mg
VPRIV (velaflucerase alfa)	Shire	J3385 Injection velaglucerase alfa, per 100 units

Current Procedural Terminology (CPT) codes used when administering enzyme replacement therapy via intravenous infusion:

- **CPT 96365** Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
- **CPT 96366** Intravenous infusion, for therapy, prophylaxis, or diagnosis; each additional hour

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Revised 8/7/12

Enzyme Replacement Therapy - Gaucher's Disease

Question:

What should the HERC determine about placement on the Prioritized List for enzyme replacement therapy for Gaucher's Disease?

Clinical Background:

Gaucher disease is characterized by a deficiency of ß-glucocerebrosidase activity, resulting in accumulation of glucocerebroside in tissue macrophages which become engorged and are typically found in the liver, spleen, and bone marrow and occasionally in lung, kidney, and intestine. Secondary hematologic sequelae include severe anemia and thrombocytopenia in addition to the characteristic progressive hepatosplenomegaly, skeletal complications, including osteonecrosis and osteopenia with secondary pathological fractures.

Gaucher's disease has three common clinical subtypes.

- Type I (or non-neuropathic type) is the most common form of the disease. Symptoms may begin early in life or in adulthood and include enlarged liver and grossly enlarged spleen. Skeletal weakness and bone disease may be extensive. Spleen enlargement and bone marrow replacement cause anemia, thrombocytopenia and leukopenia. The brain is not affected pathologically, but there may be lung and, rarely, kidney impairment. Depending on disease onset and severity, type 1 patients may live well into adulthood. Many patients have a mild form of the disease or may not show any symptoms.
- Type II (or acute infantile neuropathic Gaucher's disease) typically begins within 6 months of birth and has an incidence rate of approximately 1 in 100,000 live births. Symptoms include an enlarged liver and spleen, extensive and progressive brain damage, eye movement disorders, spasticity, seizures, limb rigidity, and a poor ability to suck and swallow. Affected children usually die by age 2.
- Type III (the chronic neuropathic form) can begin at any time in childhood or even in adulthood. It is characterized by slowly progressive but milder neurologic symptoms compared to the acute or type 2 version. Major symptoms include an enlarged spleen and/or liver, seizures, poor coordination, skeletal irregularities, eye movement disorders, blood disorders including anemia and respiratory problems. Patients often live into their early teen years and adulthood.

For type 1 and most type 3 patients, enzyme replacement treatment with intravenous recombinant glucocerebrosidase (imiglucerase) can dramatically decrease liver and spleen size, reduce skeletal abnormalities, and reverse other manifestations. Due to the low incidence, this has become an orphan drug in many countries, meaning that a government recognizes and accommodates the financial constraints that limit research into drugs that address a small population. Velaglucerase alfa was approved by the Food and Drug Administration (FDA) as an alternative treatment in February 2010. In May 2012 the FDA approved an additional treatment – Taliglucerase alfa, or *Elelyso*.

Enzyme replacement therapy (ERT) for type 1 Gaucher disease is now available and includes imiglucerase (Cerezyme), velaglucerase alfa (VPRIV), and taliglucerase alfa (Elelyso). Most patients receive the recombinant enzyme imiglucerase. This preparation is highly effective in reversing the visceral and hematologic manifestations of Gaucher disease. However, skeletal disease is slow to respond, and pulmonary involvement is relatively resistant to the enzyme. No evidence shows that ERT results in neurologic improvement. Although the enzyme affects the visceral involvement in types 2 and 3 disease, the associated brain involvement may persist or progress.

Indications and Usage From the Cerezyme website

Cerezyme® (imiglucerase for injection) is an analogue of the human enzyme ß-glucocerebrosidase, produced by recombinant DNA technology. ß-Glucocerebrosidase (ß-D-glucosyl-N-acylsphingosine glucohydrolase, E.C. 3.2.1.45) is a lysosomal glycoprotein enzyme which catalyzes the hydrolysis of the glycolipid glucocerebroside to glucose and ceramide.

Cerezyme® (imiglucerase for injection), approved since 1994, is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of Type 1 Gaucher disease that results in one or more of the following conditions:

a. anemia

b. thrombocytopenia

c. bone disease

d. hepatomegaly or splenomegaly

Current Prioritized List Status

ICD 9 272.7 Lipoidosis

Line	Condition	Treatment
67	METABOLIC DISORDERS INCLUDING HYPERLIPIDEMIA	MEDICAL THERAPY
78	NEUROLOGICAL DYSFUNCTION IN BREATHING, EATING, SWALLOWING, BOWEL, OR BLADDER CONTROL CAUSED BY CHRONIC CONDITIONS	MEDICAL AND SURGICAL TREATMENT (EG. G-TUBES, J-TUBES, RESPIRATORS, TRACHEOSTOMY, UROLOGICAL PROCEDURES)
110	END STAGE RENAL DISEASE	RENAL TRANSPLANT
318	NEUROLOGICAL DYSFUNCTION IN POSTURE AND MOVEMENT CAUSED BY CHRONIC CONDITIONS	MEDICAL AND SURGICAL TREATMENT (EG. DURABLE MEDICAL EQUIPMENT AND ORTHOPEDIC PROCEDURE)
375	NEUROLOGICAL DYSFUNCTION IN COMMUNICATION CAUSED BY CHRONIC CONDITIONS	MEDICAL THERAPY
407	DYSFUNCTION RESULTING IN LOSS OF ABILITY TO MAXIMIZE LEVEL OF INDEPENDENCE IN SELF-DIRECTED CARE CAUSED BY CHRONIC CONDITIONS THAT CAUSE NEUROLOGICAL DYSFUNCTION	MEDICAL THERAPY (SHORT TERM REHABILITATION WITH DEFINED GOALS)
684	ENDOCRINE AND METABOLIC CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY	EVALUATION

ICD 10 E75.22 Gaucher disease

Code	Code Description	Current Placement
C9271	INJECTION, VELAGLUCERASE ALFA, 100 UNITS	DMAP Ancillary Codes File
J0205	INJECTION, ALGLUCERASE, PER 10 UNITS	DMAP Ancillary Codes File
J1785	INJECTION, IMIGLUCERASE, PER UNIT	DMAP Ancillary Codes File
J1786	INJECTION, IMIGLUCERASE, 10 UNITS	DMAP Ancillary Codes File
J3385	INJECTION, VELAGLUCERASE ALFA, 100 UNITS	DMAP Ancillary Codes File
S9357	HOME INFUSION THERAPY, ENZYME REPLACEMENT INTRAVENOUS THERAPY; (E.G. IMIGLUCERASE); ADMINISTRATIVE SERVICES, PROFESSIONAL PHARMACY SERVICES, CARE COORDINATION, AND ALL NECESSARY SUPPLIES AND EQUIPMENT (DRUGS AND NURSING VISITS CODED SEPARATELY), PER DIEM	67 METABOLIC DISORDERS INCLUDING HYPERLIPIDEMIA

Evidence summary

There is no currently available Cochrane review nor high quality randomized controlled trials on the use of imiglucerase in Gaucher's disease. The FDA approved velaglucerase alfa based on 3 clinical studies of 82 patients aged 4 and older. Studies appear to focus on primary endpoints of hemoglobin concentrations and not patient-oriented outcomes.

HERC Staff Recommendation

1. Place S9357 on Lines 264 GLYCOGENOSIS and Line 684 ENDOCRINE AND METABOLIC CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (as per modified guideline note).

Enzyme Replacement Therapy - Hunter's Disease

Question:

What should the HERC determine about coverage for enzyme replacement therapy for Hunter's Disease?

Current Prioritized List Status

Guideline Note 67 Enzyme Replacement Therapy
Line 684
Enzyme replacement therapy for Hunter's syndrome is included on this Line.

Clinical Background:

Hunter syndrome, or mucopolysaccharidosis Type II, is a lysosomal storage disease caused by a deficient (or absent) enzyme, iduronate-2-sulfatase (I2S). In Hunter syndrome, glycosaminoglycans (GAG) builds up in cells throughout the body due to a deficiency or absence of the enzyme iduronate-2-sulfatase (I2S). Physical manifestations for some people with Hunter syndrome include distinct facial features and large head. In some cases of Hunter syndrome, central nervous system involvement leads to developmental delays and nervous system problems. Not all people with Hunter syndrome are affected by the disease in exactly the same way, and the rate of symptom progression varies widely. However, Hunter syndrome is always severe, progressive, and life-limiting.

The continued storage of GAG in cells can lead to organs being affected in important ways. The thickening of the heart valves along with the walls of the heart can result in progressive decline in cardiac function. The walls of the airway may become thickened as well, leading to breathing problems while sleeping (obstructive airway disease). People with Hunter syndrome may also have limited lung capacity due to pulmonary involvement. As the liver and spleen grow larger with time, the belly may become distended, making hernias more noticeable. All major joints (including the wrists, elbows, shoulders, hips, and knees) may be affected by Hunter syndrome, leading to joint stiffness and limited motion. Progressive involvement of the finger and thumb joints results in decreased ability to pick up small objects. The effects on other joints, such as hips and knees, can make it increasingly difficult to walk normally. If carpal tunnel syndrome develops, a further decrease in hand function can occur. The bones themselves may be affected, resulting in short stature. In addition, pebbly, ivory-colored skin lesions may be found on the upper arms and legs and upper back of some people with Hunter syndrome. The presence or absence of the skin lesions is not helpful, however, in predicting clinical severity in Hunter syndrome. Finally, the storage of GAG in the brain can lead to delayed development with subsequent mental retardation. Many children with Hunter syndrome develop severe mental impairment and have life expectancies of 15 years or fewer.

On July 24, 2006, a synthetic version of I2S, called Elaprase (Idursulfase), was approved by the FDA as an enzyme replacement treatment for Hunter syndrome. Elaprase is a purified form of the lysosomal enzyme iduronate-2-sulfatase.

Indications and Usage From Idursulfase website

ELAPRASE IS INDICATED FOR PATIENTS WITH HUNTER SYNDROME. ELAPRASE HAS BEEN SHOWN TO IMPROVE WALKING CAPACITY IN THESE PATIENTS.

Risk of anaphylactic reactions: Life-threatening, anaphylactic reactions have been observed in some patients during ELAPRASE infusions. Therefore, appropriate medical support should be readily available when ELAPRASE is administered. Biphasic anaphylactic reactions have also been observed after ELAPRASE administration and patients who have experienced anaphylactic reactions may require prolonged observation. Patients with compromised respiratory function or acute respiratory disease may be at risk of serious acute exacerbation of their respiratory compromise due to infusion reactions, and require additional monitoring.

Evidence summary

daSilva, Cochrane systematic review, 2011

One study (96 patients) met the inclusion criteria, although the primary outcome of this review - z score for height and weight, was not assessed in the study. Following 53 weeks of treatment, patients in the weekly idursulfase 0.5 mg/kg group demonstrated a significant improvement rate compared with placebo for the primary outcome: distance walked in six minutes on the basis of the sum of ranks of change from baseline, mean difference 37.00 (95% confidence interval 6.52 to 67.48). Idursulfase was generally well tolerated, but infusion reactions did occur. Idursulfase antibodies were detected in 31.7% of patients at the end of the study and they were related to a smaller reduction in urine glycosaminoglycan levels.

The current evidence is limited. While the randomised clinical trial identified was considered to be of good quality, it failed to describe important outcomes. There is no available evidence in the included study and in the literature on outcomes such as improvement in growth, sleep apnea, cardiac function, quality of life and mortality. More studies are needed to obtain more information on the long-term effectiveness and safety of enzyme replacement therapy.

Summary

The evidence is extremely limited at this time for benefit and for clinically important outcomes

HERC Staff Recommendation

Make no change to modified Guideline Note 67.

Enzyme replacement therapy with idursulfase for mucopolysaccharidosis type II (Hunter syndrome) (Review)

da Silva EMK, da Silva EMK, Strufaldi MWL, Andriolo RB, Silva LA

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[Intervention Review]

Enzyme replacement therapy with idursulfase for mucopolysaccharidosis type II (Hunter syndrome)

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ABSTRACT

Background

Mucopolysaccharidosis II, also known as Hunter syndrome, is a rare, X-linked disease caused by a deficiency of the lysosomal enzyme iduronate-2-sulfatase, which catalyses a step in the catabolism of glycosaminoglycans. The glycosaminoglycans accumulate within tissues affecting multiple organs and physiologic systems. The clinical manifestations include neurologic involvement, severe airways obstruction, skeletal deformities and cardiomyopathy. The disease has a variable age of onset and variable rate of progression. In those with severe disease, death usually occurs in the second decade of life, whereas those patients with less severe disease may survive into adulthood. Enzyme replacement therapy with intravenous infusions of idursulfase has emerged as a new treatment for mucopolysaccharidosis type II.

Objectives

To evaluate the effectiveness and safety of enzyme replacement therapy with idursulfase compared to other interventions, placebo or no intervention, for treating mucopolysaccharidosis type II.

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group's Trials Register (date of last search 01 September 2011).

We also searched EMBASE, PubMed and the Literature Latino-Americana e do Caribe em Ciências da Saúde (LILACS) (date of last search October 2009).

Selection criteria

Randomised and quasi-randomised controlled trials of enzyme replacement therapy with idursulfase compared to no intervention, placebo or other options (e.g. behavioral strategies, transplantation).

Data collection and analysis

Two authors independently screened the trials identified, appraised quality of papers and extracted data.

Main results

One study (96 patients) met the inclusion criteria, although the primary outcome of this review - z score for height and weight, was not assessed in the study. Following 53 weeks of treatment, patients in the weekly idursulfase 0.5 mg/kg group demonstrated a significant improvement rate compared with placebo for the primary outcome: distance walked in six minutes on the basis of the sum of ranks of change from baseline, mean difference 37.00 (95% confidence interval 6.52 to 67.48). The every-other-week idursulfase 0.5 mg/kg group also showed an improvement, which was not significant compared with placebo, mean difference 23.00 (95% confidence interval -4.49 to 50.49). After 53 weeks, there was no statistical significance difference in per cent predicted forced vital capacity between the three groups and absolute forced vital capacity was significantly increased from baseline in the weekly dosing group compared to placebo, mean difference 0.16 (95% confidence interval CI 0.05 to 0.27). No difference was observed between the every-other-week idursulfase 0.5 mg/kg group and placebo.

In addition, liver and spleen volumes and urine glycosaminoglycan excretion were significantly reduced from baseline by both idursulfase dosing regimens. Idursulfase was generally well tolerated, but infusion reactions did occur. Idursulfase antibodies were detected in 31.7% of patients at the end of the study and they were related to a smaller reduction in urine glycosaminoglycan levels.

Authors' conclusions

The current evidence is limited. While the randomised clinical trial identified was considered to be of good quality, it failed to describe important outcomes. It has been demonstrated that enzyme replacement therapy with idursulfase is effective in relation to functional capacity (distance walked in six minutes and forced vital capacity), liver and spleen volumes and urine glycosaminoglycan excretion in patients with mucopolysaccharidosis type II compared with placebo. There is no available evidence in the included study and in the literature on outcomes such as improvement in growth, sleep apnoea, cardiac function, quality of life and mortality. More studies are needed to obtain more information on the long-term effectiveness and safety of enzyme replacement therapy.

PLAIN LANGUAGE SUMMARY

Enzyme replacement therapy with idursulfase for mucopolysaccharidosis type II (Hunter syndrome)

Hunter syndrome or mucopolysaccharidosis II is a rare genetic disease that occurs when an enzyme that the body needs is either missing or malfunctioning. The body doesn't have adequate supplies of this enzyme to break down certain complex molecules, so these molecules build up in harmful amounts in certain cells and tissues. The build-up that occurs in Hunter syndrome eventually causes permanent, progressive damage affecting appearance, mental development, organ function and physical abilities. Hunter syndrome appears in children as young as the age of two years and it nearly always occurs in males. In the past, treatment of Hunter syndrome has been limited to the relief of symptoms and complications. Enzyme replacement therapy with idursulfase aims to replace iduronate-2-sulfatase, the enzyme that is deficient or absent in people with Hunter syndrome. However, given its high cost it is essential to assess how effective and safe this treatment is. Current evidence is limited because there was only one randomised clinical trial found in the medical literature. Compared with placebo, enzyme replacement therapy with idursulfase in people with Hunter syndrome, led to some improvement in the patients' ability to walk and a reduction in the excretion of abnormal mucopolysaccharides in the urine. To date there is no evidence available in the literature showing that treatment reduces complications of the disease related to quality of life and mortality.

BACKGROUND

Description of the condition

Mucopolysaccharidosis II (MPS II or Hunter syndrome) belongs to a group of inherited diseases of glycosaminoglycan (GAG) catabolism called mucopolysaccharidoses. The GAGs are oligosaccharide components of the proteoglycans, macromolecules responsible for the integrity and function of connective tissue. Mucopolysaccharidoses are caused by a lysosomal enzyme deficiency for the stepwise degradation of the GAGs. All of the mucopolysac-

Revised 8/7/12

Enzyme replacement Therapy - Pompe's Disease

Question:

What should the HERC determine about placement on the Prioritized List for enzyme replacement therapy for Pompe's Disease?

Clinical Background:

Pompe disease is a rare inherited and often fatal disorder that disables the heart and skeletal muscles. It is caused by mutations in a gene that makes an enzyme called acid alpha-glucosidase (GAA). Normally, the body uses GAA to break down glycogen, a stored form of sugar used for energy. In Pompe disease, mutations in the GAA gene reduce or completely eliminate this essential enzyme. Excessive amounts of lysosomal glycogen accumulate everywhere in the body, but the cells of the heart and skeletal muscles are the most seriously affected. The severity of the disease and the age of onset are related to the degree of enzyme deficiency**.**

Early onset (or infantile form) is the result of complete or near complete deficiency of GAA. Symptoms begin in the first months of life, with feeding problems, poor weight gain, muscle weakness, floppiness, and head lag. Most babies die from cardiac or respiratory complications before their first birthday.

Late onset (or juvenile/adult) Pompe disease is the result of a partial deficiency of GAA. The onset can be as early as the first decade of childhood or as late as the sixth decade of adulthood. The primary symptom is muscle weakness progressing to respiratory weakness and death from respiratory failure after a course lasting several years. The heart is usually not involved.

A drug called alglucosidase alfa (Myozyme©), has received FDA approval for the treatment of infants and children with Pompe disease. Another algluosidase alfa drug, Lumizyme©, has been approved for late-onset (non-infantile) Pompe disease.

Codes

ICD 9 271.0 Glycogenosis

ICD 10 E74.02 Pompe Disease

Current Placement

Line	Condition	Treatment
78	NEUROLOGICAL DYSFUNCTION IN BREATHING, EATING, SWALLOWING, BOWEL, OR BLADDER CONTROL CAUSED BY CHRONIC CONDITIONS	MEDICAL AND SURGICAL TREATMENT (EG. G-TUBES, J-TUBES, RESPIRATORS, TRACHEOSTOMY, UROLOGICAL PROCEDURES)
255	ACUTE AND SUBACUTE NECROSIS OF LIVER; SPECIFIED INBORN ERRORS OF METABOLISM (EG. MAPLE SYRUP URINE DISEASE, TYROSINEMIA)	LIVER TRANSPLANT
264	GLYCOGENOSIS	MEDICAL THERAPY
318	NEUROLOGICAL DYSFUNCTION IN POSTURE AND MOVEMENT CAUSED BY CHRONIC CONDITIONS	MEDICAL AND SURGICAL TREATMENT (EG. DURABLE MEDICAL EQUIPMENT AND ORTHOPEDIC PROCEDURE)
375	NEUROLOGICAL DYSFUNCTION IN COMMUNICATION CAUSED BY CHRONIC CONDITIONS	MEDICAL THERAPY
407	DYSFUNCTION RESULTING IN LOSS OF ABILITY TO MAXIMIZE LEVEL OF INDEPENDENCE IN SELF-DIRECTED CARE CAUSED BY CHRONIC CONDITIONS THAT CAUSE NEUROLOGICAL DYSFUNCTION	MEDICAL THERAPY (SHORT TERM REHABILITATION WITH DEFINED GOALS)

Indications and Usage From the Myozyme website

MYOZYME (alglucosidase alfa) is a lysosomal glycogen-specific enzyme indicated for use in patients with Pompe disease (GAA deficiency). MYOZYME has been shown to improve ventilator-free survival in patients with infantile-onset Pompe disease as compared to an untreated historical control, whereas use of MYOZYME in patients with other forms of Pompe disease has not been adequately studied to assure safety and efficacy.

Life-threatening anaphylactic reactions, severe allergic reactions and immune mediated reactions have been observed in some patients during MYOZYME infusions. Therefore, appropriate medical support should be readily available when MYOZYME is administered.
Risk of Cardiorespiratory Failure Patients with compromised cardiac or respiratory function may be at risk of serious acute exacerbation of their cardiac or respiratory compromise due to infusion reactions, and require additional monitoring.

Indications and Usage From the Lumizyme website

LUMIZYME (alglucosidase alfa) is a lysosomal glycogen-specific enzyme indicated for patients 8 years and older with late (non-infantile) onset Pompe disease (GAA

deficiency) who do not have evidence of cardiac hypertrophy. The safety and efficacy of LUMIZYME have not been evaluated in controlled clinical trials in infantile-onset patients, or in late (non-infantile) onset patients less than 8 years of age.

Life-threatening anaphylactic reactions, severe allergic reactions and immune mediated reactions have been observed in some patients during LUMIZYME infusions. Therefore, appropriate medical support should be readily available when LUMIZYME is administered.

Because of the potential risk of rapid disease progression in Pompe disease patients less than 8 years of age, LUMIZYME is available only through a restricted distribution program called the LUMIZYME ACE Program. Only prescribers and healthcare facilities enrolled in the program may prescribe, dispense or administer LUMIZYME. LUMIZYME may be administered only to patients who are enrolled in and meet all the conditions of the LUMIZYME ACE Program.

Evidence summary

There is no currently available Cochrane review on the use of alglucosidase alfa in Pompe's disease.

CEDAC FINAL RECOMMENDATION, ALGLUCOSIDASE ALFA, 2009

> The Canadian Expert Drug Advisory Committee (CEDAC) recommends that alglucosidase alfa be listed in patients with infantile-onset Pompe disease, as demonstrated by onset of symptoms and confirmed cardiomyopathy within the first 12 months of life. The Committee further recommends that drug plans develop specific criteria for monitoring and stopping alglucosidase, in consultation with experts in the management of lysosomal storage diseases.
>
> Information from uncontrolled trials in patients with infantile–onset Pompe disease indicate that alglucosidase alfa significantly improves survival in comparison to historical controls who did not receive enzyme replacement therapy. There is insufficient evidence to evaluate the effectiveness and safety of alglucosidase alfa in other forms of Pompe disease.

Van der Ploeg et al, NEJM, 2010

> Ninety patients who were 8 years of age or older, ambulatory, and free of invasive ventilation were randomly assigned to receive biweekly intravenous alglucosidase alfa (20 mg per kilogram of body weight) or placebo for 78 weeks at eight centers in the United States and Europe. The two primary end points were distance walked during a 6-minute walk test and percentage of predicted forced vital capacity (FVC). In this study population, treatment with alglucosidase alfa was associated with improved walking distance and stabilization of pulmonary function over an 18-month period.

Chien et al, Pediatrics, 2009

> The 6 infants with Pompe disease identified by our newborn screening pilot program had uniformly positive responses, including normalization of cardiac size and normal growth and motor development at 14 -32 months, to treatment with alglucosidase alfa.

HERC Staff Recommendation

1. Add ICD 9 271.0 *Glycogenosis* (and ICD 10 E74.02 *Pompe Disease*) to Line 684 ENDOCRINE AND METABOLIC CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY for inclusion of enzyme replacement therapy late onset Pompe's disease. Revise guideline for to include ERT for children with infantile onset Pompe's disease on Line 264.

Alglucosidase alfa

Product:
ALGLUCOSIDASE ALFA
(Myozyme®) 50 mg/vial injection

Class of drugs:
Enzyme replacement therapy

Indication: Treatment of Pompe disease (lysosomal glycogen storage disease type II [GSD II])

Manufacturer: Genzyme Canada Inc.

CED Recommendation

The CED recommended that alglucosidase alfa (Myozyme) be funded through the Ontario Public Drug Programs via the Exceptional Access Program for the treatment of infantile/early onset Pompe disease, according to specific criteria. The Committee acknowledged that Pompe disease is rare and it is difficult to generate adequate data to clearly demonstrate clinical benefit and value for money. In the absence of a pan-Canadian policy for drugs for rare diseases, the CED's recommendation was made on the basis of the high fatality rate in untreated infants with early onset disease, the reported early survival benefits and reduction in ventilator dependence observed in the limited clinical trials, coupled with the lack of treatment options available.

The CED also reviewed the available evidence for adult/late onset Pompe disease and recommended no reimbursement. When the initial review for alglucosidase alfa (Myozyme) for the treatment of infantile and adult/late onset was done, the Drugs for Rare Diseases (DRD) evaluation framework was not in place.

After the DRD evaluation framework was developed, the adult/late onset indication was reviewed under the DRD evaluation framework. For additional information on the review and reimbursement guidelines for the adult/late onset indication, please see:
http://www.health.gov.on.ca/english/providers/program/drugs/pdf/myozyme_reimbursement_adult.pdf

For additional information on the review and reimbursement guidelines for the infantile/early onset indication, please see:
http://www.health.gov.on.ca/english/providers/program/drugs/pdf/myozyme_reimbursement_infantile.pdf

Executive Officer Decision

Based on the CED's recommendation the Executive Officer decided to fund alglucosidase alfa (Myozyme) through the Ontario Public Drug Programs via the Exceptional Access Program for the treatment of infantile/early Pompe disease, according to specific criteria.

Status

Funding is available through the Exceptional Access Program according to specific criteria.

For further information, please see
http://www.health.gov.on.ca/english/providers/program/drugs/eap_criteria.html

Highlights of Recommendation:

- The Committee noted that the evidence submitted for infantile/early onset Pompe disease does not meet conventional standards for public drug funding reviews, but acknowledges that the rarity of the disease makes it difficult to produce strong clinical evidence and value for money. The observed survival benefits and reduction in ventilator dependence seen in the small numbers of infant patients who have received treatment is compelling.
- Long term evidence is required to evaluate the true clinical benefit, safety profile, and quality of life improvements for this product.
- Treatment with this product is very expensive, with an estimated a cost of $155,000 per year for a child with infantile/early onset disease. A full cost analysis was not provided by the manufacturer; therefore value for money of this product could not be determined by the Committee.
- The available information for adult/late onset Pompe disease was also reviewed. The Committee noted the available evidence in this population was more immature and difficult to interpret; therefore, recommended against reimbursement. At the time the initial review was done for the adult/late onset indication, Ontario's DRD evaluation framework was not in place. After the DRD evaluation framework had been established, this indication was reviewed through the DRD evaluation framework where funding was recommended, according to specific criteria.

continued...

- **Overall, the Committee acknowledged that Pompe disease is a rare disease and therefore difficult to produce adequate data to demonstrate clinical benefit and value for money. In the absence of a pan-Canadian policy for drugs for rare diseases, given the high fatality rate in untreated infants with early onset disease, the lack of treatment options, and the compelling survival benefits and reduction in ventilator dependence observed in the limited clinical trials data available, the Committee recommended that alglucosidase alfa (Myozyme) not be approved for listing in the Formulary/CDI but be considered for reimbursement on an Exceptional Access basis according to specific criteria for infant/early onset Pompe Disease.**

Background:

Pompe disease (lysosomal glycogenstorage disease type II [GSD II]) is caused by the buildup of excess amounts of glycogen in the muscles including the heart. Glycogen is a form of stored carbohydrate that is used by muscles as an energy source. Patients with Pompe disease are lacking an enzyme that is needed to break down and convert glycogen to sugars that can be used properly by muscle tissue.

Pompe disease is rare. The predominant form of Pompe disease affects adults and results in gradual muscle weakness often leading over many years to ventilator-dependency for breathing later in life. The heart is typically not consistently affected in patients with adult/late onset of the disease. The less common but more severe form affects infants and can be diagnosed as early as several weeks after birth and almost always affects the heart muscle. Most cases of infantile/early onset Pompe disease result in death before the age of 18 months due to heart failure.

There is no standard treatment for Pompe disease at this time; current treatments are generally supportive in nature, assisting with breathing and heart problems and providing nutritional supplementation. Alglucosidase alfa (Myozyme) is an enzyme replacement therapy to provide patients with the missing enzyme.

Infants with Pompe disease may require lifelong treatment with alglucosidase alfa (Myozyme). Due to the rare nature of this disease and the very high likelihood of death in the infantile-onset type, it is difficult to know the long-term effects of the drug and whether or not treatment will produce a normal lifespan or reduce long-term outcomes.

Detailed Discussion:

- The manufacturer, Genzyme Canada Inc., asked the Ministry of Health and Long-Term Care to list alglucosidase alfa (Myozyme) on the Ontario Drug Benefit Formulary. Due to the high fatality rate in infantile onset type Pompe disease and the promising results in small groups of patients, the Committee approved the drug for Rapid Review. At that time, Ontario's DRD Evaluation Framework had not been established.
- The CED first reviewed alglucosidase alfa (Myozyme) for reimbursement consideration in December 2006. During this review, the Committee reviewed two trials related to infantile/early onset disease.
- Study AGLU01602 was an open label study of 18 patients less than six months of age with a historical control group. Although the trial had a few number of patients and was short in duration, the Committee found the evidence compelling in terms of improvement in survival and reduction in ventilator dependence. However, because the data available was short term, the Committee questioned how long the benefits of alglucosidase alfa (Myozyme) treatment could be maintained. It was further noted that alglucosidase alfa (Myozyme) does not cross the blood brain barrier and the Committee questioned whether long-term treatment in young patients will be curative or simply slow the progression of disease.
- Study AGLU01702 was an open label study of 21 patients between 6 months to 36 months of age. This study showed evidence of improvement in cardiac function, particularly in those patients who were less affected from a motor perspective. The data for survival in this group was not as well established as for the early infantile form; however there was an improvement in survival and fewer than expected children required ventilator support.
- The most common adverse effects to alglucosidase alfa (Myozyme) are hypersensitivity reactions which have ranged in severity from mild to life-threatening, including anaphylaxis.

continued...

- No formal pharmacoeconomic analysis was submitted by the manufacturer; therefore, value for money could not be determined.
- Treatment is very expensive with alglucosidase alfa (Myozyme) with an estimated a cost of $155,000 per year for a child with infantile/early onset disease (*assuming 17.5 kg body weight*). A full cost analysis was not provided by the manufacturer; therefore value for money of this product could not be determined by the Committee. The budgetary impact was difficult to predict. The Committee noted that diagnoses of Pompe disease may increase with the availability of active treatment and better screening for the disease.
- After a review of the clinical and economic evidence, the Committee noted that alglucosidase alfa (Myozyme) did not meet the conventional criteria for value for money. However, given the invariable risk of death in the first 12-18 months in the untreated infantile/early onset population, the evidence for benefit due to alglucosidase alfa (Myozyme) in this population is compelling. It was also noted that the evidence provided is from small, short term trials and longer term data is required in order to understand impact on disease and patient quality of life.
- In light of the policy and evidentiary issues highlighted by the CED, a subcommittee of clinicians including an expert in metabolic disease and genetics was convened in February 2007. The mandate of this subcommittee was to identify a niche population where reimbursement of alglucosidase alfa (Myozyme) therapy might be clinically beneficial.
- Upon review of the available evidence, and in consultation with several clinical experts from across the country, the subcommittee recommended start and stop criteria for endorsement by the CED.
- In June 2007, the CED reviewed and endorsed the subcommittee's recommendation on funding criteria for alglucosidase in the treatment of infantile/early onset Pompe Disease *(i.e. onset of generalized weakness before 12 months of age*). In the absence of a pan-Canadian policy for drugs for rare diseases, the CED's recommendation to fund treatment was based on the high fatality rate in untreated infants with infantile/early onset disease, the lack of treatment options available, and the compelling survival benefits and reduction in ventilator dependence observed in the limited clinical trial evidence.

CEDAC Recommendation:

(http://www.cadth.ca/index.php/en/cdr/recommendations)

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that alglucosidase alfa (Myozyme) be listed in patients with infantile-onset Pompe disease, as demonstrated by onset of symptoms and confirmed cardiomyopathy within the first 12 months of life. The CEDAC also recommended that drug plans develop specific criteria for monitoring and stopping alglucosidase alfa (Myozyme), in consultation with experts in the management of lysosomal storage diseases.

In September 2007, the Advisory Committee on Pharmaceuticals (ACP) supported the incorporation of Ontario's funding criteria when jurisdictions implement the CEDAC recommendation.

Ontario

Ministry of
Health and Long-Term Care
Ontario Public Drug Programs

For more information, please contact:

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or click: http://www.health.gov.on.ca/english/providers/program/drugs/ced_rec_table.html

ORIGINAL ARTICLE

A Randomized Study of Alglucosidase Alfa in Late-Onset Pompe's Disease

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ABSTRACT

BACKGROUND

Pompe's disease is a metabolic myopathy caused by a deficiency of acid alpha glucosidase (GAA), an enzyme that degrades lysosomal glycogen. Late-onset Pompe's disease is characterized by progressive muscle weakness and loss of respiratory function, leading to early death. We conducted a randomized, placebo-controlled trial of alglucosidase alfa, a recombinant human GAA, for the treatment of late-onset Pompe's disease.

METHODS

Ninety patients who were 8 years of age or older, ambulatory, and free of invasive ventilation were randomly assigned to receive biweekly intravenous alglucosidase alfa (20 mg per kilogram of body weight) or placebo for 78 weeks at eight centers in the United States and Europe. The two primary end points were distance walked during a 6-minute walk test and percentage of predicted forced vital capacity (FVC).

RESULTS

At 78 weeks, the estimated mean changes from baseline in the primary end points favored alglucosidase alfa (an increase of 28.1±13.1 m on the 6-minute walk test and an absolute increase of 3.4±1.2 percentage points in FVC; $P=0.03$ and $P=0.006$, respectively). Similar proportions of patients in the two groups had adverse events, serious adverse events, and infusion-associated reactions; events that occurred only in patients who received the active study drug included anaphylactic reactions and infusion-associated reactions of urticaria, flushing, hyperhidrosis, chest discomfort, vomiting, and increased blood pressure (each of which occurred in 5 to 8% of the patients).

CONCLUSIONS

In this study population, treatment with alglucosidase alfa was associated with improved walking distance and stabilization of pulmonary function over an 18-month period. (ClinicalTrials.gov number, NCT00158600.)

From the Departments of Pediatrics, Internal Medicine, Clinical Genetics, Neurology, and Hospital Pharmacy, Center for Lysosomal and Metabolic Diseases, Erasmus MC University Medical Center, Rotterdam, the Netherlands (A.T.P., C.I.C., N.A.B.); the Department of Neurology, University of Pittsburgh, and Neurology Service, Department of Veterans Affairs Medical Center, Pittsburgh (P.R.C., S.A.Z.); Genzyme, Cambridge, MA (D.C., G.J.G., S.L.L., C.M., A.S.); the Department of Neurology–Center for Genetic Medicine, Children's National Medical Center, Washington, DC (D.M.E., R.T.L., J.E.M.); the Department of Neurology, Washington University School of Medicine, St. Louis (J.F., K.N., A.P.); Centre de Référence Pathologie Neuromusculaire Paris-Est, Hôpital Pitié–Salpêtrière, Assistance Publique–Hôpitaux de Paris, Paris (S.H., P.L.); the Department of Pediatrics, Division of Medical Genetics, Duke University Medical Center, Durham, NC (P.S.K.); the Department of Genetics and Genomic Sciences, Mount Sinai School of Medicine, New York (D.J.L., M.W.); and Tower Hematology Oncology, Beverly Hills, CA (D.J.P., B.R.). Address reprint requests to Dr. van der Ploeg at the Department of Pediatrics, Division of Metabolic Diseases and Genetics, Center for Lysosomal and Metabolic Diseases, Erasmus MC University Medical Center, Dr. Molewaterplein 60, 3015 GJ Rotterdam, the Netherlands, or at a.vanderploeg@erasmusmc.nl.

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Pompe Disease in Infants: Improving the Prognosis by Newborn Screening and Early Treatment

Yin-Hsiu Chien, Ni-Chung Lee, Beth L. Thurberg, Shu-Chuan Chiang, Xiaokui Kate Zhang, Joan Keutzer, Ai-Chu Huang, Mei-Hwan Wu, Pei-Hsin Huang, Fuu-Jen Tsai, Yuan-Tsong Chen and Wuh-Liang Hwu

Pediatrics 2009;124;e1116
DOI: 10.1542/peds.2008-3667

Pompe Disease in Infants: Improving the Prognosis by Newborn Screening and Early Treatment

WHAT'S KNOWN ON THIS SUBJECT: Newborn screening program is now technically feasible in ultrarare diseases and can successfully identify patients with Pompe disease before symptoms have progressed to the point where they would be likely to be identified through routine pediatric care.

WHAT THIS STUDY ADDS: This is the first report of improved clinical outcomes in patients with Pompe disease who were identified by a national newborn-screening program and were treated before the onset of clinically recognizable symptoms of Pompe disease.

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KEY WORDS

inborn errors of metabolism, neuromuscular disorders, newborn screening, outcome, treatment

ABBREVIATIONS

GAA—acid α-glucosidase
rhGAA—recombinant human acid α-glucosidase
CRIM—cross-reactive immunologic material
DBS—dried blood spot
NTUH—National Taiwan University Hospital
NAG—neutral glucosidase
CXR—chest radiograph
ECG—electrocardiogram
CK—creatinine kinase
BNP—b-type natriuretic peptide
LVMI—left ventricular mass index
PAS—periodic acid-Schiff
H&E—hematoxylin and eosin
AIMS—Alberta Infant Motor Scales
PDMS-II—Peabody Developmental Motor Scales, Second Edition

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FINANCIAL DISCLOSURE: *Drs Thurberg, Zhang, and Keutzer are full-time employees of Genzyme Corporation; Dr Chien has received honoraria and research grant funding from Genzyme; Dr Chen has received research grant funding from and serves as a consultant for Genzyme; Dr Hwu has received honoraria, travel funding, and research grant funding from and serves on an advisory board for Genzyme. The other authors have indicated they have no financial relationships relevant to this article to disclose.*

abstract

OBJECTIVE: Pompe disease causes progressive, debilitating, and often life-threatening musculoskeletal, respiratory, and cardiac symptoms. Favorable outcomes with early intravenous enzyme-replacement therapy and alglucosidase alfa have been reported, but early clinical diagnosis before the development of severe symptoms has rarely been possible in infants.

METHODS: We recently conducted a newborn screening pilot program in Taiwan to improve the early detection of Pompe disease. Six of 206 088 newborns screened tested positive and were treated for Pompe disease. Five had the rapidly progressive form of Pompe disease, characterized by cardiac and motor involvement, and were treated soon after diagnosis. The sixth patient was started on treatment at 14 months of age because of progressive muscle weakness. Outcomes were compared with treated patients whose disease was diagnosed clinically and with untreated historical control subjects.

RESULTS: At the time of this report, patients had been treated for 14 to 32 months. The 5 infants who had early cardiac involvement demonstrated normalization of cardiac size and muscle pathology with normal physical growth and age-appropriate gains in motor development. The infant without cardiac involvement also achieved normal motor development with treatment. Survival in patients who had newborn screening was significantly improved compared with those in the untreated reference cohort ($P = .001$). Survival in the treated clinical comparators was reduced but not statistically different from that in the newborn screening group ($P = .48$).

CONCLUSIONS: Results from this study indicate that early treatment can benefit infants with Pompe disease and highlight the advantages of early diagnosis, which can be achieved by newborn screening. *Pediatrics* 2009;124:e1116–e1125

Revised 8/7/12

Enzyme replacement therapy guideline clarification

Question: How should Guideline Note 67 be modified to better demonstrate HERC intent regarding enzyme replacement therapy?

Question Source: VbBS, and HERC Staff

Issue:
At the June VBBS meeting there was a discussion raised about enzyme replacement therapy guideline, specifically in the contest of treatment of Fabry's disease. Coffman discussed the current guideline note 67 which refers to enzyme replacement therapies but only specifically calls out Hunter's disease; however, other ICD-9 codes (including for Fabry's disease) were included on this line, with the intent that future applications of enzyme replacement therapy would need to be individually reviewed (with automatic mapping to Line 684), and decided upon. It was agreed the guideline needed to be clarified further, to better demonstrate HERC intent.

When Guideline Note 67 was approved by the HSC in August 2008, the language was as follows: "J3490 (Unspecified drug) on this [684] line represents treatment using enzyme replacement therapy." At the same time the HSC added other ICD-9-CM codes, including 272.7 for Fabry's disease, to Line 684. This was later modified by staff based on a DMAP request to specify Hunter's syndrome in the guideline note, and the change was made between meetings due to deadlines.

The manufacturers of Fabrazyme have inquired about noncoverage of enzyme replacement for Fabry's disease. At the June 2012 Value-based Benefits Subcommittee, those members that were on the Health Services Commission in 2008 were asked what their intent had been. They said their intent had been to prioritize all enzyme replacement therapies on Line 684 with the idea that if they were presented evidence of effectiveness for one or more of these treatments that warranted a higher placement, the List/guidelines could be revised to indicate a higher priority at that time. They acknowledged the ambiguity in the multiple placement of the codes for Fabry's disease and the wording of Line 684's guideline and have agreed to address this at their August 9th meeting.

Current List Status

> Guideline Note 67 Enzyme Replacement Therapy
> *Line 684*
> Enzyme replacement therapy for Hunter's syndrome is included on this Line.

HERC Staff Recommendation:

1. Modify Guideline Note 67 as follows:
   Guideline Note 67 Enzyme Replacement Therapy
   Line 264, 684
   Enzyme replacement therapy for infantile Pompe's disease is included on Line 264. All other enzyme replacement therap**ies**~~y for Hunter's syndrome is~~ **are** included on **Line 684**~~this line~~.

Pancreas transplantation in Type 2 diabetics

Question: Should combined pancreas-kidney transplant and pancreas after kidney transplant pair with type 2 diabetes?

Question source**:** ICD 10 Abdominal transplant specialists

Issue:

At the April 12, 2012 VBBS meeting, the ICD 10 expert reviews for transplant of abdominal organs had recommended adding ICD10 codes for Type 2 diabetes to the Line 92, DIABETES MELLITUS WITH END STAGE RENAL DISEASE, with treatment: SIMULTANEOUS PANCREAS/KIDNEY (SPK) TRANSPLANT, PANCREAS AFTER KIDNEY (PAK) TRANSPLANT

UNOS allows for transplant into Type 2 diabetics and nationally about 9% occur in diabetes. There was a discussion about UNOS and whether an evidence-based process that was clearly delinated existed. It was felt that further information on the effectiveness and utility of pancreas and pancreas after kidney transplants was necessary in Type 2 diabetics to evaluate if these codes should be added to Line 92.

From David Scott (expert and requesting transplant surgeon) in a series of emails:
As the papers point out the term type one and type 2 may not be all that useful or accurate. The terms may also lead to potential bias against certain racial and ethnic groups. I have included a couple of other papers which tried to use more rigorous definitions of diabetes type and found similar outcomes. I have also included a slide demonstrating the outcomes of those on the national waiting list which shows that the chance of dying while waiting for a transplant is the same for type 1 and type 2 patients. Patients waiting for combined kidney pancreas transplant have a much higher death rate than patients waiting for Pancreas after Kidney regardless of diabetes type. This shows that spk patients, tend to benefit much more in terms of years of life gained than PAK. If as a society we have to choose I think the weight of evidence would suggest that there is greater justice, utility and cost effectiveness in transplanting selected patients with type 2 diabetes rather than PAKs. The value of PAKs is really that it may encourage living donation which allows a deceased donor organ to be utilized for other recipients. This strategy is hard to put numbers on.

The literature comparing spk and kidney transplant alone is a little bit older and comes down very heavily in favor of SPK transplants. It has been looked at over and presented in a variety of ways. I don't think anyone has published data specifically looking at the survival comparing patients with type 2 diabetes transplanted with spk transplants verses kidney transplants alone. Since the outcomes following SPK are essentially the same between the type 1 and type 2 patients one can infer that the type 2 patients will have the same survival advantage from spk transplant. I'm not sure that one would even be able to publish an article showing the survival advantage of spk over kidney transplant alone in type 2 patients because the patients selected for spk transplant are really a highly selected group. I think you would be comparing apples and oranges.

I would advocate for covering PAKs but practically the benefit vs cost ratio is much lower than for SPKs. The new criteria say that if you are an insulin dependent diabetic with a c-peptide less than 2 you can be transplanted at any BMI. If your c-peptide is more then 2 then your BMI will need to be less than 28 for now. It would be very reasonable to have your criteria match the unos criteria. The unos criteria have been approved by the board but won't go into effect for several years because there is a backlog of programming issues. One could have a local criteria which was more loose than the national criteria but the patients would not accrue any waiting time. The national criteria seem pretty reasonable so I don't know why one would want to do that.

Evidence summary

Orlando, 2010

a. Review article of outcomes of SPKT in Type 1 versus Type 2 diabetics.
b. No trials exist comparing type 2 diabetics with renal failure receiving kidney alone or kidney with pancreas
c. few single center retrospective studies have reported comparable outcomes in terms of patient survival, improvement in quality of life, and allograft survival and function among T2DM and T1DM patients undergoing SPKT
    i. Selection criteria for SPKT in T2DM include:
        1. Patients less than 55–60 years of age
        2. BMI less than 30–32 kg/m2
        3. Insulin-requiring for a minimum of 5 years with a total daily insulin requirement less than 1 u/kg/day
        4. Fasting C-peptide level less than 10 ng/ml
        5. Absence of severe vascular disease or tobacco abuse
        6. Adequate cardiac function
        7. Presence of 'complicated' diabetes
    ii. Outcomes
        1. Outcomes in these patients are comparable to those undergoing SPKT and classified as having T1DM..
    iii. Conclusions:
        1. Consequently, characterization of the 'type' of diabetes may be irrelevant and insulin requiring diabetic patients with ESRD should be evaluated for PTX based exclusively on their predicted ability to tolerate the surgical procedure and requisite immunosuppression as well as comply with a stringent posttransplant follow-up regimen.

Santos-Sampaio, 2011

1. Retrospective cohort study using the United Network for Organ Sharing database
2. N = 6756, Type 1 diabetics - 6141 and Type 2 - 582
    a. **Results** Of the 6756 SPK transplants, 8.6% were performed in recipients with a type 2 diabetes diagnosis.

    Rates of delayed kidney graft function and primary kidney nonfunction were higher in the type 2 diabetics. Five-year overall and death-censored kidney graft survival were inferior in type 2 diabetics. After adjustment for other risk factors, including recipient (age, race, body weight, dialysis time, and cardiovascular comorbidities), donor, and transplant immune characteristics, type 2 diabetes was not associated with increased risk for death or kidney or pancreas failure when compared with type 1 diabetic recipients.
    b. Conclucsions: SPK in Type 2 diabetics non inferior to Type 1 diabetics

Mohan, 2003

1. Retrospective cohort study
2. N=101 patients with Type 1 diabetes (no type 2)
    a. 51 patients had kidney transplant alone
    b. 50 patients had simultaneous kidney-pancreas transplant
3. Results: Patient survival significantly different (P = 0·018 at 8 years).

	Survival 1 year	Survival 3 years	Survival 5 years	Survival 8 years
Simultaneous pancreas/kidney transplant	96%	93%	89%	77%
Kidney transplant alone	93%	75%	57%	47%

4. Conclusion: The addition of pancreatic transplantation prolongs life in type 1 diabetic patients with renal failure compared with renal transplantation alone.

<u>Summary</u>

There is no direct evidence comparing type 2 diabetics with renal failure to receiving a kidney alone, or a simultaneous pancreas-kidney, or pancreas after kidney transplant. By extrapolation from type 1 diabetic treatment, and from non-inferiority studies, there is an assumption that type 2 diabetics will also do better with the addition of the pancreas.

<u>HERC Staff Recommendation</u>

1) Decide whether or not to add Type 2 Diabetes codes to Line 92 to allow for simultaneous pancreas-kidney transplants
    a. Secondary diabetes: 249.xx
    b. Type II diabetes: 250.00, 250.02, 250.10, 250.12, 250.20, 250.22, 250.30, 250.32, 250.40, 250.42, 250.50.250.52, 250.60. 250.62, 250.70, 250.72, 250.80. 250.82, 250.90, 250.92
2) Do not add pancreas-after-kidney transplants (PAK) for type 2 diabetics
3) If Type 2 diabetes is added to line 92 in #1 above, will need to add the following guideline:

GUIDELINE XXX PANCREAS-KIDNEY TRANSPLANTS

Line 92

Secondary diabetes and type II diabetes ICD-9 codes are included on this line only for pairing with simultaneous pancreas-kidney transplants. Pancreas-after-kidney transplants are not covered for these diagnoses.

Pancreas transplantation for type 2 diabetes mellitus

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Current Opinion in Organ Transplantation 2011, 16:110–115

Purpose of review

This review will provide evidence that selected patients with type 2 diabetes mellitus (T2DM) may benefit from vascularized pancreas transplantation (PTX).

Recent findings

Initial experience with simultaneous pancreas–kidney transplantation (SPKT) in patients with T2DM and end-stage renal disease (ESRD) suggested that augmentation of endogenous insulin production by PTX in patients with C-peptide-positive, insulin-requiring diabetes resulted in insulin independence, improved glucose counter-regulation, and enhanced quality of life. A number of single-center retrospective studies have documented equivalent outcomes in patients with either type 1 diabetes mellitus (T1DM) or T2DM undergoing predominantly SPKT, although clearly a selection bias exists for patients in the latter category. Selection criteria for SPKT in T2DM include patients less than 55–60 years of age with a BMI less than 30–32 kg/m^2, insulin-requiring for a minimum of 5 years with a total daily insulin requirement less than 1 u/kg/day, a fasting C-peptide level less than 10 ng/ml, absence of severe vascular disease or tobacco abuse, adequate cardiac function, and presence of 'complicated' diabetes. Data from the International Pancreas Transplant Registry show that up to 7% of SPKT recipients are classified as having T2DM and that outcomes in these patients are comparable to those undergoing SPKT and classified as having T1DM.

Summary

Consequently, characterization of the 'type' of diabetes may be irrelevant and insulin-requiring diabetic patients with ESRD should be evaluated for PTX based exclusively on their predicted ability to tolerate the surgical procedure and requisite immunosuppression as well as comply with a stringent posttransplant follow-up regimen.

Keywords

metabolic syndrome, obesity, pancreas transplantation, type 2 diabetes mellitus

Curr Opin Organ Transplant 16:110–115

1087-2418

Introduction: diabetes mellitus – scope and magnitude of the problem

Diabetes mellitus is a chronic disease that has reached pandemic proportions and exerts a heavy burden on society. According to the WHO, more than 220 million people are afflicted with diabetes worldwide and nearly 80% live in low-income to middle-income countries (www.who.int/diabetes/en/, provides essential knowledge and access to the topic of diabetes mellitus). Projections envision that the worldwide burden of diabetes and diabetes-related deaths will both double in the next 20 years (www.who.int/diabetes/en/). According to the 2007 national diabetes statistics in the USA, diabetes mellitus affects approximately 7.8% of the overall population, 13% of the adult population, and 23% of persons older than 60 years (http://diabetes.niddk.nih.gov/dm/pubs/statistics/, provides essential knowledge and data on diabetes mellitus in the USA). Of the estimated 23.6 million diabetic patients in the USA, about 17.9 million are diagnosed, 4.8 million take insulin, and 1.6 million new cases of diabetes are diagnosed each year in Americans aged more than 20 years (http://diabetes.niddk.nih.gov/dm/pubs/statistics/). In the USA, diabetes mellitus is the leading cause of end-stage renal disease (ESRD), accounting for 48 215 new cases (44%) of kidney failure in 2006 [1•]. Patients with diabetes mellitus currently comprise more than 40% of the kidney transplant waiting list in the USA.

Classification and pathophysiology of diabetes mellitus

Historically, diabetes mellitus has been classified as either type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM), according to the presumed mechanisms of disease as well as the epidemiologic features and clinical manifestations [see Table 1].

T2DM accounts for up to 95% of all cases, affected patients are usually diagnosed when older and obese, and patients exhibit both insulin resistance as well as relative insulin deficiency (www.who.int/diabetes/en/; http://diabetes.niddk.nih.gov/dm/pubs/statistics/). The T2DM 'phenotype' is associated with the metabolic syndrome and higher preexisting cardiovascular morbidity [2,3]. In contrast, T1DM individuals are usually diagnosed as children or young adults, do not produce any insulin and are immediately insulin-requiring, and may have signs of autoimmunity. However, notwithstanding the supposed inherent biological differences, the two groups often overlap clinically. For example, T1DM patients may develop the disease later in life and not show any signs of autoimmune disease whereas T2DM patients may present signs of autoimmunity and develop the disease at a younger age [3]. Therefore, the classic distinction between these two 'types' of diabetes mellitus has been questioned and has become less clear with the formulation of the 'accelerator hypothesis', in which T1DM and T2DM are believed to be the same disorder of insulin resistance set against different genetic backgrounds [4••]. T1DM is distinguished from T2DM only by the time of onset that is determined by the impact of environmental and behavioral variables on a specific genetic milieu. The faster tempo in T1DM may merely reflect the more susceptible genotype and inevitable earlier presentation [4••].

Differentiation of the different types of diabetes mellitus may be difficult. No clinical or laboratory tests exist that can reliably distinguish between the two major types of diabetes mellitus with consistent accuracy. Although several diagnostic criteria have been proposed to discriminate between T1DM and T2DM [Table 1], many diabetic patients do not strictly fit into one category [2,3,4••]. For example, fasting C-peptide serum levels have long been considered a discriminating factor between T1DM and T2DM [3,5]. However, when diabetes mellitus is subjected to phenotypic analysis in patients presenting with concomitant ESRD, C-peptide levels (fasting or stimulated) are not accurate predictors of insulin production [6,7]. In fact, in such patients, C-peptide catabolism and excretion, which normally occur in the kidneys, are impaired and the resultant C-peptide levels do not accurately reflect the actual functioning β-cell mass [6,7]. In addition, total daily insulin dose does not necessarily correlate with the actual degree of insulin resistance.

Key points

- Differentiation between type 1 and type 2 diabetes mellitus (T2DM) may be difficult.
- Initial experience with predominantly simultaneous pancreas–kidney transplantation in patients with insulin-treated diabetes mellitus and end-stage renal disease has reported equivalent outcomes regardless of the 'type' of diabetes.
- The belief that T2DM should be considered a contraindication to pancreas transplantation is not substantiated by published data.

Treatment options for diabetes mellitus

Traditionally, management of diabetes mellitus has been medical (based on oral antidiabetic agents and insulin injections) and behavioral (dietary restrictions and regular physical activity). Although exogenous insulin therapy is effective at preventing acute metabolic decompensation and is life-saving for T1DM, less than 40% of diabetic patients achieve recommended therapeutic goals. Overall, a large number of diabetic patients are inadequately controlled, complete and steady remission of hyperglycemia is rare, treatment may be complicated by hypoglycemia, and most patients with diabetes mellitus will develop one or more end organ complications during their lifetime. This situation means that standard exogenous insulin-based intensive control of glucose can significantly reduce, but not completely protect against, the long-term microvascular and macrovascular complications of diabetes mellitus [8]. Pancreas transplantation (PTX) and islet transplantation are currently the only known therapies that reliably establish a long-term stable euglycemic state. Little to no data are available regarding

Table 1 Epidemiologic features and clinical manifestations distinguishing type 1 diabetes mellitus from type 2 diabetes mellitus

Characteristic	Type 1	Type 2
Age at diagnosis	<25 years	>40 years
Onset	Abrupt	Gradual
Body habitus	Thin	Overweight
Family history	Autoimmune disease	Diabetes: 1st and 2nd degree relatives
Associated disease	Thyroid disease	Elevated lipids, acanthosis
HLA-association	Positive	Negative
Diabetic ketoacidosis	Yes	No
Islet cell antibody	Present at onset	Absent
C-peptide	Undetectable	Detectable
Immediate need for insulin	Yes	No
Ethnicity	Predominantly non-Hispanic Caucasian	More common in African–American, Hispanic, and Native Americans

HLA, human leukocyte antigen.

Outcomes of Simultaneous Pancreas-Kidney Transplantation in Type 2 Diabetic Recipients

Marcelo Santos Sampaio,† Hung-Tien Kuo,*‡ and Suphamai Bunnapradist**

Summary

Background and objectives Type 2 diabetic patients with end-stage renal disease may receive a simultaneous pancreas-kidney (SPK) transplant. However, outcomes are not well described. Risks for death and graft failure were examined in SPK type 2 diabetic recipients.

Design, setting, participants, & measurements Using the United Network for Organ Sharing database, outcomes of SPK transplants were compared between type 2 and type 1 diabetic recipients. All primary SPK adult recipients transplanted between 2000 and 2007 (n = 6756) were stratified according to end-stage pancreas disease diagnosis (type 1: n=6141, type 2: n=582). Posttransplant complications and risks for death and kidney/pancreas graft failure were compared.

Results Of the 6756 SPK transplants, 8.6% were performed in recipients with a type 2 diabetes diagnosis. Rates of delayed kidney graft function and primary kidney nonfunction were higher in the type 2 diabetics. Five-year overall and death-censored kidney graft survival were inferior in type 2 diabetics. After adjustment for other risk factors, including recipient (age, race, body weight, dialysis time, and cardiovascular comorbidities), donor, and transplant immune characteristics, type 2 diabetes was not associated with increased risk for death or kidney or pancreas failure when compared with type 1 diabetic recipients.

Conclusions After adjustment for other risk factors, SPK recipients with type 2 diabetes diagnosis were not at increased risk for death, kidney failure, or pancreas failure when compared with recipients with type 1 diabetes.

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Introduction

Simultaneous pancreas-kidney transplantation (SPK) is one of the treatment options for type 1 diabetes mellitus (T1DM) patients with end-stage renal disease (ESRD) (1). Compared with kidney transplant alone, a successful SPK may improve quality of life (2,3), diminish the progression of diabetic complications (4,5), and possibly prolong patient and kidney allograft survival (6–9). In T1DM, SPK transplant outcomes are excellent, with a reported 5-year patient, kidney, and pancreas graft survival of 88%, 77% (10), and 69% (11), respectively.

The outcomes of SPK in type 2 diabetes mellitus (T2DM) are less well described and mostly represent single-center experiences. The largest published study included 38 SPK T2DM recipients, defined by a serum C-peptide level >0.8 ng/ml (12–14). In T1DM and T2DM, 5-year patient survival was 85% and 73%, pancreas survival was 71% and 67%, and kidney survival was 77% and 72%, respectively. Another smaller study defined T2DM by a C-peptide level ≥2.0 ng/ml (n = 7) and compared SPK outcomes with T1DM recipients. In T1DM and T2DM, recipients' 3-year patient survival was 94% and 71%, death-censored pancreas survival was 87% and 100%, and death-censored kidney survival was 95% and 100%, respectively (15). Two additional studies reported outcomes in T2DM patients with pancreas transplants. One study with 17 recipients (7 were SPK) had 94% pancreas survival in 1 year, and 11 of the 12 recipients were alive and euglycemic after 3 years (16). The second study included only four SPK transplants, and the outcomes were one death, one pancreas failure within 2 years, and two recipients with euglycemic after 7 years (17).

In this study we analyzed data from the Organ Procurement and Transplant Network/United Network for Organ Sharing (OPTN/UNOS), described characteristics of ESRD T2DM recipients who underwent a SPK transplant in the United States, and compared their outcomes with T1DM recipients. Diabetes was defined based on the diagnosis of end-stage pancreas disease (ESPD) as declared by each pancreas transplant center to UNOS. The objectives of this study were to describe characteristics of T2DM ESRD recipients considered for a SPK and to identify risks for death and graft failure compared with T1DM recipients.

Original article

Improved patient survival in recipients of simultaneous pancreas–kidney transplant compared with kidney transplant alone in patients with type 1 diabetes mellitus and end-stage renal disease

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Background: There are emerging data that simultaneous pancreas–kidney transplant (SPK) prolongs life compared with kidney transplant alone (KTA) in type 1 diabetics with end-stage renal disease. This study was a retrospective comparison of SPK with KTA in patients with type 1 diabetes.
Methods: Between 1 January 1992 and 30 April 2002, 101 patients with type 1 diabetes were transplanted. Fifty-one of these patients received a KTA and 50 had a SPK. All patients underwent coronary angiography with surgical correction of any coronary artery disease before being listed. All patients who underwent SPK received quadruple immunosuppressive therapy consisting of antilymphocyte globulin, calcineurin inhibitor (tacrolimus or cyclosporin), azathioprine and steroids. Those who underwent KTA received calcineurin inhibitor (tacrolimus or cyclosporin), azathioprine and steroids.
Results: Patient survival at 1, 3, 5 and 8 years was 96, 93, 89 and 77 per cent respectively after SPK, and 93, 75, 57 and 47 per cent respectively after KTA ($P = 0{\cdot}018$ at 8 years).
Conclusion: The addition of pancreatic transplantation prolongs life in type 1 diabetic patients with renal failure compared with renal transplantation alone.

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Introduction

It is estimated that the management of diabetes and all its complications accounts for 11 per cent of bed occupancy and 9 per cent of National Health Service hospital expenditure in England and Wales (equivalent to £1·9 billion in 2000)[1]. The American Diabetes Association estimates the total annual direct costs of management at US $44 billion, with an additional cost of US $54 billion associated with disability, lost productivity and premature death[2]. Despite the increasing incidence and cost of managing patients with insulin-dependent diabetes mellitus (IDDM) and end-stage renal disease (ESRD), the application of pancreas transplantation to the care of these patients has been very slow to gain acceptance in the UK. The perception of poor results, high mortality and complication rates[3], and a historical lack of discernible benefit may be some of the reasons for this attitude.

However, as the current results of simultaneous pancreas–kidney transplant (SPK) are now equal to or better than those for other solid-organ transplants[4], and positive effects of the procedure on diabetic nephropathy[5], microangiopathy[6], cardiac function[7], lipid profile[8] and neuropathy[9] are now apparent, this procedure is now considered the treatment of choice for type 1 diabetic patients with ESRD by the American Diabetes Association[10].

A survival advantage in SPK recipients compared with recipients of a kidney transplant alone (KTA) has also been deomonstrated[11–15]. The present study was a retrospective analysis of the results of renal transplantation in diabetic patients with renal failure to determine the impact of the addition of a pancreatic transplant on patient survival.

The Editors are satisfied that all authors have contributed significantly to this publication

Overview of Recommendations for Converting Lines to ICD-10-CM

Orthopedics

Specialty consultants: Dr. Robert Orfaly, Dr. Alex Herzberg

Note: code movements not requiring line movements were not completely reviewed and will be brought back as interim List changes at a later date

CREATE NEW LINES

1) Divide line 297 DEFORMITY/CLOSED DISLOCATION OF JOINT into two lines, "MAJOR DEFORMITY/CLOSED DISLOCATION OF JOINT" AND "MINOR DEFORMITY/CLOSED DISLOCATION OF JOINT"
    a. Having dislocation of toe and dislocation of hip on same line does not make prioritization sense. Any dislocation associated with vascular or nerve injury or of major joint should be on higher line. Higher line should include sternoclacivular, shoulder, knee, and hip dislocations. Lower line should include finger and toe dislocations
    b. Note: line split requires approval at August, 2012 meeting. Diagnoses for inclusion on each line may be approved/modified at a later date
    c. No line scoring recommendations received from experts
        i. current scoring shown below is for line 297

Lower dislocation line:

Line XXX MINOR DEFORMITY/CLOSED DISLOCATION OF JOINT

ICD-10: M20.021-M21.769, M24.074-M24.30, M24.40, M24.444-M24.446, M24.477-M24.479, Q69.0-1, Q70.00-Q70.13, S63.200A-S63.299A, S93.101A-S93.149A (boutonniere and swan neck deformity of fingers, acquired clawfoot, unequal limb length acquired, loose body in toe joint, pathologic dislocation of unspecified joint, recurrent dislocation of unspecified joint, recurrent dislocation finger/toe, accessory finger(s)/thumb(s), fused fingers, webbed fingers, dislocation/subluxation of finger/toe)

CPT: all CPT and HCPCS from line 297

Category 7
Impact on Healthy Life Years 6
Impact on Pain and Suffering 4
Population effects 0
Vulnerable populations 0
Tertiary prevention 2
Effectiveness 5
Need for treatment 1
Net cost 2
SCORE , PUTS ON LINE

Higher dislocation line:

Line XXX MAJOR DEFORMITY/CLOSED DISLOCATION OF JOINT

ICD-10: M22.00-M24.073, M24.321-M24.376, M24.411-M24.443, M24.451-M24.476, M24.811-M99.19, Q66.0, Q66.2, Q66.4, Q66.6, Q66.7, S03.0xxA-S63.146A, S73.001A-S93.06xA, S93.301A-S93.336A, Z47.1 (recurrent dislocation/subluxation of patella, loose body in elbow/ankle, pathologic/recurrent dislocation of elbow/wrist/hip/knee/ankle/foot/shoulder, other specified joint derangements, recurrent vertebral dislocation, Dypuytren contracture, osteochondrosis of patella, congenital talipes equinovarus, congenital deformities of feet, congenital pes cavus, congenital deformity of knee, dislocation/subluxation of upper limb joints shoulder through thumb, lower limb through foot)

Overview of Recommendations for Converting Lines to ICD-10-CM

CPT: all CPT and HCPCS from line 297

Category 7
Impact on Healthy Life Years 6
Impact on Pain and Suffering 4
Population effects 0
Vulnerable populations 0
Tertiary prevention 2
Effectiveness 5
Need for treatment 1
Net cost 2
SCORE , PUTS ON LINE

2) Create new line for recurrent instability of joint
    a. Include M24.40-M24.476 (recurrent dislocations, except M24.477-9 toe dislocations)
    b. All of currently on line 297 DEFORMITY/CLOSED DISLOCATION OF JOINT
    c. Affect young healthy people, easily treatable, effective with rehab and surgery. Success of surgery 95%. Percent of people needing surgery = 80% with unidirectional, 20% multidirectional. All need physical therapy. Unidirectional will fail therapy.
    d. Should be below acute broken bones, above chronic osteo, below acute tendon injuries, below dislocations
    e. If this line is approved, remove these codes from Major Deformity line above
    f. No line scoring recommendations received from experts
        i. scores shown below are for line 297

LINE XXX RECURRENT JOINT DISLOCATIONS
ICD-10 M24.40-M24.476
CPT: all from line 297

Category 7
Impact on Healthy Life Years 6
Impact on Pain and Suffering 4
Population effects 0
Vulnerable populations 0
Tertiary prevention 2
Effectiveness 5
Need for treatment 1
Net cost 2
SCORE , PUTS ON LINE

COMBINE MULTIPLE LINES

1) Combine line 536 CLOSED FRACTURE OF GREAT TOE with line 382 CLOSED FRACTURE OF EXTREMITIES (EXCEPT TOES)
    a. Combined line should have all CPT/HCPCS codes from both lines and be located at the location of line 382
    b. Thinks great toe should be with forefoot, and treatment should be covered due to affect on ability to walk
    c. Change name of line 382 to CLOSED FRACTURE OF EXTREMITIES (EXCEPT MINOR TOES)

Overview of Recommendations for Converting Lines to ICD-10-CM

DELETE LINES
None

RESCORE LINES
None

GUIDELINES

1) Collapsed vertebra codes are currently on lines 158 CERVICAL VERTEBRAL DISLOCATIONS/FRACTURES, OPEN OR CLOSED; OTHER VERTEBRAL DISLOCATIONS/FRACTURES, OPEN OR UNSTABLE; SPINAL CORD INJURIES WITH OR WITHOUT EVIDENCE OF VERTEBRAL INJURY and 507 CLOSED DISLOCATIONS/FRACTURES OF NON-CERVICAL VERTEBRAL COLUMN ~~WITHOUT SPINAL CORD INJURY~~ WITHOUT NEUROLOGIC INJURY OR STRUCTURAL INSTABILITY. Create guideline to indicate that collapsed vertebra are on line 158 if there is an unstable burst fracture, a fracture that qualified for trauma system entry, or a fracture with spinal cord injury.

GUIDELINE XXX COLLAPSED VERTEBRA
Lines 158, 507
Collapsed vertebra (ICD-10 M48.50xA- M48.58xA) are included on line 158 for unstable burst fractures, a fracture that qualified for trauma system entry, or a fracture with spinal cord injury.

2) Add benign neoplasms of various bones to lines with fractures of those bones. Add guideline to all of these lines specifying that these benign tumors are included on the upper fractures lines for benign neoplasms associated with pathologic fractures, at high risk of fracture, or which case function problems including impeding joint function due to size, causing nerve compression, have malignant potential or are considered precancerous.
    a. These codes are currently on line 549 BENIGN NEOPLASM BONE AND ARTICULAR CARTILAGE INCLUDING OSTEOID OSTEOMAS; BENIGN NEOPLASM OF CONNECTIVE AND OTHER SOFT TISSUE and should remain there as well
    b. Add D16.00-D16.32 (benign neoplasm of scapula and long bones of upper and lower limbs) to line 382 CLOSED FRACTURE OF EXTREMITIES (EXCEPT TOES)
    c. Add D16.6 (benign neoplasm of vertebral column) to line 158 CERVICAL VERTEBRAL DISLOCATIONS/FRACTURES, OPEN OR CLOSED; OTHER VERTEBRAL DISLOCATIONS/FRACTURES, OPEN; SPINAL CORD INJURIES WITH OR WITHOUT EVIDENCE OF VERTEBRAL INJURY and 507 CLOSED DISLOCATIONS/FRACTURES OF NONCERVICALVERTEBRAL COLUMN WITHOUT SPINAL CORD INJURY
    d. Add D16.7 (Benign neoplasm of ribs, sternum and clavicle) to lines 382 CLOSED FRACTURE OF EXTREMITIES and 519 CLOSED FRACTURES OF RIBS, STERNUM AND COCCYX
    e. Add D16.8 (Benign neoplasm of pelvic bones, sacrum and coccyx) to lines 507 CLOSED DISLOCATIONS/FRACTURES OF NON-CERVICAL VERTEBRAL COLUMN WITHOUT SPINAL CORD INJURY, 519 CLOSED FRACTURES OF RIBS, STERNUM AND COCCYX

Overview of Recommendations for Converting Lines to ICD-10-CM

GUIDELINE XXX BENIGN BONE TUMORS

Lines 158, 382, 507, 519, 549

Treatment of benign tumors of bones are included on lines 158, 382, 507, and 519 for those neoplasms associated with pathologic fractures, at high risk of fracture, or which case function problems including impeding joint function due to size, causing nerve compression, have malignant potential or are considered precancerous. Treatment of all other benign tumors are included on line 549.

RENAME LINES

1) Line 158 CERVICAL VERTEBRAL DISLOCATIONS/FRACTURES, OPEN OR CLOSED; OTHER VERTEBRAL DISLOCATIONS/FRACTURES, OPEN OR UNSTABLE; SPINAL CORD INJURIES WITH OR WITHOUT EVIDENCE OF VERTEBRAL INJURY
2) Line 315 CRUSH AND OTHER INJURIES OF DIGITS
3) Line 507 CLOSED DISLOCATIONS/FRACTURES OF NON-CERVICAL VERTEBRAL COLUMN ~~WITHOUT SPINAL CORD INJURY~~ WITHOUT NEUROLOGIC INJURY OR STRUCTURAL INSTABILITY

CODE PLACEMENT

1) Move unstable burst fracture and fractures resulting from neoplastic disease from line 507 CLOSED DISLOCATIONS/FRACTURES OF NON-CERVICAL VERTEBRAL COLUMN ~~WITHOUT SPINAL CORD INJURY~~ WITHOUT NEUROLOGIC INJURY OR STRUCTURAL INSTABILITY to line 158 CERVICAL VERTEBRAL DISLOCATIONS/FRACTURES, OPEN OR CLOSED; OTHER VERTEBRAL DISLOCATIONS/FRACTURES, OPEN OR UNSTABLE; SPINAL CORD INJURIES WITH OR WITHOUT EVIDENCE OF VERTEBRAL INJURY
    a. M84.58xA Pathological fracture in neoplastic disease, vertebrae, initial encounter for fracture
    b. M84.68xA Pathological fracture in other disease, other site, initial encounter for fracture
2) Move congenital absence of upper limb/hand/fingers/lower limb/foot, congenital shortening of upper or lower limb, longitudinal reduction defect of limbs, split foot, other congenital malformations of limbs (Q71.00-Q77.0) from line 297 DEFORMITY/CLOSED DISLOCATION OF JOINT to line 550: DEFORMITIES OF UPPER BODY AND ALL LIMBS
3) Move Mallet finger (M20.011-9) to line with other extension injuries of fingers. Mallet finger is currently on line 550 DEFORMITIES OF UPPER BODY AND ALL LIMBS. Will move to new line MINOR DEFORMITY/CLOSED DISLOCATION OF JOINT
4) Move physeal arrest (M89.121-M89.18) to covered line, as these should be treated. Occur in children and cause a significant range of problems. Currently on line 550 DEFORMITIES OF UPPER BODY AND ALL LIMBS, move to line 143 OPEN FRACTURE/DISLOCATION OF EXTREMITIES

Sleep Disorders

Question**:** Should certain sleep disorders be moved into the funded region?

Question Source: Drs. Kyle Johnson, Akram Khan, Michael Lefor, Holger Link

Issue The Oregon sleep medicine specialists consulting on the ICD 10 conversion also provided input on changes to Medicaid coverage for a number of additional sleep diagnoses. One of more of the consultants recommended that the following diagnoses be move to the funded region:

- Parasomnias
- Kleine-Levin Syndrome
- Circadian Rhythm sleep disorder-delayed sleep phase type
- Circadian Rhythm Disorder-free running type
- REM Sleep Behavior Disorder
- Primary Insomnia

Current Prioritized List Status

The ICD10 codes for these disorders map to the lower sleep line 636, on the current ICD-9 list

Line: 636 Condition: DISORDERS OF SLEEP WITHOUT SLEEP APNEA

Line Ranking

Score	Category	HLY	Suffering	Pop Effects	Vulnerable Pop	Tertiary Prev	Effectiveness	Need For Services	Net Cost	Text
2.7	9	0	2	0	1		3	0.3	4	**660**

Evidence Review:

I. ***Parasomnias*** have been subdivided according to 2 major classification schemes, the American Sleep Disorders Association's *International Classification of Sleep Disorders (ICSD)and* the American Psychiatric Association's *Diagnostic Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR*) .[1] Here we will used the *DSM-IV-TR* classifications which lists 4 major types of parasomnias, as follows: Nightmare disorder, Sleep terror disorder, Sleepwalking disorder, Parasomnias not otherwise specified

a. ***Nightmare disorder*** (also called dream anxiety attacks) typically occurs during the latter third of the night, usually during REM sleep, but without any motoric dream enactment. It may be associated with tachycardia, tachypnea, diaphoresis, and arousal. Complete alertness and subsequent recollection of the dreams differentiates nightmares from sleep terrors. Nightmares are another form of dreams, but one with documented emotional and physiologic consequences often invoking anger and embarrassment. 4% adults and a larger proportion of children

are affected, as are 80% of those suffering from PTSD. It can impair quality of life and exacerbate psychiatric disorders.

i. Systematic and Evidence-based Reviews: None identified

ii. Professional Society Guidelines

1. American Association of Sleep Medicine (AASM) Best Practice Guideline, Aurora 2010
    a. The only adult data available is for PTSD associated nightmares
    b. Prazosin (3 Level 1 placebo-controlled studies(total N=57) and 4 Level 4 studies) and Cognitive Behavioral Therapy (1 Level 1(N=168), 1 Level 2, 1 Level 3, and 7 Level 4 studies) are effective at reducing recurrent distressing dreams.
    c. Some drugs are ineffective for nightmares (e.g. venlafaxine) and should not be used

b. ***Sleep terror disorder*** is a disorder of arousal that primarily occurs during stages III and IV of NREM sleep. It is manifested by extreme panic and a loud scream during sleep, followed by motor activities such as hitting objects or moving in and out of the bedroom. Subsequent recollection of these episodes either does not occur or is partial. Most sleep terrors occur in young children.

i. Systematic and Evidence-based Reviews

1. Bruni, O. and Novelli, L. Sleep Disorders in Children. BMJ Clinical Evidence 2010:09:2304
    a. Behavioral and pharmacologic therapy for parasomnias in children are of unknown effectiveness

ii. Professional Society Guidelines: None identified

c. ***Sleepwalking*** disorder arises from slow-wave stages of NREM sleep. The subject performs complex automatic behaviors, such as wandering aimlessly, carrying objects, going outdoors, and performing other activities of varying complexity and duration. This disorder occurs across the lifespan but is much more common in pre-adolescent children.

i. Systematic and Evidence-based Reviews

1. Bruni, O. and Novelli, L. Sleep Disorders in Children. BMJ Clinical Evidence 2010:09:2304
    a. Behavioral and pharmacologic therapy for parasomnias in children are of unknown effectiveness

ii. Professional Society Guidelines: None identified

II. ***Kleine-Levin Syndrome*** (KLS) is a rare disorder which mainly affects adolescent men. It is characterized by recurrent episodes lasting days to weeks of hypersomnia, usually accompanied by hyperphagia, cognitive and mood disturbances, abnormal behavior such as hypersexuality, and signs of dysautonomia. In 1990 the diagnostic

criteria for Kleine-Levin Syndrome were modified in the International Classification of Sleep Disorders, where it was defined as a syndrome composed of recurring episodes of undue sleepiness lasting some days, which may or may not be associated with hyperphagia and abnormal behavior. [3]

a. Systematic and Evidence-based Reviews
    i. A 2012 Cochrane Collaboration on the Pharmacologic treatment for Kleine-Levin Syndrome did not find any studies meeting inclusion criteria.
b. Professional Society Guidelines: None identified
c. Standard Treatment (eMedicine)
    i. For Kleine-Levin syndrome, somnolence can decrease with stimulants (mainly amphetamines), while neuroleptics and antidepressants are of poor benefit. Lithium, rather than carbamazepine or other antiepileptics, was found to have a higher success rate for stopping relapses (Primary Hypersomnia, eMedicine, Adrian Preda Updated May 2012. http://emedicine.medscape.com/article/291699-overview Accessed June 21, 2012.
d. Expert input:
    i. From Holger Link: I would include Kleine-Levin Syndrome as a covered condition for the following reasons: a) it is a very rare condition and hence will have no noticeable impact on the budget. B) it can be very debilitating if not treated

III. ***Circadian Rhythm sleep disorder-delayed sleep phase type*** Delayed sleep phase disorder (DSPD) is characterized by a stable delay of the habitual nocturnal sleep period. Individuals with DSPD are often unable to fall asleep until the early morning hours and unable to awaken until late morning or early afternoon. During their preferred sleep schedules, sleep duration and quality are generally normal. However, sleep-onset insomnia and morning sleepiness occur if sleep and waking are attempted at an earlier time.

a. Systematic and Evidence-based Reviews: None identified
b. Professional Society Guidelines
    i. American Association of Sleep Medicine Review, 2007
        1. Melatonin is effective in shifting biomarkers of circadian rhythms and reducing sleep onset latency without changing total sleep time or daytime alertness(1 Level 1, 2 Level 2 studies).
        2. One level 1 and one level 2 study found that exposure to 2500 lux for 2-3 hours at or prior to arising causes phase advance and increases daytime alertness.
        3. No evidence for hypnotics or stimulants

IV. ***Circadian Rhythm Disorder-free running type*** Patients with free-running (FRD) rhythms are thought to reflect a failure of entrainment, the synchronization of internal cycles to external cues of light and dark. This condition is most common in blind individuals (about 50% of whom have FRD) and is highly unusual in sighted individuals. In blind people who have free-running rhythms, periodic symptoms of insomnia and daytime sleepiness commonly occur when the circadian pacemaker and, therefore, the circadian rhythm of sleepiness drift out of phase with the desired time

for sleeping.(Nakagawa H, Sack RL, Lewy AJ. Sleep propensity free-runs with the temperature, melatonin and cortisol rhythms in a totally blind person. Sleep 1992;15:330-336) These symptoms vary considerably but can be among the most burdensome aspects of blindness.(Sack RL, Brandes RW, Kendall AR, Lewy AJ N Engl J Med. 2000 Oct 12;343(15):1070). Roughly one-fourth of sighted individuals with FRD have related psychiatric diagnoses. (Standards of Practice Committee of the AASM, Practice Parameters for the Clinical Evaluation and Treatment of Circadian Rhythm Sleep Disorders)

a. Systematic and Evidence-based Reviews: None identified
b. Professional Society Guidelines
    i. American Association of Sleep Medicine Review, 2007
        1. In blind individuals, small level 2 trials and level 4 data supports the use of melatonin. In the level 2 controlled trials, 15 of 24 subjects entrained their sleep cycles with melatonin.
        2. In sighted individuals, both morning bright light exposure and melatonin are reported to entrain patients but the data available is case reports only(level 4); the rarity of the disorder precludes larger trials

V. ***REM Sleep Behavior Disorder*** Rapid eye movement sleep behavior disorder (RBD) is a parasomnia, first described in cats and later described in human beings. RBD is typically characterized by abnormal or disruptive behaviors emerging during rapid eye movement sleep having the potential to cause injury or sleep disruption such as talking, laughing, shouting, gesturing, grabbing, flailing arms, punching, kicking, and sitting up or leaping from bed. Vigorous, violent episodes may occur rarely or up to several times nightly

a. Systematic and Evidence-based Reviews: None identified
b. Professional Society Guidelines
    i. American Association of Sleep Medicine Best Practice Guide, 2010
        1. No RCT; all level 4 evidence.
        2. Safer sleep environment recommended
        3. Cautious pharmacologic treatment with clonazepam to prevent injury
            a. Recommendation for clonazepam based on 22 studies. None of the studies exceeded Level 4 evidence. These include 16 case series and 6 case reports. A majority of the studies evaluated sleep clinic populations, whereas only 1 studied a community sample. In total, 249 (73%) of 339 subjects had a complete response to clonezepam; an additional 57 (17%) partially responded.
        4. Melatonin was effective in small level 4 studies; overall, 31(82%) of 38 patients improved.

VI. ***Primary Insomnia*** In the American Academy of Sleep Medicine guideline, an insomnia disorder is defined as a subjective report of difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity for sleep, and that results in some form of daytime impairment

a. Evidence-based Reviews

i. AHRQ, 2005:
    1. There is evidence that chronic insomnia is associated with older age, female gender, present or past psychiatric illness and psychological problems, medical conditions and poor general health, increased healthcare utilization, lower quality of life and social relationships, socioeconomic status (marital separation, unemployment, poorer working conditions and lower social status), and decrements in memory, mood and cognitive function.
    2. There is evidence that benzodiazepines and non-benzodiazepines are effective in the management of chronic insomnia. There is some evidence that antidepressants are effective in the management of chronic insomnia: more research is required in this area. There is evidence that benzodiazepines, non-benzodiazepines and antidepressants pose a risk of harm.
    3. There is some evidence that melatonin is effective in the management of chronic insomnia in subsets of the chronic insomnia population, and there is no evidence that melatonin poses a risk of harm. However, more research is required in this area, given that the results are based on a small number of studies.
    4. There is evidence that relaxation therapy and cognitive/behavioral therapy are effective in the management of chronic insomnia in subsets of the chronic insomnia population.
    5. There is evidence that benzodiazepines have a greater risk of harm than non-benzodiazepines.
    6. Publication bias noted among drug studies.
ii. NICE Guidance on Short-term Management of Insomnia, 2004
    1. Summary: Severe insomnia can be treated with cheapest available drug; no value in changing unless serious side-effects occur
    2. Specific Recommendations(quoted):
    3. 1.1 When, after due consideration of the use of nonpharmacological measures, hypnotic drug therapy is considered appropriate for the management of severe insomnia interfering with normal daily life, it is recommended that hypnotics should be prescribed for short periods of time only, in strict accordance with their licensed indications.
    4. 1.2 It is recommended that, because of the lack of compelling evidence to distinguish between zaleplon, zolpidem, zopiclone or the shorter-acting benzodiazepine hypnotics, the drug with the lowest purchase cost (taking into account daily required dose and product price per dose) should be prescribed.
    5. 1.3 It is recommended that switching from one of these hypnotics to another should only occur if a patient experiences adverse effects considered to be directly related to a specific agent. These are the only circumstances in which the drugs with the higher acquisition costs are recommended.

6. 1.4 Patients who have not responded to one of these hypnotic drugs should not be prescribed any of the others.

b. Professional Society Guidelines
    i. American Association of Sleep Medicine, Report, 2006
        1. Psychological and behavioral interventions are effective and recommended in the treatment of chronic primary and secondary insomnia
        2. Effective and recommended for the treatment of chronic insomnia
            a. Stimulus control therapy
            b. Relaxation training
            c. Sleep restriction
            d. Cognitive behavior therapy, with or without relaxation therapy
            e. Multicomponent therapy (without cognitive therapy) is effective and recommended therapy in the treatment of chronic insomnia.
            f. Paradoxical intention
            g. Biofeedback
        3. Insufficient evidence available
            a. Sleep hygiene education to be an option as a single therapy
            b. imagery training to be an option as a single therapy
            c. cognitive therapy to be recommended as a single therapy.
        4. Insufficient evidence was available to recommend one single therapy over another, or to recommend single therapy versus a combination of psychological and behavioral interventions.
        5. Psychological and behavioral interventions are effective and recommended in the treatment of insomnia in older adults
        6. Psychological and behavioral interventions are effective and recommended in the treatment of insomnia among chronic hypnotic users
    ii. AASM Chronic Insomnia Clinical Guideline, 2008
        1. Treatment Recommendations
            a. Cognitive behavioral therapies are first line (standard)
            b. Pharmacologic treatment, if used, should be with CBT(consensus)
            c. Combination therapy has no advantage over CBT alone
            d. Superiority of CBT vs long-term pharmacologic treatment is unknown

Staff Recommendations:

1) No changes recommended:

a. no effective treatments found or no clear need for coverage identified

a. Parasomnias (nightmares, sleep terrors, and sleepwalking)

b. Klein Levinson Syndrome

c. Circadian rhythm sleep disorder-delayed sleep phase

d. Circadian rhythm sleep disorder-free-running type

i. Blindness is a co-morbidity. The disorder in sighted individuals is too rare for treatment to be well established

e. Insomnia

i. Insomnia is common. Any coverage change would have significant fiscal impact.

ii. Behavioral and standard, widely used, pharmacologic treatments appear to have some value; neither should require specialist referral or repeated visits. Single visit for diagnosis with primary care clinician should be sufficient to initiate treatment; however, medications may not be covered.

2) Add coverage for REM sleep behavior disorder

a. Risk of physical harm to the patient and sleeping partners and the evidence of the value of clonazepam treatment

b. Move REM sleep behavior disorder (ICD-9 327.42) from Line 636 to Line 210 SLEEP APNEA AND NARCOLEPSY

c. Rename Line 210, SLEEP APNEA, ~~AND~~ NARCOLEPSY, AND REM BEHAVIORAL DISORDER

SPECIAL ARTICLES

JCSM
Journal of Clinical Sleep Medicine

Best Practice Guide for the Treatment of Nightmare Disorder in Adults

Standards of Practice Committee:

R. Nisha Aurora, M.D.[1]; Rochelle S. Zak, M.D.[2]; Sanford H. Auerbach, M.D.[3]; Kenneth R. Casey, M.D.[4]; Susmita Chowdhuri, M.D.[5]; Anoop Karippot, M.D.[6]; Rama K. Maganti, M.D.[7]; Kannan Ramar, M.D.[8]; David A. Kristo, M.D.[9]; Sabin R. Bista, M.D.[10]; Carin I. Lamm, M.D.[11]; Timothy I. Morgenthaler, M.D.[8]

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Summary of Recommendations: Prazosin is recommended for treatment of Posttraumatic Stress Disorder (PTSD)-associated nightmares. Level A

Image Rehearsal Therapy (IRT) is recommended for treatment of nightmare disorder. Level A

Systematic Desensitization and Progressive Deep Muscle Relaxation training are suggested for treatment of idiopathic nightmares. Level B

Venlafaxine is *not* suggested for treatment of PTSD-associated nightmares. Level B

Clonidine may be considered for treatment of PTSD-associated nightmares. Level C

The following medications may be considered for treatment of PTSD-associated nightmares, but the data are low grade and sparse: trazodone, atypical antipsychotic medications, topiramate, low dose cortisol, fluvoxamine, triazolam and nitrazepam, phenelzine, gabapentin, cyproheptadine, and tricyclic antidepressants. Nefazodone is not recommended as first line therapy for nightmare disorder because of the increased risk of hepatotoxicity. Level C

The following behavioral therapies may be considered for treatment of PTSD-associated nightmares based on low-grade evidence: Exposure, Relaxation, and Rescripting Therapy (ERRT); Sleep Dynamic Therapy; Hypnosis; Eye-Movement Desensitization and Reprocessing (EMDR); and the Testimony Method. Level C

The following behavioral therapies may be considered for treatment of nightmare disorder based on low-grade evidence: Lucid Dreaming Therapy and Self-Exposure Therapy. Level C

No recommendation is made regarding clonazepam and individual psychotherapy because of sparse data.

Keywords: Nightmare disorder, nightmares, prazosin, clonidine, cyproheptadine, nefazodone, trazodone, olanzapine, topiramate, risperidone, cortisol, tricyclics, fluvoxamine, triazolam, nitrazepam, phenelzine, aripiprazole, gabapentin, venlafaxine, clonazepam, cognitive behavioral therapy, imagery rehearsal therapy, lucid dreaming therapy, sleep dynamic therapy, exposure relaxation and rescripting therapy, hypnosis, self-exposure therapy, systematic desensitization, progressive deep muscle training, psychotherapy, testimony method

Citation: Aurora RN; Zak RS; Auerbach SH; Casey KR; Chowduri S; Krippot A; Maganti RK; Ramar K; Kristo DA; Bista SR; Lamm CI; Morgenthaler TI. Best practice guide for the treatment of nightmare disorder in adults. *J Clin Sleep Med* 2010;6(4):389-401.

1.0 INTRODUCTION

There has been a burgeoning literature about pharmacotherapy and behavioral treatment of nightmare disorder in adults, but no systematic review has been available. The Standards of Practice Committee (SPC) of the American Academy of Sleep Medicine (AASM) commissioned a task force to assess the literature on the treatment of nightmare disorder. The Board of Directors authorized the task force to draft a Best Practice Guide based on review and grading of the literature and clinical consensus.

2.0 METHODS

The SPC of the AASM commissioned among its members 7 individuals to conduct this review and develop best practice principles. Work began in December 2007 to review and grade evidence in the peer-reviewed scientific literature regarding the treatment of nightmare disorder in adults. A search for articles on the medical treatment of nightmare disorder was conducted using the PubMed database, so that clinically relevant articles on the treatment of nightmare disorder could be collected and evaluated. Other databases such as PsychLit and Ovid were not searched, since it was felt that these databases would not include clinically relevant material. The PubMed search was conducted with no start date limit until February 2008, and subsequently updated in March 2009 to include the most current literature. The key words were: [(Nightmares OR nightmare OR nightmare disorder OR nightmare disorders OR recurrent nightmares) AND (treatment OR drug therapy OR therapy)] as well as [Post-traumatic stress disorder AND (nightmare disor-

ClinicalEvidence

Sleep disorders in children

Search date September 2009

Oliveiero Bruni and Luana Novelli

ABSTRACT

INTRODUCTION: Sleep disorders may affect between 20% and 30% of young children, and include problems getting to sleep (dyssomnias), or undesirable phenomena during sleep (parasomnias), such as sleep terrors and sleepwalking. Children with physical or learning disabilities are at increased risk of sleep disorders. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of treatments for dyssomnias in children? What are the effects of treatments for parasomnias in children? We searched: Medline, Embase, The Cochrane Library, and other important databases up to September 2009 (Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 28 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: antihistamines; behavioural therapy plus antihistamines, plus benzodiazepines, or plus chloral and derivatives; benzodiazepines alone; exercise; extinction and graduated extinction; 5-hydroxytryptophan; light therapy; melatonin; safety/protective interventions for parasomnias; scheduled waking (for parasomnias); sleep hygiene; and sleep restriction.

QUESTIONS

INTERVENTIONS

DYSSOMNIA TREATMENTS

Likely to be beneficial

Trade off between benefits and harms

Unknown effectiveness

PARASOMNIAS TREATMENTS

Unknown effectiveness

Covered elsewhere in Clinical Evidence

Insomnia in the elderly

Nocturnal enuresis

Footnote

* Based on consensus; few RCT data

Key points

- Sleep disorders may affect between 20% and 30% of young children, and include problems getting to sleep (dyssomnias) or undesirable phenomena during sleep (parasomnias), such as sleep terrors and sleepwalking.

Pharmacological treatment for Kleine-Levin Syndrome (Review)

Oliveira MM, Conti C, Saconato H, Prado GF

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2012, Issue 4

http://www.thecochranelibrary.com

[Intervention Review]

Pharmacological treatment for Kleine-Levin Syndrome

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Editorial group: Cochrane Epilepsy Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 4, 2012.
Review content assessed as up-to-date: 24 October 2011.

Citation: Oliveira MM, Conti C, Saconato H, Prado GF. Pharmacological treatment for Kleine-Levin Syndrome. *Cochrane Database of Systematic Reviews* 2009, Issue 2. Art. No.: CD006685. DOI: 10.1002/14651858.CD006685.pub2.

ABSTRACT

Background

This is an updated version of the original Cochrane review published in Issue 2, 2009.

Kleine-Levin Syndrome (KLS) is a rare disorder which mainly affects adolescent men. It is characterized by recurrent episodes of hypersomnia, usually accompanied by hyperphagia, cognitive and mood disturbances, abnormal behavior such as hypersexuality, and signs of dysautonomia.

In 1990 the diagnostic criteria for Kleine-Levin Syndrome were modified in the International Classification of Sleep Disorders, where it was defined as a syndrome composed of recurring episodes of undue sleepiness lasting some days, which may or may not be associated with hyperphagia and abnormal behavior.

The etiology of Kleine-Levin Syndrome remains unknown and several treatment strategies have been used. Some medications have been reported to provide some benefit for the treatment of Kleine-Levin Syndrome patients, but because of the rarity of the condition no long-term follow-up therapies have yet been described.

Objectives

This review aimed to evaluate:

1. whether pharmacological treatment for Kleine-Levin Syndrome is effective and safe; and

2. which drug or category of drugs is effective and safe.

Search methods

We obtained relevant trials from the following sources: the Cochrane Epilepsy Group Specialized Register (24 October 2011); the Cochrane Central Register of Controlled Trials (CENTRAL Issue 4 of 4, *The Cochrane Library* 2011); MEDLINE (1948 to October week 2, 2011); LILACS (24 October 2011); reference lists of sleep medicine textbooks; review articles and reference lists of articles identified by the search strategies.

Selection criteria

All randomized controlled trials (RCTs) and quasi-randomized controlled trials looking at pharmacological interventions for Kleine-Levin Syndrome. We included both parallel group and cross-over studies.

Practice Parameters for the Clinical Evaluation and Treatment of Circadian Rhythm Sleep Disorders

An American Academy of Sleep Medicine Report

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The expanding science of circadian rhythm biology and a growing literature in human clinical research on circadian rhythm sleep disorders (CRSDs) prompted the American Academy of Sleep Medicine (AASM) to convene a task force of experts to write a review of this important topic. Due to the extensive nature of the disorders covered, the review was written in two sections. The first review paper, in addition to providing a general introduction to circadian biology, addresses "exogenous" circadian rhythm sleep disorders, including shift work disorder (SWD) and jet lag disorder (JLD). The second review paper addresses the "endogenous" circadian rhythm sleep disorders, including advanced sleep phase disorder (ASPD), delayed sleep phase disorder (DSPD), irregular sleep-wake rhythm (ISWR), and the non–24-hour sleep-wake syndrome (nonentrained type) or free-running disorder (FRD). These practice parameters were developed by the Standards of Practice Committee and reviewed and approved by the Board of Directors of the AASM to present recommendations for the assessment and treatment of CRSDs based on the two accompanying comprehensive reviews. The main diagnostic tools considered include sleep logs, actigraphy, the Morningness-Eveningness Questionnaire (MEQ), circadian phase markers, and polysomnography. Use of a sleep log or diary is indicated in the assessment of patients with a suspected circadian rhythm sleep disorder (Guideline). Actigraphy is indicated to assist in evaluation of patients suspected of circadian rhythm disorders (strength of recommendation varies from "Option" to "Guideline," depending on the suspected CRSD). Polysomnography is not routinely indicated for the diagnosis of CRSDs, but may be indicated to rule out another primary sleep disorder (Standard). There is insufficient evidence to justify the use of MEQ for the routine clinical evaluation of CRSDs (Option). Circadian phase markers are useful to determine circadian phase and confirm the diagnosis of FRD in sighted and unsighted patients but there is insufficient evidence to recommend their routine use in the diagnosis of SWD, JLD, ASPD, DSPD, or ISWR (Option). Additionally, actigraphy is useful as an outcome measure in evaluating the response to treatment for CRSDs (Guideline). A range of therapeutic interventions were considered including planned sleep schedules, timed light exposure, timed melatonin doses, hypnotics, stimulants, and alerting agents. Planned or prescribed sleep schedules are indicated in SWD (Standard) and in JLD, DSPD, ASPD, ISWR (excluding elderly-demented/nursing home residents), and FRD (Option). Specifically dosed and timed light exposure is indicated for each of the circadian disorders with variable success (Option). Timed melatonin administration is indicated for JLD (Standard); SWD, DSPD, and FRD in unsighted persons (Guideline); and for ASPD, FRD in sighted individuals, and for ISWR in children with moderate to severe psychomotor retardation (Option). Hypnotic medications may be indicated to promote or improve daytime sleep among night shift workers (Guideline) and to treat jet lag-induced insomnia (Option). Stimulants may be indicated to improve alertness in JLD and SWD (Option) but may have risks that must be weighed prior to use. Modafinil may be indicated to improve alertness during the night shift for patients with SWD (Guideline).

Keywords: Circadian, light therapy, melatonin, naps, jet lag, shift work

Citation: Morgenthaler TI; Lee-Chiong T; Alessi C; Friedman L; Aurora N; Boehlecke B; Brown T; Chesson AL; Kapur V; Maganti R; Owens J; Pancer J; Swick TJ; Zak R; Standards of Practice Committee of the AASM. Practice Parameters for the Clinical Evaluation and Treatment of Circadian Rhythm Sleep Disorders. *SLEEP* 2007;30(11):1445-1459.

Disclosure Statement

This is not an industry supported study. The authors have indicated no financial conflicts of interest.

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1.0 INTRODUCTION

THIS PRACTICE PARAMETER PAPER IS WRITTEN AS A COMPANION ARTICLE TO THE TWO ACCOMPANYING REVIEW ARTICLES ON CIRCADIAN RHYTHM SLEEP disorders (CRSDs) authored by a task force of experts convened by the American Academy of Sleep Medicine (AASM).[1,2] The companion review papers summarize the peer-reviewed scientific literature published through October 2006. The authors of the review papers evaluated the evidence presented by the reviewed studies according to the Oxford System for Evidence-Based Medicine[3] http://www.cebm.net/index.aspx?o=1025. Using this infor-

Circadian Rhythm Sleep Disorders: Part II, Advanced Sleep Phase Disorder, Delayed Sleep Phase Disorder, Free-Running Disorder, and Irregular Sleep-Wake Rhythm

An American Academy of Sleep Medicine Review

Robert L Sack, MD[1]; Dennis Auckley, MD[2]; R. Robert Auger, MD[3]; Mary A. Carskadon, PhD[4]; Kenneth P. Wright Jr, PhD[5]; Michael V. Vitiello, PhD[6]; Irina V. Zhdanova, MD[7]

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Objective: This the second of two articles reviewing the scientific literature on the evaluation and treatment of circadian rhythm sleep disorders (CRSDs), employing the methodology of evidence-based medicine. We herein report on the accumulated evidence regarding the evaluation and treatment of Advamced Sleep Phase Disorder (ASPD), Delayed Sleep Phase Disorder (DSPD), Free-Running Disorder (FRD) and Irregular Sleep-Wake Rhythm ISWR).

Methods: A set of specific questions relevant to clinical practice were formulated, a systematic literature search was performed, and relevant articles were abstracted and graded.

Results: A substantial body of literature has accumulated that provides a rational basis the evaluation and treatment of CRSDs. Physiological assessment has involved determination of circadian phase using core body temperature and the timing of melatonin secretion. Behavioral assessment has involved sleep logs, actigraphy and the Morningness-Eveningness Questionnaire (MEQ). Treatment interventions fall into three broad categories: 1) prescribed sleep scheduling, 2) circadian phase shifting ("resetting the clock"), and 3) symptomatic treatment using hypnotic and stimulant medications.

Conclusion: Circadian rhythm science has also pointed the way to rational interventions for CRSDs and these treatments have been introduced into the practice of sleep medicine with varying degrees of success. More translational research is needed using subjects who meet current diagnostic criteria.

Keywords: Circadian rhythm sleep disorders

Citation: Sack R; Auckley D; Auger RR; Carskadon MA; Wright KP; Vitiello MV; Zhdanova IV. Circadian rhythm sleep disorders: Part II, advanced sleep phase disorder, delayed sleep phase disorder, free-running disorder, and irregular sleep-wake rhythm. *SLEEP* 2007;30(11):1484-1501.

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Disclosure Statement

This is not an industry supported study. Dr. Sack has received research support from GlaxoSmithKline, Takeda, and Cephalon and has consulted for Minimitter Company. Dr. Auckley has received research support from Invacare and TAP Pharmaceuticals. Dr. Carskadon has received research support from Evotec and Cephalon and has participated in speaking engagements for World Class and Cephalon. Dr. Wright has received research support from and has participated in speaking engagements for Cephalon and Takeda, and has consulted for Takeda. Dr. Vitiello is on the speakers bureau for Takeda. Drs. Auger and Zhdanova have indicated no financial conflicts of interest.

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SPECIAL ARTICLES

JCSM
Journal of Clinical Sleep Medicine

Best Practice Guide for the Treatment of REM Sleep Behavior Disorder (RBD)

Standards of Practice Committee:

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Summary of Recommendations: Modifying the sleep environment is recommended for the treatment of patients with RBD who have sleep-related injury. Level A

Clonazepam is suggested for the treatment of RBD but should be used with caution in patients with dementia, gait disorders, or concomitant OSA. Its use should be monitored carefully over time as RBD appears to be a precursor to neurodegenerative disorders with dementia in some patients. Level B

Clonazepam is suggested to decrease the occurrence of sleep-related injury caused by RBD in patients for whom pharmacologic therapy is deemed necessary. It should be used in caution in patients with dementia, gait disorders, or concomitant OSA, and its use should be monitored carefully over time. Level B

Melatonin is suggested for the treatment of RBD with the advantage that there are few side effects. Level B

Pramipexole may be considered to treat RBD, but efficacy studies have shown contradictory results. There is little evidence to support the use of paroxetine or L-DOPA to treat RBD, and some studies have suggested that these drugs may actually induce or exacerbate RBD. There are limited data regarding the efficacy of acetylcholinesterase inhibitors, but they may be considered to treat RBD in patients with a concomitant synucleinopathy. Level C

The following medications may be considered for treatment of RBD, but evidence is very limited with only a few subjects having been studied for each medication: zopiclone, benzodiazepines other than clonazepam, Yi-Gan San, desipramine, clozapine, carbamazepine, and sodium oxybate. Level C

Keywords: REM sleep behavior disorder, synucleinopathy, clonazepam, melatonin, pramipexole, L-DOPA, acetylcholinesterase inhibitor, paroxetine, zopiclone, benzodiazepine, Yi-Gan San, desipramine, carbamazepine, clozapine, sodium oxybate, sleep-related injury

Citation: Aurora RN; Zak RS; Maganti RK; Auerbach SH; Casey KR; Chowdhuri S; Karippot A; Ramar K; Kristo DA; Morgenthaler TI. Best practice guide for the treatment of REM sleep behavior disorder (RBD). *J Clin Sleep Med* 2010;6(1):85-95.

1. INTRODUCTION

REM sleep behavior disorder (RBD) was first defined in 1986.[1] Since then, a number of reviews but no evidence-based treatment recommendations have been published. To address this issue, the Standards of Practice Committee of the American Academy of Sleep Medicine (AASM) commissioned a task force to assess the literature on the treatment of RBD. The task force found that although the literature is voluminous, much of the data are low-level studies, mostly case series and case reports with no randomized controlled clinical trials. These studies were deemed insufficient to support the standards or guidelines of a practice parameter. Thus, the Board of Directors authorized the task force to draft a Best Practice Guide on the treatment of RBD based on a systematic review and compilation of recommended evaluation or management strategies.

2. METHODS

The Standards of Practice Committee of the AASM commissioned among its members 7 individuals to conduct this review and develop best practice principles. Work began in December 2007 to review and grade evidence in the peer-reviewed scientific literature regarding the treatment of RBD in adults. A search for articles on the medical treatment of RBD was conducted using the PubMed database, first in February 2008, and subsequently updated in June 2009, to include the most current literature. The key words for the searches were the following: [(RBD OR Rapid Eye Movement Sleep Disorder OR REM Sleep behavior disorder) AND (treatment OR medication OR drug therapy] as well as [Rapid eye movement behavior disorder AND evaluation AND (neurological diseases OR dementia OR stroke OR sleep disorders OR Lewy body dementia OR drug induced OR multiple systems atrophy OR narcolepsy OR Parkinson's OR synucleinopathies)]. Each search was run separately and findings were merged. When the search was limited to articles published in English and regarding human adults (age 19 years and older), a total of 315 articles was identified. Abstracts from these articles were reviewed to determine if they met inclusion criteria. The literature on medical treatment of RBD was noted to comprise mostly small case series. In order to be inclusive, latitude in

Evidence Report/Technology Assessment
Number 125

Manifestations and Management of Chronic Insomnia in Adults

Prepared for:
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AHRQ Publication No. 05-E021-2
June 2005

Structured Abstract

Context: Approximately 40 to 70 million Americans are affected by either intermittent or chronic sleep problems, representing approximately 20 percent of the population.

Objectives: To conduct a systematic review of (1) the prevalence, natural history, incidence, risk factors and consequences of chronic insomnia in adults and (2) the efficacy and safety of treatments used in the management of chronic insomnia in adults.

Data Sources: A systematic search of twenty-one electronic databases was conducted. We searched MEDLINE®, EMBASE, CINAHL®, Ovid MEDLINE In-Process & Other Non-Indexed Citations, Ovid OLDMEDLINE®, PsycINFO®, EBM Reviews-Cochrane Central Register of Controlled Trials, International Pharmaceutical Abstracts, AMED (Allied and Complementary Medicine), HealthSTAR/Ovid Healthstar, EBM Reviews-Cochrane Database of Systematic Reviews (CDSR), ACP Journal Club (ACPJC), Database of Abstracts of Reviews of Effects (DARE), Science Citation Index Expanded™, Biological Abstracts, Cochrane Complementary Medicine Field Registry, CAB Abstracts, SIGLE, OCLC Proceedings First, Dissertation Abstracts, Alt HealthWatch, NLM Gateway and PubMed®.

Study Selection: Cohort, case-control and cross-sectional studies were eligible for questions on manifestations of chronic insomnia. Randomized controlled trials were eligible for the question on management of chronic insomnia.

Quality Assessment: One of three instruments was used to assess the quality of studies relevant to the manifestations of chronic insomnia. The Jadad Scale was used to assess the quality of studies relevant to the management of chronic insomnia. The concealment of treatment allocation was also assessed in the latter studies.

Data Analysis: Data were analyzed both qualitatively and quantitatively. The Random Effects Model was used for quantitative analyses.

Main Results: The interquartile range of prevalence of chronic insomnia varied from 8.5-24.3 percent across high quality studies of general populations, to 19.8-53.7 percent across moderate quality studies of outpatient populations, to 27.8-43.0 percent across moderate quality studies of clinical populations. Sleep onset latency (SOL) was significantly decreased by benzodiazepines (Mean Difference (MD): -16.5, 95% Confidence Interval (CI): [-20.5, -12.5]), non-benzodiazepines (MD: -18.1, 95% CI: [-22.5, -13.7]), antidepressants (MD: -7.4, 95% CI: [-10.5, -4.4]) and melatonin (MD: -8.3, 95% CI: [-14.5, -2.0]). All of the preceding interventions, except melatonin, had a significantly higher risk of harm compared to placebo: benzodiazepines (Risk Difference [RD]: 0.15, 95% CI: [0.10, 0.20]), non-benzodiazepines (RD 0.05, 95% CI: [0.01, 0.09]), antidepressants (RD: 0.09, 95% CI: [0.01, 0.18]) and melatonin (RD: 0.09, 95% CI: [-0.11, 0.29]). Wakefulness after sleep onset (WASO) was not significantly reduced by melatonin (MD: -9.7, 95% CI: [-33.6, 14.3]). SOL was significantly decreased by relaxation therapy with short-term treatment (less than 4 weeks) (MD: -22.0, 95% CI: [-41.0, -2.9]); however, WASO was not significantly reduced by relaxation therapy (MD: -1.6, 95% CI: [-14.1,

10.8]). WASO was significantly decreased by cognitive/behavioral therapy (MD: -18.2, 95% CI: [-30.4, -6.0]); however, SOL was not significantly reduced by cognitive/behavioral therapy (MD: -4.6, 95% CI: -9.8, 0.6).

Main Conclusions

- There is evidence that chronic insomnia is associated with older age, female gender, present or past psychiatric illness and psychological problems, medical conditions and poor general health, increased healthcare utilization, lower quality of life and social relationships, socioeconomic status (marital separation, unemployment, poorer working conditions and lower social status), and decrements in memory, mood and cognitive function.

- There is evidence that benzodiazepines and non-benzodiazepines are effective in the management of chronic insomnia. There is some evidence that antidepressants are effective in the management of chronic insomnia: more research is required in this area. There is evidence that benzodiazepines, non-benzodiazepines and antidepressants pose a risk of harm.

- There is some evidence that melatonin is effective in the management of chronic insomnia in subsets of the chronic insomnia population, and there is no evidence that melatonin poses a risk of harm. However, more research is required in this area, given that the results are based on a small number of studies.

- There is evidence that relaxation therapy and cognitive/behavioral therapy are effective in the management of chronic insomnia in subsets of the chronic insomnia population.

- There is evidence that benzodiazepines have a greater risk of harm than non-benzodiazepines.

NHS

National Institute for Clinical Excellence

Guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia

Technology Appraisal 77

April 2004

Technology Appraisal Guidance 77

Guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia

Issue date: April 2004
Review date: April 2007

This document, which contains the Institute's full guidance for this appraisal, is available from the NICE website (www.nice.org.uk/TA077guidance).

An abridged version of this guidance (a 'quick reference guide') is also available from the NICE website (www.nice.org.uk/TA077quickrefguide). Printed copies of the quick reference guide can be obtained from the NHS Response Line: telephone 0870 1555 455 and quote reference number N0545.

Information for the Public is available from the NICE website or from the NHS Response Line (quote reference number N0546 for a version in English and N0547 for a version in English and Welsh).

The quick reference guide has been distributed to the following:

- Primary Care Trust (PCT) Chief Executives
- Local Health Board (LHB) chief executives
- NHS Trust Chief Executives in England and Wales
- Strategic health authority chief executives in England and Wales
- Medical and nursing directors in England and Wales
- Clinical governance leads in England and Wales
- Audit leads in England and Wales
- NHS trust, PCT and LHT libraries in England and Wales,
- Patient advice and liaison coordinators in England and Wales
- Consultant psychiatrists in England and Wales
- Consultant psychologists in England and Wales
- GPs in England and Wales
- Chief pharmacists, heads of drug purchasing, heads of drug information, GP prescribing advisors and purchasing advisors in England and Wales
- Mental health nurse consultants
- Community psychiatric nurses
- NHS Director Wales
- Chief Executive of the NHS in England
- Chief Medical, Nursing and Pharmaceutical Officers in England and Wales
- Medical Director & Head of NHS Quality – Welsh Assembly Government
- Community health councils in Wales
- Commission for Healthcare Audit and Inspection
- NHS Clinical Governance Support Team
- Patient advocacy groups
- Representative bodies for health services, professional organisations and statutory bodies, and the Royal Colleges

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This guidance is written in the following context:
This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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PRACTICE PARAMETER

Practice Parameters for the Psychological and Behavioral Treatment of Insomnia: An Update. An American Academy of Sleep Medicine Report

An American Academy of Sleep Medicine Report

Standards of Practice Committee of the American Academy of Sleep Medicine

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Abstract: Insomnia is highly prevalent, has associated daytime consequences which impair job performance and quality of life, and is associated with increased risk of comorbidities including depression. These practice parameters provide recommendations regarding behavioral and psychological treatment approaches, which are often effective in primary and secondary insomnia. These recommendations replace or modify those published in the 1999 practice parameter paper produced by the American Sleep Disorders Association. A Task Force of content experts was appointed by the American Academy of Sleep Medicine to perform a comprehensive review of the scientific literature since 1999 and to grade the evidence regarding non-pharmacological treatments of insomnia. Recommendations were developed based on this review using evidence-based methods. These recommendations were developed by the Standards of Practice Committee and reviewed and approved by the Board of Directors of the American Academy of Sleep Medicine. Psychological and behavioral interventions are effective in the treatment of both chronic primary insomnia (Standard) and secondary insomnia (Guideline). Stimulus control therapy, relaxation training, and cognitive behavior therapy are individually effective therapies in the treatment of chronic insomnia (Standard) and sleep restriction therapy, multicomponent therapy (without cognitive therapy), biofeedback and paradoxical intention are individually effective therapies in the treatment of chronic insomnia (Guideline). There was insufficient evidence to recommend sleep hygiene education, imagery training and cognitive therapy as single therapies or when added to other specific approaches. Psychological and behavioral interventions are effective in the treatment of insomnia in older adults and in the treatment of insomnia among chronic hypnotic users (Standard).

Keywords: Practice guidelines, practice parameters, insomnia primary, insomnia secondary, treatment, behavioral, psychological, non-pharmacological, stimulus control therapy, relaxation training, sleep restriction, cognitive behavior therapy, multicomponent therapy, paradoxical intention, sleep hygiene education.

Citation: Morgenthaler T; Kramer M; Alessi C et al. Practice parameters for the psychological and behavioral treatment of insomnia: an update. An American Academy of Sleep Medicine report. *SLEEP* 2006;29(11): 1415-1419.

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1.0 INTRODUCTION

INSOMNIA IS A COMMON CONDITION, REPORTED TO OCCUR IN ONE THIRD OF THE ADULT POPULATION.[1] CHRONIC INSOMNIA IS ASSOCIATED WITH A reduced quality of life, impaired daytime functioning, increased loss of time from work and higher health costs. Chronic insomnia is also associated with an increased risk of depression and chronic use of hypnotic medication.[2-4]

The diagnosis of insomnia is based on subjective complaints of difficulty falling asleep or staying asleep, or non-restorative sleep associated with marked distress or significant daytime impairment.[5,6] Insomnia-related complaints may include reports of daytime fatigue, problems with memory and concentration and mood disturbance. Insomnia can be a primary disorder, as in primary insomnia (e.g. psychophysiological insomnia, paradoxical insomnia, idiopathic insomnia, physiological insomnia-unspecified, etc.), or (what we term here as) secondary insomnia, where insomnia is a symptom of or associated with other conditions including medical or psychiatric illness, substance abuse disorder or another sleep disorder.[5-7] It is often difficult to distinguish the cause of insomnia in patients with concurrent medical disorders. However, insomnia, whether primary or secondary to a comorbid illness, merits attention. Indicators of the severity of insomnia

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SPECIAL ARTICLE

Clinical Guideline for the Evaluation and Management of Chronic Insomnia in Adults

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Insomnia is the most prevalent sleep disorder in the general population, and is commonly encountered in medical practices. Insomnia is defined as the subjective perception of difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity for sleep, and that results in some form of daytime impairment.[1] Insomnia may present with a variety of specific complaints and etiologies, making the evaluation and management of chronic insomnia demanding on a clinician's time. The purpose of this clinical guideline is to provide clinicians with a practical framework for the assessment and disease management of chronic adult insomnia, using existing evidence-based insomnia practice parameters where available, and consensus-based recommendations to bridge areas where such parameters do not exist. Unless otherwise stated, "insomnia" refers to chronic insomnia, which is present for at least a month, as opposed to acute or transient insomnia, which may last days to weeks.

Citation: Schutte-Rodin S; Broch L; Buysse D; Dorsey C; Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med 2008*;4(5):487-504.

SUMMARY RECOMMENDATIONS

General:

- ❖ Insomnia is an important public health problem that requires accurate diagnosis and effective treatment. **(Standard)**
- ❖ An insomnia diagnosis requires associated daytime dysfunction in addition to appropriate insomnia symptomatology. **(ICSD-2 definition)**

Evaluation:

- ❖ Insomnia is primarily diagnosed by clinical evaluation through a thorough sleep history and detailed medical, substance, and psychiatric history. **(Standard)**
  - The sleep history should cover specific insomnia complaints, pre-sleep conditions, sleep-wake patterns, other sleep-related symptoms, and daytime consequences. **(Consensus)**
  - The history helps to establish the type and evolution of insomnia, perpetuating factors, and identification of comorbid medical, substance, and/or psychiatric conditions. **(Consensus)**
- ❖ Instruments which are helpful in the evaluation and differential diagnosis of insomnia include self-administered questionnaires, at-home sleep logs, symptom checklists, psychological screening tests, and bed partner interviews. **(Guideline)**
  - At minimum, the patient should complete: (1) A general medical/psychiatric questionnaire to identify comorbid disorders (2) The Epworth Sleepiness Scale or other sleepiness assessment to identify sleepy patients and comorbid disorders of sleepiness (3) A two-week sleep log to identify general patterns of sleep-wake times and day-to-day variability. **(Consensus)**
  - Sleep diary data should be collected prior to and during the course of active treatment and in the case of relapse or reevaluation in the long-term. **(Consensus)**
  - Additional assessment instruments that may aid in the baseline evaluation and outcomes follow-up of patients with chronic insomnia include measures of subjective sleep quality, psychological assessment scales, daytime function, quality of life, and dysfunctional beliefs and attitudes. **(Consensus)**
- ❖ Physical and mental status examination may provide important information regarding comorbid conditions and differential diagnosis. **(Standard)**
- ❖ Polysomnography and daytime multiple sleep latency testing (MSLT) are not indicated in the routine evaluation of chronic insomnia, including insomnia due to psychiatric or neuropsychiatric disorders. **(Standard)**
  - Polysomnography is indicated when there is reasonable clinical suspicion of breathing (sleep apnea) or movement disorders, when initial diagnosis is uncertain, treatment fails (behavioral or pharmacologic), or precipitous arousals occur with violent or injurious behavior. **(Guideline)**

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Hyperbaric oxygen issue summary

Question: How should the ICD-10 code mapping be changed for the two hyperbaric oxygen lines, Line 358 ANAEROBIC INFECTIONS REQUIRING HYPERBARIC OXYGEN and Line 399 TOXIC EFFECT OF GASES, FUMES, AND VAPORS REQUIRING HYPERBARIC OXYGEN?

Issue: No ICD-10 consultant volunteered to assist in reviewing the hyperbaric oxygen line. HERC staff has identified suggested coding changes.

Evidence:

1) **Scottish NHS 2008: systematic review on clinical indications and cost effectiveness of hyperbaric oxygen; European Consensus Conference Recommendations**
    - **a.** Strongly recommend use:
        - **i.** Gas embolism
        - **ii.** Osteoradionecrosis of the mandible
    - **b.** Recommend use:
        - **i.** Decompression illness
        - **ii.** Treatment of compromised skin grafts and myocutaneous flaps
        - **iii.** Radionecrosis of bones other than the mandible
        - **iv.** Adjunctive therapy for stage IV neurolabstoma
        - **v.** Chronic refractory osteomyelitis
        - **vi.** Sudden deafness
    - **c.** Recommend use in specific cases:
        - **i.** Carbon monoxide poisoning for patients at high risk (unconscious; clinical neurological, cardiac, respiratory or psychological symptoms; pregnant women) or immediate or long-term complications
        - ii. Diabetic lower extremity ulcers if peri-lesional transcutaneous oxygen pressures, measured under hyperbaric conditions, are higher than 100 mgHg
        - **iii.** Venous ulcers if peri-lesional transcutaneous oxygen pressures, measured under hyperbaric conditions, are higher than 50 mgHg
        - **iv.** Crush injuries of Gustilo type III B and C
        - **v.** Necrotising soft-tissue infections of anaerobic or mixed bacterial nature
        - **vi.** Optional for second or third degree burns exceeding 20% of body surface area

vii. Optional for acute ophthalmological ischemia

d. Use NOT recommended

i. Pressure ulcers
ii. Other chronic wounds
iii. Blunt chest injury
iv. Calciphylaxis
v. Surgical site infections
vi. Livedoid vasculopathy
vii. Acute coronary syndrome
viii. Stroke
ix. Traumatic brain injury
x. Soft tissue radionecrosis
xi. Treatment of cancer and tumor sensitization to radiotherapy, other than adjunctive therapy for stage IV neuroblastoma
xii. Surgery
xiii. Cardiopulmonary bypass
xiv. Urology
xv. Headache
xvi. Multiple sclerosis
xvii. Sports injuries
xviii. Osteonecrosis of the mandible
xix. Peridontitis
xx. Chronic hepatitis
xxi. Crohn's disese
xxii. Bell's palsy
xxiii. Pain syndromes
xxiv. Cognitive impairment
xxv. Infertility
xxvi. Severe anemia
xxvii. Malignant otitis externa

2) NICE

a. NICE guidances do not recommend use of hyperbaric oxygen for diabetic foot ulcers or for treatment of multiple sclerosis
b. Other indications for use of hyperbaric oxygen were not reviewed

3) Other policies

a. CMS 2006

i. Covers hyperbaric oxygen for the following indications:
1. Acute carbon monoxide intoxication
2. Decompression illness
3. Gas embolism

4. Gas gangrene
5. Acute traumatic peripheral ischemia. HBO therapy is a valuable adjunctive treatment to be used in combination with accepted standard therapeutic measures when loss of function, limb, or life is threatened.
6. Crush injuries and suturing of severed limbs. As in the previous conditions, HBO therapy would be an adjunctive treatment when loss of function, limb, or life is threatened.
7. Progressive necrotizing infections (necrotizing fasciitis)
8. Acute peripheral arterial insufficiency
9. Preparation and preservation of compromised skin grafts (not for primary management of wounds)
10. Chronic refractory osteomyelitis, unresponsive to conventional medical and surgical management
11. Osteoradionecrosis as an adjunct to conventional treatment
12. Soft tissue radionecrosis as an adjunct to conventional treatment
13. Cyanide poisoning
14. Actinomycosis, only as an adjunct to conventional therapy when the disease process is refractory to antibiotics and surgical treatment
15. Diabetic wounds of the lower extremities in patients who meet the following three criteria:
    a. Patient has type I or type II diabetes and has a lower extremity wound that is due to diabetes;
    b. Patient has a wound classified as Wagner grade III or higher; and
    c. Patient has failed an adequate course of standard wound therapy.

ii. Non-covered indications:

1. Cutaneous, decubitus, and stasis ulcers
2. Chronic peripheral vascular insufficiency
3. Anaerobic septicemia and infection other than clostridial
4. Skin burns (thermal)
5. Senility
6. Myocardial infarction
7. Cardiogenic shock
8. Sickle cell anemia
9. Acute thermal and chemical pulmonary damage, i.e., smoke inhalation with pulmonary insufficiency
10. Acute or chronic cerebral vascular insufficiency

11. Hepatic necrosis
12. Aerobic septicemia
13. Nonvascular causes of chronic brain syndrome (Pick's disease, Alzheimer's disease, Korsakoff's disease)
14. Tetanus
15. Systemic aerobic infection
16. Organ transplantation
17. Organ storage
18. Pulmonary emphysema
19. Exceptional blood loss anemia
20. Multiple Sclerosis
21. Arthritic Diseases
22. Acute cerebral edema

4) Specialty society recommendations
   - **a. Undersea and Hyperbaric Medical Society**
     - **i.** Air or gas embolism
     - **ii.** Carbon monoxide poisoning
     - **iii.** Clostridial Myositis and Myonecrosis (Gas Gangrene)
     - **iv.** Crush Injury, Compartment Syndrome and Other Acute Traumatic Ischemias
     - **v.** Decompression Sickness
     - **vi.** Arterial Insufficiencies:
       1. **1.** Central Retinal Artery Occlusion
       2. **2.** Enhancement of Healing In Selected Problem Wounds
     - **vii.** Severe Anemia
     - **viii.** Intracranial Abscess
     - **ix.** Necrotizing Soft Tissue Infections
     - **x.** Osteomyelitis (Refractory)
     - **xi.** Delayed Radiation Injury (Soft Tissue and Bony Necrosis)
     - **xii.** Compromised Grafts and Flaps
     - **xiii.** Acute Thermal Burn Injury
     - **xiv.** Idiopathic Sudden Sensorineural Hearing Loss

HERC Staff recommendations

1) Changes to current Prioritized List in ICD-9 as shown in first table below for implementation October 1, 2012
    a. Do not include diabetic ulcers per NICE review
    b. Add guideline as shown below
    c. Note: all conditions recommended for addition are recommendations of the European Consensus Conference and also are included for coverage by CMS. Conditions recommended by the European Consensus Conference but not by CMS (i.e. neuroblastoma, skin burns, sudden deafness, venous ulcers) are not recommended for addition
2) Changes to Prioritized List in ICD-10 as shown in second table below for implementation with the Biennial Review List in October, 2014 (tentative)
3) Consider combining the two hyperbaric oxygen lines into one line
    a. Placement location would need discussion
    b. Recommendation(s) for line placement unable to be made by HERC staff; no expert input available
    c. Current line scoring:
        i. Line Ranking—line 358

Score	Category	HLY	Suffering	Pop Effects	Vulnerable Pop	Tertiary Prev	Effectiveness	Need For Services	Net Cost	Text
2.7	6	7	3	0	0	2	2	1	1	**960**

        ii. Line ranking—line 399

Score	Category	HLY	Suffering	Pop Effects	Vulnerable Pop	Tertiary Prev	Effectiveness	Need For Services	Net Cost	Text
2.7	6	4	1	0	0	0	3	1	2	**600**

GUIDELINE NOTE XXX HYPERBARIC OXYGEN

Lines 358, 399

Hyperbaric oxygen is a covered services for pairing with 526.4 for osteomyelitis of the jaw only; 526.89/M27.8 for osteoradionecrosis of the jaw only; 639.0, 670.02, and 670.04/O08.0, M60.000-M60.09 only if the infection is a necrotizing soft-tissue infection; 730.10-9/M46.20-M46.39, M86.9 only for chronic refractory osteomyelitis unresponsive to conventional medical and surgical management; 927-929 only for posttraumatic crush injury of Gustilo type III B and C; 990/T66.xxxA only for osteoradionecrosis; 996.7/T82.898A, T82.9xxA, T83.89xA, T83.9xxA, T84.89xA, T84.9xxA, T85.89xA, T859xxA only for compromised myocutaneous flaps.

Line 358 Recommended Changes to Prioritized List effective October 1, 2012 in ICD-9 Format

ICD-9 Code	Code description	Recommendation	Comments
040.0	Gas gangrene	Keep	
526.4	Inflammatory conditions of jaw	Keep	Includes chronic osteomyelitis of the jaw, see guideline
526.89	Other specified diseases of the jaws	Keep	Includes osteoradionecrosis of jaw, see guideline
639.0	Genital tract and pelvic infection following abortion or ectopic and molar pregnancies	Keep	With limitation in guideline to necrotizing soft tissue infection
639.6	Embolism following abortion or ectopic and molar pregnancies	DELETE	Air embolism only treatable type of embolism with hyperbaric oxygen; covered under 673.00
670.02	Major puerperal infection, delivered, with mention of postpartum complication	Keep	With limitation in guideline to necrotizing soft tissue infection
670.04	Major puerperal infection, postpartum condition or complication	Keep	With limitation in guideline to necrotizing soft tissue infection
673.00-4	Obstetrical air embolism	Keep	
686.00	Pyoderma, unspecified	DELETE	Broad category; only gangrenosum would be considered necrotizing
686.01	Pyoderma gangrenosum	Keep	
686.09	Other pyoderma	DELETE	See 686.00 above
709.3	Degenerative skin disorders	DELETE	Includes calcinosis; colloid milium; skin degeneration; skin deposits; senile dermatosis NOS; subcutaneous calcification
728.86	*Necrotizing fasciitis*	ADD	Currently on line 250
730.10-9	*Chronic osteomyelitis*	Added previously	See guideline with CMS

			limitations
730.91-99	Unspecified infection of bone	DELETE	Also on line 271; ICD-9 specifies not to be used for chronic osteomyelitis
785.4	Gangrene	Keep	
927-929	Crush injuries of extremities and multiple sites	ADD	On line 142; add with guideline
958.0	Air embolism	Keep	
990	Effects of radiation, unspecified	Keep	Keep with guideline restricting to osteoradionecrosis
996.52	Mechanical complication due to graft of other tissue, not elsewhere classified	Keep	Applies to skin graft failure or rejection
996.70-79	Other complications due to device, implant, and graft	Keep	With guideline restricting to use with compromised myocutaneous flaps
999.1	Air embolism as a complication of medical care, not elsewhere classified	Keep	

Line 399

ICD-9 Codes	Code description	Recommendation	Notes
986	Toxic effect of carbon monoxide	Keep	Consider guideline with European consensus conference recommended restrictions
987.0-9	Toxic effect of gas	DELETE	Not included in European consensus conference recommendations or CMS coverage guidance
993.3	Caisson disease (aka decompression sickness)	Keep	

Recommended Changes to Prioritized List effective October 1, 2014 in ICD-10 Format

frmOPLICD10			
Code	**Description**	**Recommendation**	**txtMpTp**
A34	Obstetrical tetanus	DELETE	
A48.0	Gas gangrene		
E08.52	Diabetes mellitus due to underlying condition with diabetic peripheral angiopathy with gangrene	DELETE	
E09.52	Drug or chemical induced diabetes mellitus with diabetic peripheral angiopathy with gangrene	DELETE	
E13.52	Other specified diabetes mellitus with diabetic peripheral angiopathy with gangrene	DELETE	
I70.361	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with gangrene, right leg		
I70.362	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with gangrene, left leg		
I70.363	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with gangrene, bilateral legs		
I70.368	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with gangrene, other extremity		
I70.369	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with gangrene, unspecified extremity		
I70.461	Atherosclerosis of autologous vein bypass graft(s) of the extremities with gangrene, right leg		
I70.462	Atherosclerosis of autologous vein bypass graft(s) of the extremities with gangrene, left leg		
I70.463	Atherosclerosis of autologous vein bypass graft(s) of the extremities with gangrene, bilateral legs		
I70.468	Atherosclerosis of autologous vein bypass graft(s) of the extremities with gangrene, other extremity		
I70.469	Atherosclerosis of autologous vein bypass graft(s) of the extremities with		

frmOPLICD10			
Code	**Description**	**Recommendation**	**txtMpTp**
	gangrene, unspecified extremity		
I70.561	Atherosclerosis of nonautologous biological bypass graft(s) of the extremities with gangrene, right leg		
I70.562	Atherosclerosis of nonautologous biological bypass graft(s) of the extremities with gangrene, left leg		
I70.563	Atherosclerosis of nonautologous biological bypass graft(s) of the extremities with gangrene, bilateral legs		
I70.568	Atherosclerosis of nonautologous biological bypass graft(s) of the extremities with gangrene, other extremity		
I70.569	Atherosclerosis of nonautologous biological bypass graft(s) of the extremities with gangrene, unspecified extremity		
I70.661	Atherosclerosis of nonbiological bypass graft(s) of the extremities with gangrene, right leg		
I70.662	Atherosclerosis of nonbiological bypass graft(s) of the extremities with gangrene, left leg		
I70.663	Atherosclerosis of nonbiological bypass graft(s) of the extremities with gangrene, bilateral legs		
I70.668	Atherosclerosis of nonbiological bypass graft(s) of the extremities with gangrene, other extremity		
I70.669	Atherosclerosis of nonbiological bypass graft(s) of the extremities with gangrene, unspecified extremity		
I70.761	Atherosclerosis of other type of bypass graft(s) of the extremities with gangrene, right leg		
I70.762	Atherosclerosis of other type of bypass graft(s) of the extremities with gangrene, left leg		
I70.763	Atherosclerosis of other type of bypass graft(s) of the extremities with gangrene, bilateral legs		
I70.768	Atherosclerosis of other type of bypass graft(s) of the extremities with gangrene,		

frmOPLICD10			
Code	**Description**	**Recommendation**	**txtMpTp**
	other extremity		
I70.769	Atherosclerosis of other type of bypass graft(s) of the extremities with gangrene, unspecified extremity		
I96	Gangrene, not elsewhere classified		
L08.0	Pyoderma	DELETE	
L08.81	Pyoderma vegetans	DELETE	
L08.89	Other specified local infections of the skin and subcutaneous tissue	DELETE	
L88	Pyoderma gangrenosum		
M27.8	Other specified diseases of jaws		See guideline
M46.20	Osteomyelitis of vertebra, site unspecified		See guideline
M46.21	Osteomyelitis of vertebra, occipito-atlanto-axial region		See guideline
M46.22	Osteomyelitis of vertebra, cervical region		See guideline
M46.23	Osteomyelitis of vertebra, cervicothoracic region		See guideline
M46.24	Osteomyelitis of vertebra, thoracic region		See guideline
M46.25	Osteomyelitis of vertebra, thoracolumbar region		See guideline
M46.26	Osteomyelitis of vertebra, lumbar region		See guideline
M46.27	Osteomyelitis of vertebra, lumbosacral region		See guideline
M46.28	Osteomyelitis of vertebra, sacral and sacrococcygeal region		See guideline
M46.30	Infection of intervertebral disc (pyogenic), site unspecified		See guideline
M46.31	Infection of intervertebral disc (pyogenic), occipito-atlanto-axial region		See guideline
M46.32	Infection of intervertebral disc (pyogenic), cervical region		See guideline
M46.33	Infection of intervertebral disc (pyogenic), cervicothoracic region		See guideline
M46.34	Infection of intervertebral disc (pyogenic), thoracic region		See guideline
M46.35	Infection of intervertebral disc (pyogenic), thoracolumbar region		See guideline

frmOPLICD10			
Code	**Description**	**Recommendation**	**txtMpTp**
M46.36	Infection of intervertebral disc (pyogenic), lumbar region		See guideline
M46.37	Infection of intervertebral disc (pyogenic), lumbosacral region		See guideline
M46.38	Infection of intervertebral disc (pyogenic), sacral and sacrococcygeal region		See guideline
M46.39	Infection of intervertebral disc (pyogenic), multiple sites in spine		See guideline
M60.000	Infective myositis, unspecified right arm		See guideline
M60.001	Infective myositis, unspecified left arm		See guideline
M60.002	Infective myositis, unspecified arm		See guideline
M60.003	Infective myositis, unspecified right leg		See guideline
M60.004	Infective myositis, unspecified left leg		See guideline
M60.005	Infective myositis, unspecified leg		See guideline
M60.011	Infective myositis, right shoulder		See guideline
M60.012	Infective myositis, left shoulder		See guideline
M60.019	Infective myositis, unspecified shoulder		See guideline
M60.021	Infective myositis, right upper arm		See guideline
M60.022	Infective myositis, left upper arm		See guideline
M60.029	Infective myositis, unspecified upper arm		See guideline
M60.031	Infective myositis, right forearm		See guideline
M60.032	Infective myositis, left forearm		See guideline
M60.039	Infective myositis, unspecified forearm		See guideline
M60.041	Infective myositis, right hand		See guideline
M60.042	Infective myositis, left hand		See guideline
M60.043	Infective myositis, unspecified hand		See guideline
M60.044	Infective myositis, right finger(s)		See guideline

frmOPLICD10			
Code	**Description**	**Recommendation**	**txtMpTp**
M60.045	Infective myositis, left finger(s)		See guideline
M60.046	Infective myositis, unspecified finger(s)		See guideline
M60.051	Infective myositis, right thigh		See guideline
M60.052	Infective myositis, left thigh		See guideline
M60.059	Infective myositis, unspecified thigh		See guideline
M60.061	Infective myositis, right lower leg		See guideline
M60.062	Infective myositis, left lower leg		See guideline
M60.069	Infective myositis, unspecified lower leg		See guideline
M60.070	Infective myositis, right ankle		See guideline
M60.071	Infective myositis, left ankle		See guideline
M60.072	Infective myositis, unspecified ankle		See guideline
M60.073	Infective myositis, right foot		See guideline
M60.074	Infective myositis, left foot		See guideline
M60.075	Infective myositis, unspecified foot		See guideline
M60.076	Infective myositis, right toe(s)		See guideline
M60.077	Infective myositis, left toe(s)		See guideline
M60.078	Infective myositis, unspecified toe(s)		See guideline
M60.08	Infective myositis, other site		See guideline
M60.09	Infective myositis, multiple sites		See guideline
M72.6	Necrotizing fasciitis	ADD	
M86.9	Osteomyelitis, unspecified		See guideline
O08.0	Genital tract and pelvic infection following ectopic and molar pregnancy		See guideline
O08.2	Embolism following ectopic and molar pregnancy	DELETE	

frmOPLICD10			
Code	**Description**	**Recommendation**	**txtMpTp**
O08.82	Sepsis following ectopic and molar pregnancy	DELETE	
O88.011	Air embolism in pregnancy, first trimester		
O88.012	Air embolism in pregnancy, second trimester		
O88.013	Air embolism in pregnancy, third trimester		
O88.019	Air embolism in pregnancy, unspecified trimester		
O88.02	Air embolism in childbirth		
O88.03	Air embolism in the puerperium		
S47	Crush injury, upper arm	ADD	
S57	Crush injury, lower arm	ADD	
S67	Crush injury, hand/wrist/fingers	ADD	
S77	Crush injury, hip and thigh	ADD	
S87	Crush injury, leg	ADD	
S97	Crush injury, foot and toes	ADD	
T58	Toxic effects of carbon monoxide	ADD	
T66.xxxA	Radiation sickness, unspecified, initial encounter		See guideline
T79.0xxA	Air embolism (traumatic), initial encounter		
T80.0xxA	Air embolism following infusion, transfusion and therapeutic injection, initial encounter		
T82.818A	Embolism of vascular prosthetic devices, implants and grafts, initial encounter	DELETE	
T82.828A	Fibrosis of vascular prosthetic devices, implants and grafts, initial encounter	DELETE	
T82.838A	Hemorrhage of vascular prosthetic devices, implants and grafts, initial encounter	DELETE	
T82.848A	Pain from vascular prosthetic devices, implants and grafts, initial encounter	DELETE	
T82.857A	Stenosis of cardiac prosthetic devices, implants and grafts, initial encounter	DELETE	
T82.858A	Stenosis of vascular prosthetic devices, implants and grafts, initial encounter	DELETE	

frmOPLICD10			
Code	**Description**	**Recommendation**	**txtMpTp**
T82.867A	Thrombosis of cardiac prosthetic devices, implants and grafts, initial encounter	DELETE	
T82.868A	Thrombosis of vascular prosthetic devices, implants and grafts, initial encounter	DELETE	
T82.897A	Other specified complication of cardiac prosthetic devices, implants and grafts, initial encounter	DELETE	
T82.898A	Other specified complication of vascular prosthetic devices, implants and grafts, initial encounter		See guideline
T82.9xxA	Unspecified complication of cardiac and vascular prosthetic device, implant and graft, initial encounter		See guideline
T83.81xA	Embolism of genitourinary prosthetic devices, implants and grafts, initial encounter	DELETE	
T83.82xA	Fibrosis of genitourinary prosthetic devices, implants and grafts, initial encounter	DELETE	
T83.83xA	Hemorrhage of genitourinary prosthetic devices, implants and grafts, initial encounter	DELETE	
T83.84xA	Pain from genitourinary prosthetic devices, implants and grafts, initial encounter	DELETE	
T83.85xA	Stenosis of genitourinary prosthetic devices, implants and grafts, initial encounter	DELETE	
T83.86xA	Thrombosis of genitourinary prosthetic devices, implants and grafts, initial encounter	DELETE	
T83.89xA	Other specified complication of genitourinary prosthetic devices, implants and grafts, initial encounter		See guideline
T83.9xxA	Unspecified complication of genitourinary prosthetic device, implant and graft, initial encounter		See guideline
T84.81xA	Embolism due to internal orthopedic prosthetic devices, implants and grafts, initial encounter	DELETE	
T84.82xA	Fibrosis due to internal orthopedic prosthetic devices, implants and grafts, initial encounter	DELETE	

frmOPLICD10			
Code	**Description**	**Recommendation**	**txtMpTp**
T84.83xA	Hemorrhage due to internal orthopedic prosthetic devices, implants and grafts, initial encounter	DELETE	
T84.84xA	Pain due to internal orthopedic prosthetic devices, implants and grafts, initial encounter	DELETE	
T84.85xA	Stenosis due to internal orthopedic prosthetic devices, implants and grafts, initial encounter	DELETE	
T84.86xA	Thrombosis due to internal orthopedic prosthetic devices, implants and grafts, initial encounter	DELETE	
T84.89xA	Other specified complication of internal orthopedic prosthetic devices, implants and grafts, initial encounter		See guideline
T84.9xxA	Unspecified complication of internal orthopedic prosthetic device, implant and graft, initial encounter		See guideline
T85.81xA	Embolism due to internal prosthetic devices, implants and grafts, not elsewhere classified, initial encounter	DELETE	
T85.82xA	Fibrosis due to internal prosthetic devices, implants and grafts, not elsewhere classified, initial encounter	DELETE	
T85.83xA	Hemorrhage due to internal prosthetic devices, implants and grafts, not elsewhere classified, initial encounter	DELETE	
T85.84xA	Pain due to internal prosthetic devices, implants and grafts, not elsewhere classified, initial encounter	DELETE	
T85.85xA	Stenosis due to internal prosthetic devices, implants and grafts, not elsewhere classified, initial encounter	DELETE	
T85.86xA	Thrombosis due to internal prosthetic devices, implants and grafts, not elsewhere classified, initial encounter	DELETE	
T85.89xA	Other specified complication of internal prosthetic devices, implants and grafts, not elsewhere classified, initial encounter		See guideline
T85.9xxA	Unspecified complication of internal prosthetic device, implant and graft, initial encounter		See guideline

frmOPLICD10			
Code	**Description**	**Recommendation**	**txtMpTp**
T86.820	Skin graft (allograft) rejection		
T86.821	Skin graft (allograft) (autograft) failure		
T86.822	Skin graft (allograft) (autograft) infection		
T86.828	Other complications of skin graft (allograft) (autograft)		
T86.829	Unspecified complication of skin graft (allograft) (autograft)		

Line 399 ICD-10 recommendations

ICD-10 Code	**Code description**	**Recommendation**	**Comments**
T53.5	Toxic effect of chlorofluorocarbons	DELETE	
T57.3	Toxic effect of hydrogen cyanide	DELETE	
T58	Toxic effect of carbon monoxide		
T59.0	Toxic effect of nitrogen oxides	DELETE	
T59.1	Toxic effect of sulfur dioxide	DELETE	
T59.2	Toxic effect of formaldehyde	DELETE	
T59.3	Toxic effect of lacrimogenic gas	DELETE	
T59.4	Toxic effect of chlorine gas	DELETE	
T59.5	Toxic effect of fluorine gas and hydrogen fluoride	DELETE	
T59.6	Toxic effect of hydrogen sulfide	DELETE	
T59.7	Toxic effect of carbon dioxide	DELETE	
T59.8	Toxic effect of other specified gases	DELETE	
T59.9	Toxic effect of unspecified gases	DELETE	
T70.3xxA	Caisson disease [decompression sickness]		

HTA programme: Systematic Review 2 - July 2008

The clinical and cost effectiveness of hyperbaric oxygen therapy

Authors: Ritchie K, Baxter S, Craig J, Macpherson K, Mandava L, McIntosh H, Wilson S

1 EXECUTIVE SUMMARY

A review of the range of conditions for which hyperbaric oxygen therapy (HBOT) should be used was commissioned following discussion among the UK Public Health Specialist Commissioner Group regarding National Health Service (NHS) provision of the intervention.

Hyperbaric chambers have been used to treat the effects of decompression illness since the nineteenth century, with HBOT being introduced for the condition in the early twentieth century. HBOT has subsequently been utilised for the treatment of a wide range of medical conditions for which the theoretical basis and/or the evidence of effectiveness is not convincing. The United Kingdom (UK) Department of Health and a number of professional groups have provided guidance on conditions for which they consider HBOT to be appropriate standard care or adjunctive therapy.

This review was based on a horizon scanning report produced by the Agency for Healthcare Research and Quality (AHRQ), USA[1] and attempted to identify all indications for which HBOT has been suggested as an appropriate intervention. Literature searches for reports on the clinical and/or cost effectiveness of HBOT were conducted to identify primary and secondary literature, for the period from 2005 (when the AHRQ report was published) to July 2007. Paediatric studies and reports published in languages other than English were excluded from literature searches. Reports considering the safety of HBOT were included.

A large body of published literature was identified, obtained and critically appraised. The review highlighted a number of practical and methodological challenges when assessing an intervention applicable to such a wide range of conditions. These included: management of the large volume of published reports; appropriate application of evidence hierarchies; appropriate methods for synthesising secondary literature; and making robust recommendations when data are sparse or non-existent.

Randomised controlled trial (RCT) evidence is generally considered to be the gold standard for assessing the efficacy of healthcare interventions. RCT evidence was not available for a substantial number of the HBOT treatment indications. However RCTs may be considered inappropriate for some conditions, such as decompression illness where the theoretical rationale for therapy is accepted. For those conditions where RCTs had been conducted, the quality or reporting of many trials was considered too poor to provide robust conclusions. As a result, therapeutic efficacy was suggested for a number of HBOT indications but rigorous testing is required to confirm the findings. For the majority of conditions considered within this report it is concluded that there is insufficient evidence to support the routine use of HBOT. For some conditions observational studies have suggested that HBOT may be of some benefit, but conclusive evidence in the form of RCTs is required. A large number of such trials are currently underway and this should provide a better evidence base.

The cost-effectiveness evidence base was limited, with economic evaluations having been carried out for only a few conditions. This review found that most of the cost–effectiveness evidence on HBOT relates to the treatment of diabetic foot ulcers.

A summary of the findings of this review is presented in Table 2.1-1.

Table 2.1-1 Summary of HBOT HTA findings

Condition	European consensus conference recommendations[2]	Report findings	Section
Decompression illness	Major accidents should be treated using hyperoxygenation tables at moderate or high pressure. Minor accidents (pain only) should be treated with recompression tables at a maximum of 2.8 atmospheres absolute (ATA).	Empirical evidence together with the theoretical basis and clinical consensus supports the use of HBOT as standard care.	4.2
Gas embolism	HBOT strongly recommended.	Empirical evidence is lacking, but the theoretical basis and clinical consensus supports the use of HBOT as standard care in severe cases.	4.2
Carbon monoxide (CO) poisoning	HBOT is strongly recommended for patients with diagnosed CO poisoning, who are at high risk (unconscious; clinical neurological, cardiac, respiratory or psychological symptoms; pregnant women) of immediate or long-term complications.	Empirical evidence together with theoretical basis and clinical consensus supports the use of HBOT as part of algorithms for the management of CO poisoning.	4.3

National Coverage Determination (NCD) for Hyperbaric Oxygen Therapy (20.29)

Effective Date: 6/19/2006

For purposes of coverage under Medicare, hyperbaric oxygen (HBO) therapy is a modality in which the entire body is exposed to oxygen under increased atmospheric pressure.

Indications and Limitations of Coverage

A. Covered Conditions

Program reimbursement for HBO therapy will be limited to that which is administered in a chamber (including the one man unit) and is limited to the following conditions:

1. Acute carbon monoxide intoxication,
2. Decompression illness,
3. Gas embolism,
4. Gas gangrene,
5. Acute traumatic peripheral ischemia. HBO therapy is a valuable adjunctive treatment to be used in combination with accepted standard therapeutic measures when loss of function, limb, or life is threatened.
6. Crush injuries and suturing of severed limbs. As in the previous conditions, HBO therapy would be an adjunctive treatment when loss of function, limb, or life is threatened.
7. Progressive necrotizing infections (necrotizing fasciitis),
8. Acute peripheral arterial insufficiency,
9. Preparation and preservation of compromised skin grafts (not for primary management of wounds),
10. Chronic refractory osteomyelitis, unresponsive to conventional medical and surgical management,
11. Osteoradionecrosis as an adjunct to conventional treatment,
12. Soft tissue radionecrosis as an adjunct to conventional treatment,
13. Cyanide poisoning,
14. Actinomycosis, only as an adjunct to conventional therapy when the disease process is refractory to antibiotics and surgical treatment,
15. Diabetic wounds of the lower extremities in patients who meet the following three criteria:
    a. Patient has type I or type II diabetes and has a lower extremity wound that is due to diabetes;
    b. Patient has a wound classified as Wagner grade III or higher; and
    c. Patient has failed an adequate course of standard wound therapy.

The use of HBO therapy is covered as adjunctive therapy only after there are no measurable signs of healing for at least 30 –days of treatment with standard wound therapy and must be used in addition to standard wound care. Standard wound care in patients with diabetic wounds includes: assessment of a patient's vascular status and correction of any vascular problems in the affected limb if possible, optimization of nutritional status, optimization of glucose control,

debridement by any means to remove devitalized tissue, maintenance of a clean, moist bed of granulation tissue with appropriate moist dressings, appropriate off-loading, and necessary treatment to resolve any infection that might be present. Failure to respond to standard wound care occurs when there are no measurable signs of healing for at least 30 consecutive days. Wounds must be evaluated at least every 30 days during administration of HBO therapy. Continued treatment with HBO therapy is not covered if measurable signs of healing have not been demonstrated within any 30-day period of treatment.

B. Noncovered Conditions

All other indications not specified under §270.4(A) are not covered under the Medicare program. No program payment may be made for any conditions other than those listed in §270.4(A). No program payment may be made for HBO in the treatment of the following conditions:

1. Cutaneous, decubitus, and stasis ulcers.
2. Chronic peripheral vascular insufficiency.
3. Anaerobic septicemia and infection other than clostridial.
4. Skin burns (thermal).
5. Senility.
6. Myocardial infarction.
7. Cardiogenic shock.
8. Sickle cell anemia.
9. Acute thermal and chemical pulmonary damage, i.e., smoke inhalation with pulmonary insufficiency.
10. Acute or chronic cerebral vascular insufficiency.
11. Hepatic necrosis.
12. Aerobic septicemia.
13. Nonvascular causes of chronic brain syndrome (Pick's disease, Alzheimer's disease, Korsakoff's disease).
14. Tetanus.
15. Systemic aerobic infection.
16. Organ transplantation.
17. Organ storage.
18. Pulmonary emphysema.
19. Exceptional blood loss anemia.
20. Multiple Sclerosis.
21. Arthritic Diseases.
22. Acute cerebral edema.

C. Topical Application of Oxygen

This method of administering oxygen does not meet the definition of HBO therapy as stated above. Also, its clinical efficacy has not been established. Therefore, no Medicare reimbursement may be made for the topical application of oxygen.

National Institute for Health and Clinical Excellence

Diabetic foot problems

Inpatient management of diabetic foot problems

Issued: March 2011

NICE clinical guideline 119

www.nice.org.uk/cg119

Introduction

This guidance has been incorporated into the diabetes NICE Pathway, along with other related guidance and products.

Topic

Diabetes is one of the biggest health challenges facing the UK today. In 2010, 2.3 million people in the UK were registered as having diabetes, while the number of people estimated as having either type 1 or type 2 diabetes was 3.1 million. By 2030 it is estimated that more than 4.6 million people will have diabetes (Diabetes UK, 2010).

As the longevity of the population increases, the incidence of diabetes-related complications also increases (Anderson and Roukis, 2007). Among the complications of diabetes are foot problems, the most common cause of non traumatic limb amputation (Boulton et al, 2005). The feet of people with diabetes can be affected by neuropathy, peripheral arterial disease, foot deformity, infections, ulcers and gangrene.

Diabetic foot problems have a significant financial impact on the NHS through outpatient costs, increased bed occupancy and prolonged stays in hospital. In addition, diabetic foot problems have a significant impact on patients' quality of life; for example, reduced mobility that may lead to loss of employment, depression and damage to or loss of limbs. Diabetic foot problems require urgent attention. A delay in diagnosis and management increases morbidity and mortality and contributes to a higher amputation rate (Reiber et al, 1999).

The common clinical features of diabetic foot problems include infection, osteomyelitis, neuropathy, peripheral arterial disease and Charcot arthropathy.

Laboratory evaluations include blood tests, different imaging techniques, microbiological and histological investigations, but currently there is no guidance on which tests are the most accurate and cost effective.

The primary objective in managing diabetic foot problems is to promote mobilisation. This involves managing both medical and surgical problems and involving a range of medical experts in related fields (Bridges et al, 1994).

Undersea and Hyperbaric Medical Society

Indications for Hyperbaric Oxygen Therapy

Hyperbaric oxygen (HBO_2) is a treatment, in which a patient breathes 100% oxygen intermittently while inside a treatment chamber at a pressure higher than sea level pressure (i.e., >1 atmosphere absolute; atm abs). It can be viewed as the new application of an old, established technology to help resolve certain recalcitrant, expensive, or otherwise hopeless medical problems. In certain circumstances, it represents the primary treatment modality while in others it is an adjunct to surgical or pharmacologic interventions.

Treatment can be carried out in either a mono- or multiplace chamber. The former accommodates a single patient; the entire chamber is pressurized with 100% oxygen, and the patient breathes the ambient chamber oxygen directly. The latter holds two or more people (patients, observers, and/or support personnel); the chamber is pressurized with compressed air while the patients breathe 100% oxygen via masks, head hoods, or endotracheal tubes. According to the UHMS definition and the determination of The Centers for Medicare and Medicaid Services (CMS) and other third party carriers, breathing 100% oxygen at 1 atmosphere of pressure or exposing isolated parts of the body to 100% oxygen does not constitute HBO_2 therapy. The patient must receive the oxygen by inhalation within a pressurized chamber. Current information indicates that pressurization should be to 1.4 atm abs or higher.

The following indications are approved uses of hyperbaric oxygen therapy as defined by the Hyperbaric Oxygen Therapy Committee. The Committee Report can be purchased directly through the UHMS.

INDICATIONS:

1. Air or Gas Embolism
2. Carbon Monoxide Poisoning

Carbon Monoxide Poisoning Complicated By Cyanide Poisoning

3. Clostridial Myositis and Myonecrosis (Gas Gangrene)
4. Crush Injury, Compartment Syndrome and Other Acute Traumatic Ischemias
5. Decompression Sickness
6. Arterial Insufficiencies:

Central Retinal Artery Occlusion

Enhancement of Healing In Selected Problem Wounds

7. Severe Anemia
8. Intracranial Abscess
9. Necrotizing Soft Tissue Infections
10. Osteomyelitis (Refractory)
11. Delayed Radiation Injury (Soft Tissue and Bony Necrosis)
12. Compromised Grafts and Flaps
13. Acute Thermal Burn Injury
14. Idiopathic Sudden Sensorineural Hearing Loss (New! approved on October 8, 2011 by the UHMS Board of Directors)

Dysfunction Lines

Question: Should the current Dysfunction Line format be continued for the 2014 Biennial Review Prioritized List?

Question source: HERC staff

Issue: Currently, there are 4 dysfunction lines on the Prioritized List:

78 NEUROLOGICAL DYSFUNCTION IN BREATHING, EATING, SWALLOWING, BOWEL, OR BLADDER CONTROL CAUSED BY CHRONIC CONDITIONS
318 NEUROLOGICAL DYSFUNCTION IN POSTURE AND MOVEMENT CAUSED BY CHRONIC CONDITIONS
375 NEUROLOGICAL DYSFUNCTION IN COMMUNICATION CAUSED BY CHRONIC CONDITIONS
407 DYSFUNCTION RESULTING IN LOSS OF ABILITY TO MAXIMIZE LEVEL OF INDEPENDENCE IN SELF- DIRECTED CARE CAUSED BY CHRONIC CONDITIONS THAT CAUSE NEUROLOGICAL DYSFUNCTION

As part of the biennial review of the List, HERC staff would like the current Dysfunction Line structure discussed. Options for future Lists include 1) continuing the current 4 line structure, 2) reducing the dysfunction lines to a single line to be titled "Dysfunction resulting in loss of function" or similar, 3) making some other change to the lines, such as reducing to 2 lines.

Additionally, the approximate location of these lines on the List is open to review.

The current Dysfunction Lines have multiple diagnoses and treatments on them, some of which are likely inappropriate. However, a comprehensive review of these lines is not possible at this time due to time constraints. Once the line structure for these lines is determined, then HERC staff will work to review the contents of these lines for future HERC review.

Expert input

From Tina Kitchen, MD, Medical Director

> The number and structure of the lines has been debated many times without a clear winner. I don't know if there is a benefit in collapsing them. In fact, those that are more highly placed can have life/death consequences and the lower/est ones don't. I also don't know if it is easier to place guidelines or benefit limits on separated lines vs collapsed.
>
> Just to state the obvious: the purpose of the lines was a place to "park" those services for the end-stage condition of disability, regardless of the original cause. So that someone who needs a W/C originally because of an unfunded condition would have the same access to a W/C as some who has a funded causing-condition.

Recommendations:

1) Discuss the number and type(s) of Dysfunction Lines which should be included in the biennial review List
2) Discuss possible changes to Dysfunction Line placement

Intestinal enzyme deficiencies – nonfatal

Question: How should Line 370 be ranked with the removal of the higher morbidity/mortality enzyme deficiency diagnoses?

Issue: As part of the ICD-10 review, the pediatric metabolic specialists recommended removing a series of codes from Line 370 to a higher line, given the associated morbidity. Line 370 now needs to be reexamined given the removal of these codes.

Issue Source: ICD -10 consultants, HERC Staff

Current Prioritized List Status

Line 370 INTESTINAL DISACCHARIDASE AND OTHER DEFICIENCIES

Code	Description	Comments
E72.52	Trimethylaminuria	Causes "fishy odor" when certain foods are eaten; treatment is avoidance of triggering foods. Activated charcoal and oral antibiotics may also help.
E72.53	Hyperoxaluria	Causes kidney stones. No treatment known other than renal transplant for advanced cases, with possible liver transplant
E73.0	Congenital lactase deficiency	Treatment is avoidance of dairy products or taking lactase enzyme replacements
E73.1	Secondary lactase deficiency	See above
E73.8	Other lactose intolerance	See above
E73.9	Lactose intolerance, unspecified	See above
E74.10	Disorder of fructose metabolism, unspecified	Hereditary fructose intolerance moved to higher line
E74.31	Sucrase-isomaltase deficiency	Results in diarrhea and malabsorption. Treatment is avoiding all sucrose in the diet. Artificial enzyme recently FDA approved allows limited consumption of sucrose
E74.39	Other disorders of intestinal carbohydrate absorption	Subdiagnoses include absorption problems with glucose, sucrose, or galactose

HERC decided (based on consulting pediatric metabolic experts) the following codes are to move to Line 329 DISORDERS OF AMINO-ACID TRANSPORT AND METABOLISM (NON PKU); HEREDITARY FRUCTOSE INTOLERANCE

E74.12 Hereditary fructose intolerance
E74.8 Other specified disorders of carbohydrate metabolism
E74.19 Other disorder of fructose metabolism
E74.4 Disorder of pyruvate

Current ranking for Line 370

Score	Category	HLY	Suffering	Pop Effects	Vulnerable Pop	Tertiary Prev	Effectiveness	Need For Services	Net Cost	Text65
800	7	9	1	0	0	0	4	1	4	**383**

HERC Staff Recommendations

Change:

1) Impact on Healthy Life Years from 9 to **1**
2) Effectiveness – from 4 to **2**
3) New Score 120
4) New approximate line placement **541**

DRAFT Scoring Criteria for the HERC Individual and Population Health Impact Measures

Impact on Healthy Life Years

0 – No impact on health
1 – Nonfatal with a marginal impact on health
2 – Nonfatal with a modest impact on health
3 – Nonfatal with a low probability of a significant residual effect or a high probability of a residual effect with a moderate impact on health
4 – Nonfatal with low probability (<20%) of significant disability or at least a moderate probability of a significant residual effect
5 – Nonfatal, but at least moderate (>20%) probability of significant disability (e.g., blindness); Low fatality with onset in elderly
6 – Moderately fatal with onset in elderly; low fatality with onset in middle age
7 – Highly fatal with onset in elderly; moderately fatal with onset in middle age; low fatality with onset in young adulthood
8 – Highly fatal with onset in middle aged; moderately fatal with onset in young adulthood; low fatality with onset in childhood/newborn
9 – Highly fatal with onset in young adulthood; moderately fatal with onset in childhood/newborn
10 – Highly fatal with onset in childhood/newborn

Impact on Pain and Suffering

0 – No impact on pain or suffering
1 – Intermittent pain of moderate level or frequent pain of low level and/or low level of suffering of the individual, immediate family or caregiver
2 – Frequent pain of moderate level or constant pain of low level and/or modest level of suffering of the individual, immediate family or caregiver
3 – Intermittent pain of high level or constant pain of moderate level and/or moderate level of suffering of the individual, immediate family or caregiver
4 – Frequent pain of high level and/or high level of suffering of the individual, immediate family or caregiver
5 – Constant pain of high level and/or extreme suffering of the individual, immediate family or caregiver

Population Effects

0 – No impact on population health
1 – Nontreatment would result in limited spread of a significant nonfatal disease or have a low impact on population safety (e.g. due to the nontreatment of a mental health condition)
2 – Nontreatment would result in a moderate spread of a significant nonfatal disease or have a modest impact on population safety
3 – Nontreatment would result in a limited spread of a potentially fatal disease or a wide spread of a significant nonfatal disease or have a moderate impact on population safety
4 – Nontreatment would result in a moderate spread of a potentially fatal disease or have a high impact on population safety
5 – Nontreatment would result in a wide spread of a potentially fatal disease or have a very high impact on population safety

Impact on Vulnerable Populations

0 – No impact on vulnerable populations
1 – Somewhat disproportionate impact of a condition with a moderate impact on health on one or more vulnerable populations (does not include men, women, children or pregnant women considered as separate populations or low-income individuals, since methodology is only being applied to Medicaid population at this point)
2 – Moderately disproportionate impact of a condition with a moderate impact on health on one or more vulnerable populations
3– Somewhat disproportionate impact of a condition with a significant impact on health on one or more vulnerable populations
4 – Moderately disproportionate impact of a condition with a significant impact on health on one or more vulnerable populations
5 – Highly disproportionate impact of a condition with a significant impact on health on one or more vulnerable populations

Tertiary Prevention

0 – No tertiary prevention provided by treatment and early treatment does not prevent progression of the disease
1 – Treatment will prevent of moderate complication and/or early treatment may prevent progression of the disease resulting in a moderate impact on health
2 – Low to modest likelihood that treatment will prevent a significant complication or prevent progression of the disease resulting in significant impact on health
3 –Moderate to high likelihood that treatment will prevent a significant complication or prevent progression of the disease resulting in significant impact on health
4 – Low to modest likelihood that treatment will prevent severely debilitating complication and/or early treatment with prevent progression of disease leading to severe disability or death
5 – Moderately to high likelihood that treatment will prevent severely debilitating complication and/or early treatment with prevent progression of disease leading to severe disability or death

Effectiveness

0 – No demonstrated effectiveness (<5%) or causes harm
1 - Achieves desired result in 5-25% of cases
2 - Achieves desired result in 25-50% of cases
3 – Achieves desired result in 50-75% of cases
4 – Achieves desired result in 75-95% of cases
5 – Achieves desired result in 95+% of cases

Net Cost

0 – Very high cost (>$100,000)
1 – High cost ($20,000-$100,000)
2 – Moderate cost ($5,000-$20,000) or higher cost somewhat offset by cost of treatment alternative
3 – Modest cost ($1,000-$5,000) or higher cost significantly offset by cost of treatment alternative
4 – Low cost (<$1,000) or higher cost nearly offset by cost of treatment alternative
5 – Cost savings

Hematology recommendations for ICD 10 conversion

Specialty consultants: Drs. James Gajewski and Thomas Deloughery

SPLIT LINES

1) Divide Chronic Leukemias (Line 310) into separate lines with good and poor prognosis.
    a. Good prognosis – Medical treatment for chronic myeloid leukemia (CML—should be located in the150-170 range)
        i. Can cure 95% of people with oral therapy. Very treatable.
    b. Fair prognosis -- CML should also have BMT line, but medical therapy is much more effective.
    c. Poor prognosis (low) – Remaining diagnoses in Current Line 310 – treatment up to 1 year of life at best. Down to low 400s for priority.
    d. Scoring of the newly created lines are as listed below:

        i. Chronic myeloid leukemia (CML) – Medical Therapy – highest (ICD-10 C92.10-C92.22)
        HLY=7, P&S=2, Tertiary=5, Effect=4, Need=1, Cost=0; Score=2240
        Line ~110
        ii. Acute promyelocytic leukemia (APL) – Medical Therapy – ICD-10 C92.40-C92.42
        Effectives of med tx 60-70%
        HLY=8, P&S=3, Tertiary=1, Effectiveness=3, Need=1, Cost=1; Score 1440,
        Line ~ 250
        iii. Acute myeloid leukemia (AML) – combined medical and BMT (ICD-10 C92.50-C94.6) Should be around 181 (because that line is going away).
        HLY=8, P&S=3, Tertiary=1, Effectiveness=1, Need=1, Cost=1; Score 520,
        Line ~ 425
        iv. APL – Bone Marrow Transplant – ICD-10 C92.40-C92.42 effectiveness of BMT 40-50%
        HLY=8, P&S=3, Tertiary=1, Effectiveness=2, Need=1, Cost=1; Score 960,
        Line ~ 350
        v. CML – Bone Marrow Transplant - 20% survival
        HLY=7, P&S=2, Tertiary=0, Effectiveness=2, Need=1, Cost=0; Score=720,
        Line ~380
        vi. Chronic leukemias with poor prognosis –lowest – One year survival at best
        HLY=7, P&S=2, Tertiary=0, Effect.=1, Need=1, Cost=1; Score=400,
        Line ~445

Hematology recommendations for ICD 10 conversion

COMBINE MULTIPLE LINES

1) Merge line 206 CONSTITUTIONAL APLASTIC ANEMIAS and 131 OTHER SPECIFIED APLASTIC ANEMIAS
    a. Line 1114 APLASTIC ANEMIA; AGRANULOCYTOSIS/ BONE MARROW TRANSPLANT
        i. Combination of 206 (constituitional aplastic anemias), 131 (other specified aplastic anemias) and 79 (agranulocytosis). BMT would be the longer term higher survivability compared to medical therapy.
    b. HLY=9, P&S=5, Tertiary=0, Effectiveness=4, Need=1, Cost=0; Score=2240; Line ~110

2) Merge Lines 313 CONSTITUTIONAL APLASTIC ANEMIA/MEDICAL THERAPY and aplastic anemias from 408 ANEMIAS DUE TO DISEASE OR TREATMENT AND OTHER APLASTIC ANEMIAS/MEDICAL THERAPY
    a. Line 1115 APLASTIC ANEMIA/ MEDICAL THERAPY
        i. Includes old Line 313 CONSTITUTIONAL APLASTIC ANEMIA/MEDICAL THERAPY
    b. HLY=9, P&S=5, Tertiary=0, Effectiveness=2, Need=1, Cost=0; Score=1120; Line ~325

3) Merge Lines 127 IRON DEFICIENCY ANEMIA AND OTHER NUTRITIONAL DEFICIENCIES and 128 PERNICIOUS AND SIDEROBLASTIC ANEMIA to be “NUTRITIONAL ANEMIAS”
    a. Line placement at line 127

DELETE LINES

1) Delete line 79 AGRANULOCYTOSIS, Treatment: BONE MARROW TRANSPLATATION
    a. Merge into line 1114 APLASTIC ANEMIA/BONE MARROW TRANSPLANT
2) Delete Line 280 CHRONIC NON-LYMPHOCYTIC LEUKEMIA
3) Delete Line 181 ACUTE NON-LYMPHOCYTIC LEUKEMIAS

RESCORE LINES

1) Line 198 – MULTIPLE MYELOMA - with treatment, not a cure, gives only 3-7 years.
    a) Should be prioritized lower. Should be below transplants for ALL adult or AML – done for curative. Should be below NHL, probably just above medical therapy, (258). Change effectiveness from 4 to 3 and cost from 0 to 1. Changes score from 1760 to 1320, making new rank around line 270.

Hematology recommendations for ICD 10 conversion

2) 1116 THROMBOTIC DISORDERS MEDICAL THERAPY

There is no specific treatment for thrombophilia, unless it is caused by an underlying medical illness (such as nephrotic syndrome), in which case the treatment of the underlying disease is needed. In those with unprovoked and/or recurrent thrombosis, or those with a high-risk risk form of thrombophilia (those with DVT), the most important decision is whether to use anticoagulation medications, such as warfarin, on a long-term basis to reduce the risk of further episodes. This risk needs to weighed against the risk that the treatment will cause significant bleeding, as the reported risk of major bleeding is over 3% per year, and 11% of those with major bleeding may die as a result.

HLY=6, P&S=2, Tertiary=3, Effectiveness=1, Need=0.05, Cost=2; Score=22
Line ~610

3) 1117 OTHER MYELOID DISORDERS/MEDICAL THERAPY, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY
HLY=8, P&S=3, Tertiary=1, Effectiveness=1, Need=1, Cost=1; Score=520
Line ~425

4) Rerank line 103 ACUTE LEUKEMIA, MYELODYSPLASTIC SYNDROME/BONE MARROW TRANSPLANT**.**

a) Added codes from CLL Line 280
b) Change effectiveness from 4 to 3, changing score from 2400 to 1800, moving rank to around Line 190.

5) 408 ANEMIAS DUE TO DISEASE OR TREATMENT AND OTHER APLASTIC ANEMIAS/MEDICAL THERAPY

a) Move aplastic anemias into new Line 1115
b) Move anemia due to chemotherapy to complications Line 308

Cat.=7, HLY=4, P&S=1, Tertiary=0, Effectiveness=1, Need=0.3, Cost=3; Score=30
Moves from Line 408 to around Line 600

RENAME LINES

1) LINE 102 ~~ACUTE MYELOID LEUKEMIA, MYELODYSPLASIA, AND MYELOPROLIFERATIVE DISORDERS~~ TO CHILDHOOD LEUKEMIAS
2) Line 314, Condition: Osteopetrosis. Treatment: BONE MARROW RESCUE AND TRANSPLANT
3) Line 168 from Chronic Granulomatous Disease to GRANULOCYTE DISORDERS
4) LINE 408 ANEMIAS DUE TO DISEASE ~~OR TREATMENT AND OTHER APLASTIC ANEMIAS~~/MEDICAL THERAPY

Comparison of Current Ranking of Hematologic Lines and Recommended Biennial Changes

'12 Line	Condition	Treatment
79	AGRANULOCYTOSIS	BONE MARROW TRANSPLANT
102	ACUTE LYMPHOCYTIC LEUKEMIA (CHILD)	MEDICAL THERAPY
103	ACUTE LEUKEMIAS, MYELODYSPLASTIC SYNDROME	BONE MARROW TRANSPLANT
105	HEREDITARY IMMUNE DEFICIENCIES	BONE MARROW TRANSPLANT
121	COAGULATION DEFECTS	MEDICAL THERAPY
125	HODGKIN'S DISEASE	BONE MARROW TRANSPLANT
127	IRON DEFICIENCY ANEMIA AND OTHER NUTRITIONAL DEFICIENCIES	MEDICAL THERAPY
128	PERNICIOUS AND SIDEROBLASTIC ANEMIA	MEDICAL THERAPY
131	OTHER SPECIFIED APLASTIC ANEMIAS	BONE MARROW TRANSPLANT
157	ACQUIRED HEMOLYTIC ANEMIAS	MEDICAL THERAPY
166	HODGKIN'S DISEASE	MEDICAL THERAPY
168	CHRONIC GRANULOMATOUS DISEASE	MEDICAL THERAPY
170	NON-HODGKIN'S LYMPHOMAS	BONE MARROW TRANSPLANT
181	ACUTE NON-LYMPHOCYTIC LEUKEMIAS	MEDICAL THERAPY
198	MULTIPLE MYELOMA	BONE MARROW TRANSPLANT
199	HEREDITARY ANEMIAS, HEMOGLOBINOPATHIES, AND DISORDERS OF THE SPLEEN	MEDICAL THERAPY
206	CONSTITUTIONAL APLASTIC ANEMIAS	BONE MARROW TRANSPLANT
221	NON-HODGKIN'S LYMPHOMAS	MEDICAL THERAPY
249	ACUTE LYMPHOCYTIC LEUKEMIAS (ADULT) AND MULTIPLE MYELOMA	MEDICAL THERAPY
280	CHRONIC NON-LYMPHOCYTIC LEUKEMIA	BONE MARROW TRANSPLANT

'14 Line	Condition	Treatment
97	CHILDHOOD LEUKEMIAS	MEDICAL THERAPY
99	HEREDITARY IMMUNE DEFICIENCIES	BONE MARROW TRANSPLANT
~105	CHRONIC MYELOID LEUKEMIA	MEDICAL THERAPY
~106	APLASTIC ANEMIAS; AGRANULOCYTOSIS	BONE MARROW TRANSPLANT
114	COAGULATION DEFECTS	MEDICAL THERAPY
119	HODGKIN'S DISEASE	BONE MARROW TRANSPLANT
121	NUTRITIONAL ANEMIAS	MEDICAL THERAPY
140	HODGKIN'S DISEASE	MEDICAL THERAPY
153	ACQUIRED HEMOLYTIC ANEMIAS	MEDICAL THERAPY
163	NON-HODGKIN'S LYMPHOMAS	MEDICAL THERAPY
166	GRANULOCYTE DISORDERS	MEDICAL THERAPY
168	NON-HODGKIN'S LYMPHOMAS	BONE MARROW TRANSPLANT
~190	ACUTE LEUKEMIA, MYELODYSPLASTIC SYNDROME	BONE MARROW TRANSPLANT
199	HEREDITARY ANEMIAS, HEMOGLOBINOPATHIES, AND DISORDERS OF THE SPLEEN	MEDICAL THERAPY
241	ACUTE LYMPHOCYTIC LEUKEMIAS (ADULT) AND MULTIPLE MYELOMA	MEDICAL THERAPY
~242	ACUTE PROMYELOCYTIC LEUKEMIA	MEDICAL THERAPY
~260	MULTIPLE MYELOMA	BONE MARROW TRANSPLANT
294	CHRONIC LEUKEMIAS; POLYCYTHEMIA RUBRA VERA	MEDICAL THERAPY
298	OSTEOPETROSIS	BONE MARROW RESCUE AND TRANSPLANT
~310	APLASTIC ANEMIA	MEDICAL THERAPY

Comparison of Current Ranking of Hematologic Lines and Recommended Biennial Changes

'12 Line	Condition	Treatment
310	CHRONIC LEUKEMIAS; POLYCYTHEMIA RUBRA VERA	MEDICAL THERAPY
313	CONSTITUTIONAL APLASTIC ANEMIA	MEDICAL THERAPY
314	OSTEOPETROSIS	BONE MARROW TRANSPLANT
328	THROMBOCYTOPENIA	MEDICAL & SURGICAL TREATMENT
338	DISORDERS INVOLVING THE IMMUNE SYSTEM	MEDICAL THERAPY
408	ANEMIAS DUE TO DISEASE OR TREATMENT AND OTHER APLASTIC ANEMIAS	MEDICAL THERAPY
479	DISORDERS OF PLASMA PROTEIN METABOLISM	MEDICAL THERAPY

'14 Line	Condition	Treatment
313	THROMBOCYTOPENIA	MEDICAL & SURGICAL TREATMENT
323	DISORDERS INVOLVING THE IMMUNE SYSTEM	MEDICAL THERAPY
~335	ACUTE PROMYELOCYTIC LEUKEMIA	BONE MARROW TRANSPLANT
~365	CHRONIC MYELOID LEUKEMIA	BONE MARROW TRANSPLANT
402	OTHER MYELOID DISORDERS	MEDICAL THERAPY
~410	ACUTE MYELOID LEUKEMIA	MEDICAL THERAPY & BONE MARROW TRANSPLANT
~430	OTHER CHRONIC LEUKEMIAS	BONE MARROW TRANSPLANT
461	DISORDERS OF PLASMA PROTEIN METABOLISM	MEDICAL THERAPY
~580	ANEMIAS DUE TO DISEASE	MEDICAL THERAPY
~590	THROMBOTIC DISORDERS	MEDICAL THERAPY

General Surgery ICD 10 Recommendations

Specialty consultants: Drs. Herzig, Soot, and Swensson

New areas of proposed coverage:

1) Cover symptomatic hernias
    a. Create 3 hernia lines – see separate issue summary for hernias
    b. Discontinue coverage of ventral hernias
2) Cover symptomatic cholelithiasis – see separate issue summary for cholelithiasis
    a. Create 3 cholelithiasis lines
3) Cover anal fistula
4) Cover anal fissure
5) Cover rectal prolapse

CREATE NEW LINES:

1) Create new Line – ESOPHAGITIS AND GERD; ESOPHAGEAL SPASM – should be below the funding line, adequate treatments are over the counter**.**

    This was completed in March 2012. New GERD Line 540.

A future diagnostic guideline needs to be created – this is a topic of a future EbGS coverage guidance

MERGE LINES

a. Line 177 Ruptured Spleen Repair/Splenectomy/Incision <u>into</u>
b. Line 88 Injury to internal organs Medical and Surgical Treatment

    Rationale: Ruptured spleen is an internal organ and needs similar close monitoring and surgery if indicated

DELETE LINES

<u>Line 421 ACHALASIA, NON-NEONATAL Medical and Surgical Treatment</u>

Codes all moved to other lines

Code	**Code Description**	Current Lines	**Change**

General Surgery ICD 10 Recommendations

J85.3	Abscess of mediastinum	84: DEEP ABSCESSES, INCLUDING APPENDICITIS AND PERIORBITAL ABSCESS 421: ACHALASIA, NON-NEONATAL	Moved to 84
J98.5	Diseases of mediastinum, not elsewhere classified	278: CANCER OF LUNG, BRONCHUS, PLEURA, TRACHEA, MEDIASTINUM AND OTHER RESPIRATORY ORGANS 421: ACHALASIA, NON-NEONATAL 689: RESPIRATORY CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY	Moved to 278 and 689
K22.0	Achalasia of cardia	421: ACHALASIA, NON-NEONATAL	Moved to 409
K22.4	Dyskinesia of esophagus	421: ACHALASIA, NON-NEONATAL	Moved to 692

Line 444 INCONTINENCE OF FECES; FECAL IMPACTION

Rationale: Surgically reparable fecal incontinence is usually from old obstetric injuries. This disproportionately affects the elderly. Colostomy is very effective, particularly given wound care issues with a risk of chronic infection. If someone has complications of incontinence (sacral decubiti or chronic perineal infections, then should have diverting colostomy. Sphincertoplasty, on the other hand, should NOT be covered.

Recommendations

1) Place R15.9 Full incontinence of feces on Line 78 and on Line 551.
2) Move colostomy codes to 551.
3) Rename Line 551 Treatment: Medical and Surgical Therapy
4) Do not add sphinceteroplasty codes to 551.
    a. Rationale: That way diapers are covered, but surgery for this condition would not be covered. If someone wanted a diverting colostomy, this could be covered under the comorbidity rule.
5) Move K56.41 *Fecal impaction* to Line 48 INTUSSCEPTION, VOLVULUS, INTESTINAL OBSTRUCTION, AND FOREIGN BODY IN STOMACH, INTESTINES, COLON, AND RECTUM
    a. Rationale: Fecal impaction is essentially symptomatically the same as a large bowel obstruction and places people at risk for bowel perforation.
6) R15.2 Fecal urgency and R15.0 incomplete defecation are moved to Line 551: DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS.

a. Rationale: These are more symptomatic and not as critical. There are effective medical treatments that could be taught in a single session.

RESCORE LINES

Recommend having this prioritization of conditions

Highest – anal fistula

Lowest – anal fissure vs. Incontinence of feces, but diapers should be covered

Line 506 ANAL FISTULA; CHRONIC ANAL FISSURE

Divide line into 2 lines

1) Anal fistula
    a. Rationale: Fistula should be highest (creates effective incontinence, they do not ever go away on their own). However, treatments for fissure work better than treatments for fistula.

    Proposed ranking:

    Category 7
    Impact on Healthy Life Years 3
    Pain and Suffering **increase from 1 to 2** (same as incontinence)
    Population Effects 0
    Vulnerable populations 0
    Tertiary prevention **Increase from 0 to 1** (can have recurrent abscess and ulcers)
    Effectiveness of treatment – 4
    Net cost 2
    Need for service **100** (it is a surgical disease)
    Score 480
    Approximate **Line 419**

2) Chronic anal fissure
    a. Rationale: this should be unfunded, lots of OTC treatments, can control most of them medically. Surgical treatment is very effective for fissures but 60-80% of fissures self-resolve. Fistula should not be grouped with fissures.

    Proposed ranking:

    Category 7
    Impact on Healthy Life Years **2**
    Pain and Suffering **3** (like kidney stone/childbirth, very painful)
    Population Effects 0
    Vulnerabel populations 0
    Tertiary prevention 0
    Effectiveness of treatment 4
    Net cost 3
    Need for service 0.65 (35% respond to placebo based on Cochrane analysis)

General Surgery ICD 10 Recommendations

Score 208, **Line 495** (if pain and suffering a 2, which is halfway between)

Alternatively, can use need for service of 0.4 (since 60-80% self-resolve)

Which results in a score of 128, corresponding to **Line 536**

Line 503 – RECTAL PROLAPSE

Rationale: should be in funded region because treatment of rectal prolapse can prevent complication of fecal incontinence which is a funded diagnosis. Recurrence rate 30% in 5 years. If leave rectal prolapse untreated, will inevitably lead to incontinence because the sphincter is chronically dilated.

(leaving this on 503 would be an option if too many conditions moving to the funded region)

Ranking recommendation:

Change Tertiary prevention to 1 (from 0)
Net cost to 2 (from 3)
New score 256
New Approximate Line 475

GUIDELINES

See separate hernia issue summary

See separate symptomatic cholelithiasis summary

RENAME LINES

1. Rename Line 409 to ESOPHAGEAL STRICTURE; ACHALASIA
2. Rename line 175 to COMPLICATED HERNIAS ~~(OTHER THAN DIAPHRAGMATIC HERNIA);~~ UNCOMPLICATED INGUINAL HERNIA IN CHILDREN AGE 18 AND UNDER; PERSISTENT HYDROCELE
    a. Rationale: Diaphragmatic hernia can be equally complicated, so the codes specifying diaphragmatic hernia *with obstruction or gangrene* are moved to Line 175. Uncomplicated diaphragmatic hernia moved to the Line 411/now 540 with esophagitis.
3. Rename Line 540 ESOPHAGITIS; ASYMPTOMATIC DIAPHRAGMATIC HERNIA
    a. Place code K44.9 Diaphragmatic hernia without obstruction or gangrene on Line 540

Hernia issue summary – ICD-10 General Surgery Recommendations

Question: Should hernias be divided into 3 lines and should symptomatic hernias be moved into the covered region of the List?

Question Source: ICD 10 General Surgery Consultants

Issue: There has been long contention that the Prioritized List does not cover treatment of symptomatic hernias that are not acute incarcerated or strangulated (or inguinal hernia in children). The covered line is 175 and includes "complicated hernias" which are defined as incarcerated or with symptoms of obstruction or strangulation), and also includes inguinal hernia in children. Other symptomatic hernias are located on Line 547.

Recommendations from Surgeons:

DIVIDE HERNIAS INTO 3 LINES, add coverage to symptomatic hernias

Rationale: Consulting surgeons believe hernias should be covered, with the exception of asymptomatic and ventral hernias. Currently ventral hernias can get covered because of "chronic incarceration" based on the current guideline. The consultants thought it is not sensible for OHP to cover repairs of large ventral hernias. There is a poor success rate, it is infrequently associated with patients being able to go back to work, and the evidence is very grey about improvement in quality of life. Additionally, these are very expensive surgeries, easily $50,000 to $100,000 dollars with complex recurrent ventral hernias.

Current hernia lines

Line:	**175**
Condition:	COMPLICATED HERNIAS (OTHER THAN DIAPHRAGMATIC HERNIA); UNCOMPLICATED INGUINAL HERNIA IN CHILDREN AGE 18 AND UNDER; PERSISTENT HYDROCELE (See Guideline Notes 24,63,64,65,76)
Treatment:	REPAIR
ICD-9:	550.00-550.93,551.00-551.29,551.8-551.9,552.00-552.29,552.8-552.9,603.0,603.8-603.9
CPT:	44050,44120,49491-49572,49582,49587,49590,49650-49659,55040-55060,98966-98969,99051,99060,99070, 99078,99201-99360,99366,99374,99375,99379-99444,99468-99480,99605-99607
HCPCS:	G0406-G0408,G0425-G0427,S0270-S0274

Line:	**547**
Condition:	UNCOMPLICATED HERNIA (OTHER THAN INGUINAL HERNIA IN CHILDREN AGE 18 AND UNDER OR DIAPHRAGMATIC HERNIA) (See Guideline Notes 64,65)
Treatment:	REPAIR
ICD-9:	550.90-550.93,553.00-553.29,553.8-553.9
CPT:	44050,49250,49505,49520,49525-49550,49555,49560,49565,49568,49570,49580,49585,49590,49650-49659, 55540,98966-98969,99051,99060,99070,99078,99201-99360,99366,99374,99375,99379-99444,99468-99480, 99605-99607
HCPCS:	G0406-G0408,G0425-G0427,S0270-S0274

GUIDELINE NOTE 24, COMPLICATED HERNIAS

Line 175

Complicated hernias are included on this line if they are incarcerated (defined as non-reducible by physical manipulation) or have symptoms of obstruction and/or strangulation.

Recommended new lines

1) COMPLICATED HERNIAS; UNCOMPLICATED INGUINAL HERNIA AND PERSISTENT HYDROCELE IN CHILDREN;
   No change, just Line 175

2) SYMPTOMATIC HERNIAS, OTHER THAN VENTRAL HERNIAS

   impact on healthy life years 2
   impact on pain and suffering 2 *(currently 1)*
   population effect 0
   impact on vulnerable populations 0
   tertiary prevention 1 *(Currently 0)*
   effectiveness 5 *(currently 4)*
   % requiring treatment (would eliminate smokers, diabetes controlled) – 0.8 *(currently 0.5)*
   net cost 3
   score 500
   Approximate Line 415

3) ASYMPTOMATIC HERNIAS AND VENTRAL HERNIAS

   impact on healthy life years 2
   impact on pain and suffering – pain and cosmesis 2
   population effect 0
   impact on vulnerable populations 0
   tertiary prevention 1
   effectiveness 2
   % requiring treatment (would eliminate smokers, diabetes uncontrolled) **– 50%**
   net cost 1
   score 100
   Approximate Line 554

Change guideline

GUIDELINE NOTE 24, COMPLICATED HERNIAS
Line 175
Complicated hernias (excluding ventral hernias) are included on this line if they are incarcerated (defined as non-reducible by physical manipulation) or have symptoms of obstruction and/or strangulation. Chronic incarceration that does not place the patient at risk for impending strangulation (e.g. such as a large ventral hernia with loss of domain), is placed on Line XX (Asymptomatic Hernias and Ventral Hernias).

Rationale: Large ventral hernias are at low risk for life-threatening complications, and the recurrence rate is very high.

Evidence Summary

Cochrane 2012 – Protocol - Watchful waiting versus surgical approach for asymptomatic hernia

Mizrahi, 2012

1) Systematic review of randomized trials
2) 2 RCTs, N= 880 total patients
3) Results:
    a. No significant difference in pain scores and general health status were found when comparing the patients who were followed up with the patients who had surgery.
    b. A significant crossover ratio ranging between 23% and 72% from watchful waiting to surgery was found. In patients with watchful waiting, the rates of IH strangulation were 0.27% after 2 years of follow-up and 0.55% after 4 years of follow-up. In patients who underwent elective surgery, the range of operative complications was 0% to 22.3% and the recurrence rate was 2.1%.
    c. Conversion to surgery group was largely due to pain
4) Conclusions: both options are safe

Studies primarily exam either asymptomatic candidates, or compare open to laparoscopic treatment.

HERC Staff Recommendations:

1) Modify Guideline Note 24 as recommended (depending on decision on number 2, Guideline Note 24 will refer to Line XX or Line 547).

    GUIDELINE NOTE 24, COMPLICATED HERNIAS
    Line 175
    Complicated hernias (excluding ventral hernias) are included on this line if they are incarcerated (defined as non-reducible by physical manipulation) or have symptoms of obstruction and/or strangulation. Chronic incarceration that does not place the patient at risk for impending strangulation (e.g. such as a large ventral hernia with loss of domain), is placed on Line *XX/547* (Asymptomatic Hernias and Ventral Hernias).

2) Place ventral hernia codes (without obstruction or gangrene) on lower unfunded hernia line

3) Rename Line 547 UNCOMPLICATED HERNIA AND VENTRAL HERNIA (OTHER THAN INGUINAL HERNIA IN CHILDREN AGE 18 OR UNDER OR DIAPHRAGMATIC HERNIA)

4) Discuss proposal to place symptomatic hernias in the covered region. **CHOOSE ONE:**

    a. Make no change to current line structure

    b. Adopt new 3 line structure with funded symptomatic hernia line as recommended by consultants

Management of Asymptomatic Inguinal Hernia

A Systematic Review of the Evidence

Hagar Mizrahi, MD; Michael C. Parker, FRCS

Objective: To establish a literature-based surgical approach to asymptomatic inguinal hernia (IH).

Data Sources: PubMed, the Cochrane Library database, Embase, national guidelines (including the National Library of Guidelines Specialist Library), National Institute for Health and Clinical Excellence guidelines, and the National Research Register were searched for prospective randomized trials comparing surgical treatment of patients with asymptomatic IH with conservative treatment.

Study Selection: The literature search retrieved 216 article headlines, and these articles were analyzed. Of those studies, a total of 41 articles were found to be relevant and 2 large well-conducted randomized controlled studies that published their results in several articles were reviewed.

Data Extraction: The pain and discomfort, general health status, complications, and life-threatening events of patients with asymptomatic IH managed by surgery or watchful waiting were determined.

Data Synthesis: No significant difference in pain scores and general health status were found when comparing the patients who were followed up with the patients who had surgery. A significant crossover ratio ranging between 23% and 72% from watchful waiting to surgery was found. In patients with watchful waiting, the rates of IH strangulation were 0.27% after 2 years of follow-up and 0.55% after 4 years of follow-up. In patients who underwent elective surgery, the range of operative complications was 0% to 22.3% and the recurrence rate was 2.1%.

Conclusion: Both treatment options for asymptomatic IH are safe, but most patients will develop symptoms (mainly pain) over time and will require operation.

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INGUINAL HERNIA (IH) OCCURS when a peritoneal sac protrudes through a weak point within the groin area. It often contains abdominal content and is traditionally treated with surgery.[1] As a rule, IH is diagnosed by a simple physical examination except in cases where the diagnosis is obscure; in these cases, different modalities are used for confirmation.[2] *Asymptomatic IH* is a term used to describe the condition in a patient who has a groin bulge or impulse cough with only minor or no symptoms. On the other hand, an incidental operative finding of an internal ring defect with no groin lump or other symptoms is defined as an *occult IH*, a condition prevalent since the introduction of laparoscopic surgery.

Inguinal hernia repair (IHR) is the most frequent elective operation performed in the United States and Europe, although when comparing the rate of surgery performed to treat IH there is great variety among different populations.[3,4] For example, IHR is done in 10 per 10 000 people in the United Kingdom, while the rate is 28 per 10 000 people in the United States.[5] There are several possible explanations for this observable fact, including different primary care management, costs, and insurance policies.

As in any other operation, elective IHR carries its share of complications. Surgical site infection, hematoma, urinary retention, and other short-term morbidities are well known, as are long-term complications including chronic groin pain, neuralgia, and IH recurrence.[6] However, postponing the operation might carry a risk of acute IH and visceral organ strangulation with additional risks of gangrene, perforation, and infection of the peritoneal cavity. Hence, operations in the emergency setting for incarcerated IH have higher morbidity and mortality rates.[7]

The aim of this review is to establish a surgical approach to asymptomatic IH by

Cholelithiasis Issue Summary –

ICD-10 General surgery recommendations

Question: Should cholelithiasis be divided into 3 lines?

Question Source: ICD 10 General Surgery Consultants

Issue: Currently cholelithiasis is divided into 2 lines, essentially divided between cholecystitis and bile duct involvement versus cholelithiasis by itself. There is no distinction between symptomatic or non-symptomatic cholelithiasis. There is widespread agreement that for asymptomatic cholelithiasis, conservative management is appropriate. However, for symptomatic cholelithiasis (even without cholecystitis), the standard approach is surgical treatment. Symptomatic cholelithiais involves abdominal pain, vomiting, etc.

Current Lines:

a. Line 61 CHOLELITHIASIS, CHOLECYSTITIS, COMMON BILIARY DUCT STONE
b. Line 671 GALLSTONES WITHOUT CHOLECYSTITIS

txtDline	txtScore	cmbCategory	HLY	Suffering	PopEffects	VulnerablePop	TertiaryPrev	Effectiveness	NeedForServices	NetCost
671	0	9	0	0	0	1		4	0	2

Surgeon recommendations:

Recommend dividing cholelithiasis into 3 lines and treating symptomatic cholelithiasis, based on issues of how this would be cost savings. People with symptomatic cholelithiasis will repeatedly go to the ER and miss work, and surgery provides definitive treatment. Symptomatic cholelithiasis is currently on Line 671 unless complications are present

1) 61 Highest – Cholangitis. – complicated cholelithiasis is very high cost, people have sepsis, needs urgent treatment
    a. Rename COMPLICATED STONES OF THE GALLBLADDER AND BILE DUCTS
2) New line (should be in funded region)
    a. SYMPTOMATIC CHOLELITHIASIS
    b. Recommended ranking by surgones
        i. Impact on Healthy Life Years 4
        ii. Impact on Pain and Suffering 2
        iii. Tertiary Prevention 4
        iv. Effectiveness 5
        v. Net Cost 2
        vi. Need for service 1
        vii. Score 1000
        viii. Approximate Line Placement YYY 345
3) 671 – maintain current low line: GALLSTONES OR OTHER BILIARY DISEASE WITHOUT SYMPTOMS

Evidence:
Note: no studies found with cost-effectiveness comparisons of surgery vs observation for symptomatic gallbladder disease

1) No reviews found at NICE or SIGN
2) **BMJ Clinical Evidence** (from http://bestpractice.bmj.com/best-practice/monograph/873/treatment/evidence/intervention/0411/0/sr-0411-i1193838491631.html)
    a. Systematic review comparing laparoscopic cholecystectomy versus no treatment/observation
    b. We found no systematic review or RCTs comparing only laparoscopic cholecystectomy versus no treatment. We found one RCT comparing cholecystectomy (laparoscopic or open) versus observation alone.
        i. N=1 study (64 patients)
        ii. Gallstone-related events (admissions for pain, recurrent cholecystitis, and pancreatitis)
            1. 6/31 (19%) with cholecystectomy
            2. 12/33 (36%) with observation
            3. P=0.16 (not significant)
        iii. In the cholecystectomy group, 27/31 (87%) people had the operation at a median of 3.6 months after randomisation. After 8 years, 10/33 (30%) people originally randomised to observation had undergone cholecystectomy (failure rate). In the cholecystectomy group, 4/31 (13%) refused operation on the grounds of freedom from symptoms.
        iv. Complications: The RCT found no significant difference in the rates of major or minor operative complications between those initially randomised to cholecystectomy and those who converted to cholecystectomy (major complication rate: 3/27 [11%] in the group randomised to cholecystectomy *v* 1/10 [10%] in the group randomised to observation; minor complication rate: 7/27 [26%] in the group randomised to cholecystectomy *v* 1/10 [10%] in the group randomised to observation; P = 0.66 for difference in overall postoperative complications between the groups). Major complications included bile duct injuries or haemorrhage, whereas minor complications included wound infection, subphrenic collections, or miscellaneous infections (urinary and respiratory).
    c. Conclusion: *Compared with laparoscopic cholecystectomy* Observation or no treatment seems no more effective than cholecystectomy at reducing the rate of gallstone-related complications (recurrent cholecystitis, pancreatitis, intractable pain) in people with acute cholecystitis (moderate-quality evidence).
3) **Festi 2010**
    a. Population based cohort study examining clinical outcome of gallbladder disease
    b. N=856 subjects with gallstones seen on ultrasound
    c. Results: At enrollment, 580 (73.1%) patients were asymptomatic, 94 (11.8%) had mild symptoms and 119 (15.1%) had severe symptoms. GS patients were followed up for a mean period of 8.7 years; 63 subjects (7.3%) were lost to follow up. At the end of the follow up, of the asymptomatic subjects, 453 (78.1%) remained asymptomatic; 61 (10.5%) developed mild symptoms and 66 (11.4%)

developed severe symptoms. In subjects with mild symptoms, the symptoms disappeared in 55 (58.5%), became severe in 23 (24.5%), remained stable in 16 (17%); in subjects with severe symptoms, the symptoms disappeared in 62 (52.1%), became mild in 20 (16.8%) and remained stable in 37 (31.1%). A total of 189 cholecystectomies were performed: 41.3% on asymptomatic patients, 17.4% on patients with mild symptoms and 41.3% on patients with severe symptoms.

d. Conclusions: This study indicates that: (i) asymptomatic and symptomatic GS patients have a benign natural history; (ii) the majority of GS patients with severe or mild symptoms will no longer experience biliary pain; and (iii) a significant proportion of cholecystectomies are performed in asymptomatic patients. Expectant management still represents a valid therapeutic approach in the majority of patients.

4) **Vetrhus 2007** (only abstract available)
   a. RCT of observation vs cholecystectomy for symptomatic gallbladder stone disease
   b. N=137 (68 in cholecystectomy group; 69 in expectant treatment)
   c. Median 67 months of follow up
   d. RESULTS: Eight of the patients randomized to cholecystectomy did not undergo operation, while 35 of the patients randomized to observation later had their gallbladders removed. The cumulative risk of having a cholecystectomy seemed to level off after 4 years. Gallstone-related complications occurred in 3 patients in the observation group, 1 in the operation group and 5 of 201 excluded patients. After cholecystectomy, 16 of 222 patients had a major complication and 10 a minor.
   e. CONCLUSIONS: We found that non-operative expectant treatment carries a low risk of complications. Patients should be informed that watchful waiting is a safe option.
5) **Schmidt 2011** (only abstract available)
   f. RCT examining feasibility and safety of observation after extended long-term follow-up for symptomatic gallstone disease
   g. N=137
   h. Follow up 14 yrs
   i. Results: There were no differences in outcome between the observation group and the surgical group ($p = 0.298$). Virtually no cholecystectomy was performed after 5 years of follow-up, and no clear escalation in the severity of the disease was observed. A total of 50.7% of patients from the observation group and 88.2% from the surgical group underwent surgery.
   j. Conclusion: Cholecystectomy was the preferred treatment after extended long-term follow-up, but conservative management for symptomatic gallstone disease is an alternative to surgery in the elderly.

Summary: Little evidence exists on the long term cost-effectiveness of observation/expectant management of symptomatic gallstones. Limited evidence supports the safety of expectant management of symptomatic gallstones.

Recommendations:

1) Maintain current 2 line structure. There is evidence that expectant management of symptomatic gallstones is safe and may avoid unnecessary surgeries.
    a. Rename line 61 COMPLICATED STONES OF THE GALLBLADDER AND BILE DUCTS
2) If 3 line structure is adopted, the new middle line should look as OPTION A or B below; and need to adopt the proposed guideline below.
    a. OPTION A - Proposed surgeon ranking
        i. Impact on Healthy Life Years 4
        ii. Impact on Pain and Suffering 2
        iii. Tertiary Prevention 4
        iv. Effectiveness 5
        v. Net Cost 2
        vi. Need for service 1
        vii. Score 1000
        viii. Approximate Line Placement YYY 345

    b. OPTION B Proposed staff ranking
        i. Impact on Healthy Life Years 2
        ii. Impact on Pain and Suffering 2
        iii. Tertiary Prevention 0
        iv. Effectiveness 4
        v. Net Cost 2
        vi. Need for service 0.5
        vii. Score 200
        viii. Approximate line placement YYY 496

Condition: SYMPTOMATIC CHOLELITHIASIS
ICD-9 codes: 574.20-1 (Note: These ICD-9 codes to remain on line 671)
CPT codes: all from line 61 and 671

GUIDELINE NOTE XXX SYMPTOMATIC CHOLELITHIASIS
Lines YYY, 671
Calculus of gallbladder (ICD-9 575.20, 575.21) are included on line YYY only in those cases which are symptomatic with *moderate-to severe* abdominal pain lasting 4 or more hours *on greater than one occasion*. Asymptomatic gallstones are included on line 671.

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HEPATOLOGY

Natural history of gallstone disease: Expectant management or active treatment? Results from a population-based cohort study

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Key words
biliary symptoms, cholecystectomy, epidemiology, gallstones.

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Abstract

Background and Aims: The knowledge of natural history is essential for disease management. We evaluated the natural history (e.g. frequency and characteristics of symptoms and clinical outcome) of gallstones (GS) in a population-based cohort study.

Methods: A total of 11 229 subjects (6610 men, 4619 women, age-range: 29–69 years, mean age: 48 years) were studied. At ultrasonography, GS were present in 856 subjects (338 men, 455 women) (7.1%). GS were followed by means of a questionnaire inquiring about the characteristics of specific biliary symptoms.

Results: At enrolment, 580 (73.1%) patients were asymptomatic, 94 (11.8%) had mild symptoms and 119 (15.1%) had severe symptoms. GS patients were followed up for a mean period of 8.7 years; 63 subjects (7.3%) were lost to follow up. At the end of the follow up, of the asymptomatic subjects, 453 (78.1%) remained asymptomatic; 61 (10.5%) developed mild symptoms and 66 (11.4%) developed severe symptoms. In subjects with mild symptoms, the symptoms disappeared in 55 (58.5%), became severe in 23 (24.5%), remained stable in 16 (17%); in subjects with severe symptoms, the symptoms disappeared in 62 (52.1%), became mild in 20 (16.8%) and remained stable in 37 (31.1%). A total of 189 cholecystectomies were performed: 41.3% on asymptomatic patients, 17.4% on patients with mild symptoms and 41.3% on patients with severe symptoms.

Conclusions: This study indicates that: (i) asymptomatic and symptomatic GS patients have a benign natural history; (ii) the majority of GS patients with severe or mild symptoms will no longer experience biliary pain; and (iii) a significant proportion of cholecystectomies are performed in asymptomatic patients. Expectant management still represents a valid therapeutic approach in the majority of patients.

Introduction

Gallstone disease is a very common gastrointestinal disorder, as more than 14% of adults are, or have been, affected by this disease.[1,2] Gallstone disease represents a major public health problem, and this disorder is one of the most common and costly of all digestive diseases, at least in the Western world.[3,4] In fact, in terms of inpatient physician services and hospital costs, gallstone disease is by far the most costly digestive disorder,[5] the bulk of the economic burden being mainly due to the surgical and operative procedures.[3,4,6]

Cholecystectomy is considered the treatment of choice for symptomatic gallstones;[7–9] in particular, laparoscopic cholecystectomy (LC) due to its reasonable safety (mortality less than 0.2%, morbidity less than 5.0%) and its high acceptability by both patients and physicians.[9] The latter is mainly due to minimal postoperative pain, a short recovery time, a quick return to work and cosmetic results. A recent Cochrane review,[10] comparatively evaluating LC and open cholecystectomy, has confirmed the absence of any significant difference between the two procedures in terms of mortality, complications and operating time; furthermore, LC is associated with a significantly shorter hospital stay and quicker convalescence.

However, since the introduction of LC, an increased rate (20–50%) of cholecystectomies has been documented,[6,11,12] probably due to changes in the perceived risk/benefit ratio (for patients and physicians) and changes in surgical indications. Furthermore, the recent proposal of new surgical access for performing a

Ophthamology ICD-10 Follow up issues - Chelation

Question: Where should the code for chelation of the corneal epithelium be placed?

Question Source: ICD 10 Ophthamologists and HERC Staff

Issue:

The HERC had approved a number of recommendations made by ICD-10 consulting ophthalmologists, including removal of CPT code **65436** (Removal of corneal epithelium; with application of chelating agent (eg, EDTA)) from Line 461 RECURRENT EROSION OF THE CORNEA. Staff has since identified it is not on any other line, and thus would no longer be able to be performed. The consultants stated it is appropriate that:

> "chelation pairs with band keratopathy which is calcium that accumulates in the superficial cornea. It can often block the vision and can be improved with debridement of the epithelium and then chemical chelation of the calcium. I believe band keratopathy is 371.43 on the ICD-9." Related ICD 10 codes include:

txtCode	txtCodeDesc	txtLD
H18.421	Band keratopathy, right eye	337 CORNEAL OPACITY AND OTHER DISORDERS OF CORNEA
H18.422	Band keratopathy, left eye	337 CORNEAL OPACITY AND OTHER DISORDERS OF CORNEA
H18.423	Band keratopathy, bilateral	337 CORNEAL OPACITY AND OTHER DISORDERS OF CORNEA
H18.429	Band keratopathy, unspecified eye	337 CORNEAL OPACITY AND OTHER DISORDERS OF CORNEA

Clinical background

No cochrane reviews identified. There only appears to be case series. However, it does appear that EDTA chelation is standard care.

From emedicine, Surgical Treatment of Band Keratopathy

Surgical debridement of band keratopathy is usually effective in restoring normal vision.

- The procedure can be performed in a minor operating room under topical anesthesia. Proparacaine or tetracaine drops can be used for this purpose. Use of an operating microscope is recommended.
    - Place a lid speculum to hold open the eyelids.

    - Debride the epithelium overlying the calcium with an ophthalmic surgical blade or spatula.
    - Apply 0.05 mol, 1.5% neutral disodium ethylenediaminetetraacetic acid (EDTA), to the corneal surface. Weck-cel sponges soaked in this solution can be used for this purpose. Alternatively, the solution can be placed in a water bath over the cornea to limit ocular exposure.
    - Then, remove calcium deposits with firm scraping of the corneal surface with a blunt spatula. (A Paton spatula works well.) Often, it is necessary to apply solution, followed by scraping several times to remove the plaque. The primary goal is to clear the visual axis. Thin calcium deposits may come off in 5 minutes, while thick plaques may take 30-45 minutes to dissolve.
    - Once this has been accomplished, an assessment of the smoothness of the underlying stroma can be made. If the surface is very irregular, phototherapeutic keratectomy with an excimer laser can be performed to smooth the surface. Ideally, this procedure is performed in the same setting. Note that the excimer laser should not be used to remove calcium. Attempting to remove band keratopathy with the excimer laser alone will result in significant irregular astigmatism since the cornea, not calcium, will be ablated preferentially. The role of the excimer is to polish the surface after the plaque has been removed.[13]
    - Irrigate the eye thoroughly following the procedure to remove EDTA solution from the conjunctival surface and fornices.
    - Place a bandage contact lens over the cornea. Alternatively, pressure patching or frequent antibiotic ointment can be used.
- Postoperative care includes the insertion of a bandage contact lens that is left in place until the epithelium heals. Topical nonsteroidal agents are useful for pain control immediately following the procedure and for the first few days afterwards. An antibiotic drop should be prescribed with the bandage contact lens in place. Use of a topical steroid drop (eg, prednisolone acetate [not phosphate]) is helpful for comfort and treatment of the inflammation and corneal edema that is often present in the early postprocedure period. These medications can be stopped when the epithelium is healed, and the bandage contact lens is removed (usually within the first 1-2 wk).
- Occasionally, a mild subepithelial haze can be seen weeks after EDTA chelation. This may resolve on its own. A mild topical steroid (eg, fluorometholone 0.1%) may help to resolve this haze. If there is significant damage to the Bowman membrane, the haze may be permanent.

Jhanji, 2011

Clinical (non-systematic) review (no methodology)

EDTA appears to be standard chelation treatment for calcific band keratopathy

Najjar, 2004

1) Retrospective interventional case series

2) N=230 patients; 54 patients, 65 eyes underwent EDTA chelation

3) RESULTS: The mean follow-up time after EDTA chelation was 36.6 months (range, 1 month to 29.6 years). Forty-four of 45 patients (98%) reported partial or complete symptomatic relief. Seventeen eyes (33.3%) improved 2 or more lines at 1 month and 18

eyes (35.2%) at last follow-up visit ($P \leq 0.0001$). In patients with an initial visual acuity between 20/50 and 20/400, 15 eyes (47%) improved 2 or more lines at 1 month and 16 eyes (50%) at last follow-up visit. Ten of 56 eyes (17.8%) had a recurrence at a mean time of 17.7 years (range, 1 month to 26 years). The highest number of recurrences was in three of five eyes with uveitis (60%; $P = 0.03$).

4) Article conclusions: EDTA is effective

Summary

There is poor quality data supporting the use of EDTA chelation, however it appears to be usual care, and is currently in the funded region of the List, and was inadvertently removed with a suggestion already approved.

HERC Staff Recommendation

1. Place cpt code 65436 on Line 337

Corneal calcific band keratopathy

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Current Opinion in Ophthalmology 2011, 22:283–289

Purpose of review

Calcific band keratopathy is a chronic degenerative condition characterized by the deposition of grayish to whitish opacities in the superficial layers of the cornea. It is usually associated with chronic ocular inflammatory conditions. Various treatment modalities have been used for the management of band keratopathy including mechanical debridement, chelation, and excimer laser phototherapeutic keratectomy (PTK). This review will discuss the cause and management of calcific band keratopathy.

Recent findings

Recent use of combination treatments such as chelation, excimer laser, and amniotic membrane transplantation has renewed interest in the management of cases with band keratopathy in order to achieve faster epithelial healing and better postoperative outcomes.

Summary

Careful case selection is required before deciding on the surgical management plan in cases with band keratopathy. Chelation is a cost-effective and straightforward procedure. An excimer laser PTK, although costly, can provide a smooth corneal surface. Combination treatment using amniotic membrane is reserved for selected cases to enhance epithelial healing.

Keywords

amniotic membrane transplantation, band keratopathy, chelation, ethylenediamine tetraacetic acid, phototherapeutic keratectomy, treatment

Curr Opin Ophthalmol 22:283–289

1040-8738

Introduction

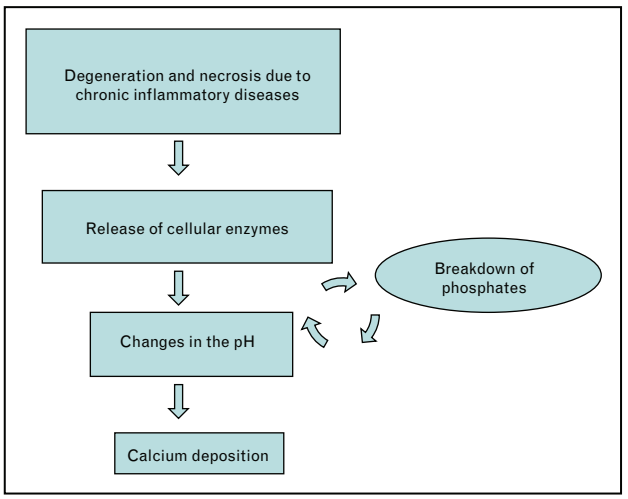
Calcific band keratopathy is a chronic degenerative condition characterized by the deposition of grayish to whitish opacities in the superficial layers of the cornea, most frequently in the interpalpebral zone. Band keratopathy was first described by Dixon [1] in 1948. It may be associated with a variety of ocular and systemic conditions, the most common ocular condition being chronic inflammation and most common systemic condition being hypercalcemia. Accumulation of calcium can disrupt the ocular surface, causing irritation, photophobia, or recurrent corneal erosions. Once the opacities extend on to the visual axis, they result in significant glare and decreased vision. Various modalities have been used in the treatment of band keratopathy, the most popular being, mechanical debridement [2], ethylenediamine tetraacetic acid (EDTA) chelation [3•,4–7], and phototherapeutic keratectomy [8,9]. The goal of treatment is to remove the calcium opacities and restore a smooth ocular surface. This review will discuss the cause, pathogenesis, and treatment modalities available for the management of calcific band keratopathy.

Pathogenesis

Bowman's membrane is prone to calcification perhaps in a similar fashion to copper being deposited in Descemet's membrane in patients with Wilson's disease, in which the molecular structure of the membrane provides a binding site for the copper ions. The mechanism of calcium deposition in the cornea is unknown, but it is associated with corneal exposure, as deposition occurs primarily in the exposed area. It may result from precipitation left as tears evaporate or because of a lower pH in this region (Fig. 1) [10]. Precipitation of calcium can also occur with an alteration in tear osmolality, elevation of the pH from corneal tissue metabolism, or increase in the concentration of either calcium or phosphate. The pH of the interpalpebral fissure is higher than that of the rest of the ocular surface because of carbon dioxide released from the exposed zone. This also enhances calcium precipitation. In an experimental model in which animals with induced ocular inflammation were given overdoses of vitamin D, band keratopathy developed only in animals with open eyelids but did not develop if the eyelids were kept closed [11]. In addition, band keratopathy can occur rapidly in patients with dry eyes, further suggesting a role for tear evaporation in the pathogenesis of this process [12]. Clinically, when the calcium phosphate solubility product is greater than 60 mg, the deposition of calcium in the cornea is to be expected.

Characteristically, the deposition of calcium occurs in Bowman's layer and in the most superficial lamellae of

Figure 1 Flow chart depicting the pathogenesis of calcific band keratopathy



the stroma leaving the remainder of the cornea clear. This distinguishes calcific band keratopathy from calcareous degeneration of the cornea, a much rarer condition, which characteristically affects the deeper parts of the cornea as well. In band keratopathy, calcium is deposited in the cornea as a horizontal pattern that begins near the corneal periphery and appears as a hazy opacity in the peripheral stroma separated from the limbus by a clear zone. It often develops a 'Swiss cheese' appearance because of the scattered holes inside the band, thought to represent spaces in which corneal nerves penetrate through Bowman's layer [13].

Usually, the most severely affected area is centered on the junction of the middle and inferior thirds of the cornea, possibly because of the amount of exposure. The deposits begin as a gray haze and can gradually assume a dense white appearance with a rough surface that elevates the epithelium consequently resulting in pain, foreign body sensation, recurrent corneal erosions, and decreased vision. It is a slow process and may take many years, although it may occur rapidly in very dry eyes [12].

Histopathologically, the earliest changes consist of basophilic staining of the basement membrane of the epithelium. This is followed by involvement of Bowman's layer with calcium deposition and eventual fragmentation. Calcium is deposited as the hydroxyapatite salt in the epithelial basement membrane, basal epithelium, and Bowman's membrane [10]. The granular deposits contain phosphate and carbonate salts of calcium in a noncrystalline form with small amounts of sulfur and silicone in advanced cases. Eventually, the granules coalesce and Bowman's layer becomes calcified. Hyaline material deposits between the fragments of calcified Bowman's layer and the overlying epithelium giving the appearance of reduplication of Bowman's layer [10,13]. The deposits are usually extracellular, although hypercalcemia may cause intracellular epithelial accumulation.

Key points

- Band keratopathy is usually associated with chronic ocular inflammation.
- Reduced visual acuity and chronic ocular irritation are the main indications for surgery.
- Chelation is a cost-effective treatment modality and has been proven to be effective in cases with calcific band keratopathy.
- Excimer laser phototherapeutic keratectomy provides a smooth surface after ablation in cases with band keratopathy.
- Amniotic membrane transplantation is a useful adjunctive treatment for faster epithelial healing in selected cases.

Cause

Deposition of calcium in the Bowman's membrane occurs in two circumstances: dystrophic calcification and metastatic calcification. Many chronic ocular and systemic conditions have been associated with calcific band keratopathy. It has been noted in many states of chronic intraocular inflammation. Most classically, it occurs in patients with the chronic uveitis of juvenile idiopathic arthritis and in eyes with intraocular silicone oil [14,15]. In addition, band keratopathy has been associated with the chronic or excessive use of older glaucoma medications and dry-eye preparations manufactured with mercury-containing preservatives. It is typically seen in eyes with chronic uveitis, corneal ulcers, or chemical burns and in phthisical eyes after multiple ocular surgeries. Conditions associated with the occurrence of band keratopathy are as follows:

(1) ocular diseases
   (a) chronic uveitis;
   (b) phthisis bulbi;
   (c) long-standing glaucoma;
   (d) interstitial keratitis;
   (e) dry eye and corneal exposure syndromes;
   (f) spheroidal keratopathy;
   (g) keratoprosthesis;
(2) hypercalcemia
   (a) hyperparathyroidism;
   (b) excessive vitamin D (e.g., oral intake, sarcoidosis, and osteoporosis);
   (c) renal failure (e.g., Fanconi's syndrome);
   (d) hypophosphatasia;
   (e) sarcoidosis;

EDTA Chelation for Calcific Band Keratopathy: Results and Long-term Follow-up

DANY M. NAJJAR, MD, ELISABETH J. COHEN, MD, CHRISTOPHER J. RAPUANO, MD, AND PETER R. LAIBSON, MD

• PURPOSE: To determine the etiologies and management of calcific band keratopathy (CBK), and assess the results and long-term follow-up after ethylenediamine-tetraacetic acid (EDTA) chelation.

• DESIGN: Retrospective interventional case series.

• METHODS: Two hundred thirty patients with clinically significant CBK were included from January 1996 to July 2002. Among these, 54 patients (65 eyes) underwent EDTA chelation. Outcome measures included symptomatic relief, visual improvement, and recurrences. The improvement or worsening of the number of lines of Snellen best-corrected visual acuity was determined at 1 month and at last follow-up visit.

• RESULTS: The most common causes of CBK were chronic corneal edema in 80 eyes (28%) and idiopathic in 74 eyes (25.9%). The mean follow-up time after EDTA chelation was 36.6 months (range, 1 month to 29.6 years). Forty-four of 45 patients (98%) reported partial or complete symptomatic relief. Seventeen eyes (33.3%) improved 2 or more lines at 1 month and 18 eyes (35.2%) at last follow-up visit ($P = .0001$). In patients with an initial visual acuity between 20/50 and 20/400, 15 eyes (47%) improved 2 or more lines at 1 month and 16 eyes (50%) at last follow-up visit. Ten of 56 eyes (17.8%) had a recurrence at a mean time of 17.7 years (range, 1 month to 26 years). The highest number of recurrences was in three of five eyes with uveitis (60%; $P = .03$).

• CONCLUSION: Chelation with EDTA is an effective treatment of CBK. Visual acuity improves most in eyes with acuity between 20/50 and 20/400. This treatment can be used as the initial surgical intervention after conservative measures fail. (Am J Ophthalmol 2004; 137:1056–1064. © 2004 by Elsevier Inc. All rights reserved.)

Biosketch and/or additional material at www.ajo.com.

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From the Cornea Service, Wills Eye Hospital, Thomas Jefferson University, Philadelphia, Pennsylvania.

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This study was presented at the Wills Eye 55th Annual Conference, Philadelphia, Pennsylvania, March 14, 2003, and was the winner of the P. Robb McDonald Award for the best scientific paper by a fellow. Data from this study were presented, in part, as a poster at the annual meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, Florida, May 4–9, 2003.

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FIRST DESCRIBED BY DIXON IN 1848, CALCIFIC BAND keratopathy (CBK) is a chronic degenerative condition characterized by the deposition of grayish to whitish opacities in the superficial layers of the cornea, most frequently in the interpalpebral zone. It is separated from the limbus by a clear area and usually develops a "swiss cheese" appearance because of the scattered holes inside the band, thought to represent spaces where corneal nerves penetrate through Bowman's layer.[1–5]

Many chronic ocular and systemic conditions have been associated with CBK. Systemic conditions are primarily those that lead to increased calcium levels in blood.[6–8] When it develops in association with ocular conditions, CBK is commonly a result of chronic ocular inflammation. It is typically seen in eyes with chronic uveitis, corneal ulcers, or chemical burns, and in phthisic eyes after multiple ocular surgeries. If no underlying cause can be determined, CBK is referred to as primary or idiopathic.[9–20] In the early stages, it remains asymptomatic; however, once it extends into the visual axis, it results in significant glare and visual disturbances. Furthermore, accumulation of calcium can disrupt the ocular surface, causing irritation, photophobia, or recurrent corneal erosions.

Various modalities have been used in the treatment of CBK. By far the most widely used method is ethylenediamine-tetraacetic acid (EDTA) chelation.[21–24] The goal of treatment is to remove the calcium opacities and restore a smooth ocular surface. In most cases, vision can be improved; however, in eyes with poor visual potential, the procedure is performed mainly to improve ocular comfort. When the calcium plaque is thick, it can be scraped off the cornea with forceps; alternatively, a superficial keratectomy can be performed.[25] Other methods described in the literature include the use of a diamond burr,[26] Nd:YAG

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Foreign body in gastrointestinal tract

Question: Should the scoring be revised for the new Line "Foreign Body in Gastrointestinal Tract?"

Question Source: HERC Staff

Issue: At the March 2012 VBBS meeting the ICD 10 pediatric surgery recommendations were reviewed and suggested scoring was approved. However, in further staff work on this, it was found that the actual score proposed for this line was incorrectly calculated to be in the low 400s, when instead it is a score of 120, which is about Line 560, a difference in a funded versus a non-funded condition. Staff is bringing back this issue for clarification.

From the proposed recommendations:

> Line XXX FOREIGN BODY IN GASTROINTESTINAL TRACT
> Treatment: Medical therapy
> ICD-10: T18.2xxA, T18.3xxA, T18.4xxA, T18.5xxA, T18.8xxA, T18.9xxA
> CPT: 43247, 44363, 44383, 44390, 45307, 45332, 45378, 45379, 45915, 46608, 98966-98969, 99051, 99060, 99070, 99078, 99201-99217, 99241-99245, 99341-99366, 99441-99444
>
> ICD-10 codes from this line are to be separated out from line 48 CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL EXCLUDING NECROSIS; CHRONIC INTESTINAL PSEUDO-OBSTRUCTION. These codes all represent foreign bodies in various parts of the GI tract. Many of the conditions to be moved don't need any treatment, or need endoscopy only. Many are just observed to ensure passage. These conditions are normally not life threatening (unlike obstruction). If obstructed, can use obstruction code (or other complications can be coded as that complication).
>
> CPT codes: 43247 (upper endoscopy with foreign body removal), 44363 (small intestinal endoscopy with foreign body removal), 44383 (ileoscopy through stoma), 44390 (colonoscopy with removal of foreign body), 45307 (proctosigmoidoscopy, rigid, with removal of foreign body), 45332 (Sigmoidoscopy, flexible, with removal of foreign body), 45378 (colonscopy, diagnostic), 45379 (colonoscopy, with removal of foreign body), 45915 (removal of fecal impaction or foreign body, under anesthesia), 46608 (anoscopy, with removal of foreign body), 98966-98969, 99051, 99060, 99070, 99078, 99201-99217, 99241-99245, 99341-99366, 99441-99444 (medical visit codes, ER codes)

> Ranking recommendations for Line XXX Foreign Body in GI Tract
> Category 7
> Vulnerable populations 0
> Population effects 0
> **Impact on healthy life years 5**
> Impact on pain/suffering 1
> Tertiary prevention – 0

Effectiveness of treatment – 5
Need for medical service 0.2
Net cost 3
Score is 240 which is in the low 400s (Score with HLY - 5 is actually 120 which is about line 560)

Summary

The new proposed scoring is actually unfunded (was incorrectly calculated to be in the 440s when approved at prior VBBS/HERC meeting). Specialty consultant Barry Newman was consulted again and thought proposed ranking appropriate, and for foreign bodies in stomach and intestines to be on a lower line.

HERC Staff Recommendations

1) Accept proposed ranking recommendations, with new Foreign Body in GI Tract Line placement around 560.

Severe Inflammatory Skin Disease Guideline wording change

Question: Should a minor modification to the new severe inflammatory skin disease guideline be made?

Question source: OHP managed care medical directors

Issue: The medical directors were concerned that the placement of the word "only" is not entirely clear. They suggested moving this word to clearly indicate that biologics are only covered for severe plaque psoriasis.

HERC Staff Recommendation:

Modify new Severe Inflammatory Skin Disease Guideline as follows:

Guideline Note XX

> For severe psoriasis, first line agents include topical agents, phototherapy and methotrexate. Second line agents include other systemic agents and oral retinoids and should be limited to those who fail, or have contraindications to, or do not have access to first line agents.
>
> Biologics are ~~only~~ covered on this line only for the indication of severe plaque psoriasis; after documented failure of first line agents and failure of (or contraindications to) a second line agent.

Breast Cancer Line 197 Issue Summary

Question: How should issues pertaining to those at high risk of breast cancer be dealt with?

Question Source: HERC Staff

Issue: At the June 2012 VBBS/HERC meeting, the code for family history of breast cancer were moved from the lower Prevention Line to Line 197 CANCER OF BREAST

Code	Description
Z80.3	Family history of malignant neoplasm of breast

Additionally, staff identified the following code that is currently not mapping anywhere on the List, and is in the DMAP Excluded File.

Code	Description	Current Placement
Z15.01	Genetic susceptibility to malignant neoplasm of breast	DMAP Excluded File

HERC Staff Recommendations

1) Rename Line 197 CANCER OF BREAST; AT HIGH RISK OF BREAST CANCER
2) Place Z15.01 *Genetic susceptibility to malignant neoplasm of breast* on Line 197
3) Modify Guideline Note 3 as follows

GUIDELINE NOTE ~~3~~ XX, PROPHYLACTIC TREATMENT FOR PREVENTION OF BREAST CANCER IN HIGH RISK WOMEN

Lines ~~4,~~197

Bilateral prophylactic breast removal is included on Line ~~4~~ 197 for women without a personal history of invasive breast cancer who are at high risk for breast cancer. Prior to surgery, women without a personal history of breast cancer must have a genetics consultation. High risk is defined as:

A) Having a BRCA1/BRCA2 mutation;
A) Having a strong family history of breast cancer, defined as one of the following:
   1) 2 first-degree or second degree relatives diagnosed with breast cancer at younger than an average age of 50 years (at least one must be a first-degree relative);
   2) 3 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years (at least one must be a first-degree relative);
   3) 4 relatives diagnosed with breast cancer at any age (at least one must be a first-degree relative);

4) 1 relative with ovarian cancer at any age and, on the same side of the family, either 1 first-degree relative (including the relative with ovarian cancer) or second-degree relative diagnosed with breast cancer at younger than age 50 years, or 2 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years, or another ovarian cancer at any age;
5) 1 first-degree relative with cancer diagnosed in both breasts at younger than an average age of 50 years;
6) 1 first-degree or second-degree relative diagnosed with bilateral breast cancer and one first-degree or second-degree relative diagnosed with breast cancer at younger than an average age of 60 years; or,
7) a male relative with breast cancer at any age and on the same side of the family at least 1 first-degree or second-degree relative diagnosed with breast cancer at younger than age 50 years, or 2 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years.

B) A history of LCIS with a family history of breast cancer; or,
C) A history of treatment with thoracic radiation between ages 10 and 30.

Contralateral prophylactic mastectomy is included on Line~~s 4 and~~ 197 for women with a personal history of breast cancer and any of the high risk categories listed above. In addition, contralateral prophylactic mastectomy of the unaffected breast is indicated for women with invasive lobular carcinoma.

Prophylactic oophorectomy is ~~included on Line 4~~ appropriate for women who have the BRCA1/BRCA2 mutation.

Gender Identity Disorder/Gender Dysphoria

Question: Should puberty suppressing hormone therapy for gender-questioning children/youth be included on the new gender identity disorder line on the Prioritized List?

Question Source: HERC staff; Office of Multicultural Health; OHA; Transactive Advocacy Group; Basic Rights Oregon

Issue:
Gender identity disorder was separated from several inappropriate diagnoses and made into its own line as part of the 2012 Biennial Review of the Prioritized List. At the March, 2012 VbBS meeting, there was discussion about what services should be included on this new line. The treatments on the old line, including psychotherapy, were included. There was considerable discussion about inclusion of puberty suppressing hormone therapy for gender-questioning children and youth. Considerable testimony was heard regarding the need for this type of puberty suppression therapy, as well as the effectiveness of such treatment. The VbBS concluded that this therapy was effective and resulted in improved outcomes for these children and youth; however, concerns were raised about possible side effects and short- and long-term harms of this type of treatment. VbBS staff were asked to bring experts to a VbBS meeting to discuss risks and harms with the subcommittee.

From the March, 2012 VbBS minutes:

> The new guideline restricting the types of treatments for gender dysphoria was discussed in detail. The experts testifying before the subcommittee recommended that puberty suppressing medications be limited to children who have attained at least Tanner stage 2 in sexual development, as children in Tanner stage 1 have not yet started puberty. The treatment should be allowed through Tanner stage 5 to allow for different stages of puberty.
>
> Heidi Allen summarized the previously presented literature on the harms of not treating transgendered children during puberty. Tyack asked if there is evidence of the safety of these medications, to which the experts replied that there was. Pollack noted that the likelihood of misdiagnosis is very rare, and the use of puberty suppressing medication was not subject to abuse. Ocker asked the experts who provided care for these patients. The response was psychiatry, in conjunction with endocrinology and primary care. Kirk had concerns for access to appropriate care outside of Portland metro area. The experts indicated that resources are available throughout the state. Pollack reviewed DSM-5 criteria for gender identity disorder, which has fairly restrictive diagnostic criteria. The group decided that there was evidence of effectiveness for treatment of adolescents with gender identity disorder and no evidence of harms. This treatment was specified as being included on this line with a guideline.

A new guideline regarding puberty suppressing hormone therapy was accepted at the March meeting; however, this guideline has been placed on hold pending the outcome for further discussions regarding the need and safety of such treatment. The accepted guideline is shown below.

Recommendation:

1) Discuss possible short- and long-term harms of puberty suppressing hormone therapy with experts
    a. If harms are seen as acceptable, include puberty suppressing hormone therapy on the new gender dysphoria line with the guideline below (wording previously accepted by the subcommittee)

GUIDELINE XXX GENDER DYSPHORIA

Line XXX

Hormone treatment is included on this line only for use in delaying the onset of puberty and/or continued pubertal development for gender questioning children and adolescents (age 17 and younger) at Tanner stage 2 and above.

DRAFT 2014-15 Prioritized List of Health Services
Reflects Decisions Through 6/14/12 Meeting

Line: **1**
Condition: PREGNANCY (See Guideline Notes 1,2,16,22,64,65,76,85,92) (See Prevention Tables)
Treatment: MATERNITY CARE

Line: **2**
Condition: BIRTH OF INFANT (See Guideline Notes 64,65)
Treatment: NEWBORN CARE

Line: **3**
Condition: PREVENTIVE SERVICES WITH EVIDENCE OF EFFECTIVENESS
Treatment: MEDICAL THERAPY

Line: **4**
Condition: ABUSE OR DEPENDENCE OF PSYCHOACTIVE SUBSTANCE (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **5**
Condition: TOBACCO DEPENDENCE (See Guideline Notes 1,4,64,65)
Treatment: MEDICAL THERAPY/BRIEF COUNSELING NOT TO EXCEED 10 FOLLOW-UP VISITS OVER 3 MONTHS

Line: **6**
Condition: REPRODUCTIVE SERVICES (See Guideline Notes 64,65,68,76)
Treatment: CONTRACEPTION MANAGEMENT; STERILIZATION

Line: **7**
Condition: MAJOR DEPRESSION, RECURRENT; MAJOR DEPRESSION, SINGLE EPISODE, SEVERE (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **8**
Condition: TYPE I DIABETES MELLITUS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **9**
Condition: ASTHMA (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **10**
Condition: GALACTOSEMIA (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **11**
Condition: RESPIRATORY CONDITIONS OF FETUS AND NEWBORN (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **12**
Condition: HIV DISEASE (INCLUDING ACQUIRED IMMUNODEFICIENCY SYNDROME) AND RELATED OPPORTUNISTIC INFECTIONS (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **13**
Condition: CONGENITAL HYPOTHYROIDISM (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **14**
Condition: PHENYLKETONURIA (PKU) (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **15**
Condition: CONGENITAL INFECTIOUS DISEASES (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **16**
Condition: CONGENITAL SYPHILIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **17**
Condition: VERY LOW BIRTH WEIGHT (UNDER 1500 GRAMS) (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **18**
Condition: NEONATAL MYASTHENIA GRAVIS (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **19**
Condition: FEEDING PROBLEMS IN NEWBORNS
Treatment: MEDICAL THERAPY

Line: **20**
Condition: HYDROCEPHALUS AND BENIGN INTRACRANIAL HYPERTENSION (See Guideline Notes 1,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **21**
Condition: SYNDROME OF "INFANT OF A DIABETIC MOTHER" AND NEONATAL HYPOGLYCEMIA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **22**
Condition: OMPHALITIS OF THE NEWBORN AND NEONATAL INFECTIVE MASTITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **23**
Condition: LOW BIRTH WEIGHT (1500-2500 GRAMS) (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **24**
Condition: CYSTIC FIBROSIS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **25**
Condition: SCHIZOPHRENIC DISORDERS (See Guideline Notes 64,65,82)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **26**
Condition: INTRACRANIAL HEMORRHAGES; CEREBRAL CONVULSIONS, DEPRESSION, COMA, AND OTHER ABNORMAL CERERAL SIGNS OF THE NEWBORN
Treatment: MEDICAL THERAPY

Line: **27**
Condition: VESICOURETERAL REFLUX (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY, REIMPLANTATION

Line: **28**
Condition: DYSPLASIA OF CERVIX AND CERVICAL CARCINOMA IN SITU, CERVICAL CONDYLOMA (See Guideline Notes 64,65,66,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **29**
Condition: BIPOLAR DISORDERS (See Guideline Notes 64,65,82)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **30**
Condition: TYPE II DIABETES MELLITUS (See Coding Specification Below) (See Guideline Notes 1,7,8,64,65,76)
Treatment: MEDICAL THERAPY, BARIATRIC SURGERY WITH BMI >= 35

Line: **31**
Condition: DRUG WITHDRAWAL SYNDROME IN NEWBORN (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **32**
Condition: REGIONAL ENTERITIS, IDIOPATHIC PROCTOCOLITIS, ULCERATION OF INTESTINE (See Guideline Notes 1,9,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **33**
Condition: EPILEPSY AND FEBRILE CONVULSIONS (See Guideline Notes 1,64,65,84)
Treatment: MEDICAL THERAPY

Line: **34**
Condition: SEVERE BIRTH TRAUMA FOR BABY (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **35**
Condition: NEONATAL THYROTOXICOSIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **36**
Condition: HEMATOLOGICAL DISORDERS OF FETUS AND NEWBORN (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **37**
Condition: SPINA BIFIDA (See Guideline Notes 1,64,65,76)
Treatment: SURGICAL TREATMENT

Line: **38**
Condition: OTHER CONGENITAL ANOMALIES OF MUSCULOSKELETAL SYSTEM
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **39**
Condition: TERMINATION OF PREGNANCY (See Guideline Notes 1,64,65,76) (Note: This line item is not priced as part of the list)
Treatment: INDUCED ABORTION

Line: **40**
Condition: ACQUIRED HYPOTHYROIDISM, DYSHORMONOGENIC GOITER (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **41**
Condition: ECTOPIC PREGNANCY; HYDATIDIFORM MOLE; CHORIOCARCINOMA (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **42**
Condition: PRIMARY, AND SECONDARY SYPHILIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **43**
Condition: DISORDERS RELATING TO LONG GESTATION AND HIGH BIRTHWEIGHT (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **44**
Condition: PANHYPOPITUITARISM, IATROGENIC AND OTHER PITUITARY DISORDERS (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **45**
Condition: HYPOCALCEMIA, HYPOMAGNESEMIA AND OTHER ENDOCRINE AND METABOLIC DISTURBANCES SPECIFIC TO THE FETUS AND NEWBORN (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **46**
Condition: INTUSSCEPTION, VOLVULUS, INTESTINAL OBSTRUCTION, AND FOREIGN BODY IN STOMACH, INTESTINES, COLON, AND RECTUM (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **47**
Condition: CLEFT PALATE WITH AIRWAY OBSTRUCTION (See Guideline Notes 36,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, ORTHODONTICS

Line: **48**
Condition: COARCTATION OF THE AORTA (See Guideline Notes 1,6,76)
Treatment: SURGICAL TREATMENT

Line: **49**
Condition: CORONARY ARTERY ANOMALY (See Guideline Notes 6,76)
Treatment: REIMPLANTATION OF CORONARY ARTERY

Line: **50**
Condition: RHEUMATOID ARTHRITIS AND OTHER INFLAMMATORY POLYARTHROPATHIES (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL THERAPY, INJECTIONS

Line: **51**
Condition: DEEP ABSCESSES, INCLUDING APPENDICITIS AND PERIORBITAL ABSCESS (See Guideline Notes 1,36,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **52**
Condition: CHRONIC RESPIRATORY DISEASE ARISING IN THE NEONATAL PERIOD (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **53**
Condition: CONGENITAL HYDRONEPHROSIS (See Guideline Notes 64,65,76)
Treatment: NEPHRECTOMY/REPAIR

Line: **54**
Condition: PULMONARY TUBERCULOSIS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **55**
Condition: ACUTE PELVIC INFLAMMATORY DISEASE (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **56**
Condition: GONOCOCCAL INFECTIONS AND OTHER SEXUALLY TRANSMITTED DISEASES OF THE ORAL, ANAL AND GENITOURINARY TRACT (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **57**
Condition: PREVENTIVE DENTAL SERVICES (See Guideline Note 17)
Treatment: CLEANING, FLUORIDE AND SEALANTS

Line: **58**
Condition: DENTAL CONDITIONS (EG. INFECTION, PAIN, TRAUMA)
Treatment: EMERGENCY DENTAL SERVICES

Line: **59**
Condition: CHOLELITHIASIS, CHOLECYSTITIS, COMMON BILIARY DUCT STONE (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **60**
Condition: ULCERS, GASTRITIS, DUODENITIS, AND GI HEMORRHAGE (See Guideline Notes 1,9,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **61**
Condition: BURN FULL THICKNESS GREATER THAN 10% OF BODY SURFACE (See Guideline Notes 1,6,64,65,76)
Treatment: FREE SKIN GRAFT, MEDICAL THERAPY

Line: **62**
Condition: BRONCHIECTASIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **63**
Condition: END STAGE RENAL DISEASE (See Guideline Notes 1,7,64,65,76)
Treatment: MEDICAL THERAPY INCLUDING DIALYSIS

Line: **64**
Condition: METABOLIC DISORDERS INCLUDING HYPERLIPIDEMIA (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **65**
Condition: TORSION OF OVARY (See Guideline Notes 64,65,76)
Treatment: OOPHORECTOMY, OVARIAN CYSTECTOMY

Line: **66**
Condition: SUBSTANCE-INDUCED MOOD ANXIETY AND DELUSIONAL DISORDERS (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **67**
Condition: SPONTANEOUS ABORTION; MISSED ABORTION (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **68**
Condition: SUBSTANCE-INDUCED DELIRIUM (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **69**
Condition: CONGENITAL ANOMALIES OF UPPER ALIMENTARY TRACT, EXCLUDING TONGUE (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **70**
Condition: LARYNGEAL STENOSIS OR PARALYSIS WITH AIRWAY COMPLICATIONS
Treatment: INCISION/EXCISION/ENDOSCOPY

Line: **71**
Condition: VENTRICULAR SEPTAL DEFECT (See Guideline Notes 1,6,64,65,76)
Treatment: CLOSURE

Line: **72**
Condition: ACUTE BACTERIAL MENINGITIS (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL THERAPY

Line: **73**
Condition: ACUTE AND SUBACUTE ISCHEMIC HEART DISEASE, MYOCARDIAL INFARCTION (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **74**
Condition: CONGENITAL PULMONARY VALVE ANOMALIES (See Guideline Notes 64,65,76)
Treatment: PULMONARY VALVE REPAIR

Line: **75**
Condition: NEUROLOGICAL DYSFUNCTION IN BREATHING, EATING, SWALLOWING, BOWEL, OR BLADDER CONTROL CAUSED BY CHRONIC CONDITIONS (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT (EG. G-TUBES, J-TUBES, RESPIRATORS, TRACHEOSTOMY, UROLOGICAL PROCEDURES)

Line: **76**
Condition: BURN, PARTIAL THICKNESS GREATER THAN 30% OF BODY SURFACE OR WITH VITAL SITE; FULL THICKNESS, LESS THAN 10% OF BODY SURFACE (See Guideline Notes 1,6,64,65,76)
Treatment: FREE SKIN GRAFT, MEDICAL THERAPY

Line: **77**
Condition: POLYCYTHEMIA NEONATORUM, SYMPTOMATIC (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **78**
Condition: DERMATOMYOSITIS, POLYMYOSITIS (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **79**
Condition: ADDISON'S DISEASE (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **80**
Condition: HYPERTENSION AND HYPERTENSIVE DISEASE (See Guideline Notes 1,6,64,65)
Treatment: MEDICAL THERAPY

Line: **81**
Condition: PATENT DUCTUS ARTERIOSUS; AORTIC PULMONARY FISTULA/WINDOW (See Guideline Notes 1,6,64,65,76)
Treatment: LIGATION

Line: **82**
Condition: INJURY TO MAJOR BLOOD VESSELS OF EXTREMITIES (See Guideline Note 76)
Treatment: LIGATION/REPAIR

Line: **83**
Condition: PHLEBITIS AND THROMBOPHLEBITIS, DEEP (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **84**
Condition: INJURY TO INTERNAL ORGANS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **85**
Condition: FRACTURE OF HIP, CLOSED (See Guideline Notes 6,15,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **86**
Condition: MYOCARDITIS, PERICARDITIS, AND ENDOCARDITIS (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **87**
Condition: DEEP OPEN WOUND OF NECK, INCLUDING LARYNX; FRACTURE OF LARYNX OR TRACHEA (See Guideline Notes 64,65,76)
Treatment: REPAIR

Line: **88**
Condition: DIABETES MELLITUS WITH END STAGE RENAL DISEASE (See Coding Specification Below) (See Guideline Notes 1,76)
Treatment: SIMULTANEOUS PANCREAS/KIDNEY (SPK) TRANSPLANT, PANCREAS AFTER KIDNEY (PAK) TRANSPLANT

Line: **89**
Condition: ENDOCARDIAL CUSHION DEFECTS (See Guideline Notes 1,6,64,65,76)
Treatment: REPAIR

Line: **90**
Condition: CONGENITAL PULMONARY VALVE ATRESIA (See Guideline Notes 6,64,65,76)
Treatment: SHUNT/REPAIR

Line: **91**
Condition: CONGENITAL ANOMALIES OF GENITOURINARY SYSTEM (See Guideline Notes 1,64,65,76)
Treatment: RECONSTRUCTION

Line: **92**
Condition: NECROTIZING ENTEROCOLITIS IN FETUS OR NEWBORN (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **93**
Condition: DISCORDANT CARDIOVASCULAR CONNECTIONS (See Guideline Notes 1,6,64,65,76)
Treatment: REPAIR

Line: **94**
Condition: CONGENITAL MITRAL VALVE STENOSIS/INSUFFICIENCY (See Guideline Notes 6,64,65,76)
Treatment: MITRAL VALVE REPAIR/REPLACEMENT

Line: **95**
Condition: GUILLAIN-BARRE SYNDROME (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL THERAPY

Line: **96**
Condition: SEVERE/MODERATE HEAD INJURY: HEMATOMA/EDEMA WITH LOSS OF CONSCIOUSNESS, COMPOUND/DEPRESSED FRACTURES OF SKULL (See Guideline Notes 1,6,64,65,76,90)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **97**
Condition: ACUTE MYELOID LEUKEMIA, MYELODYSPLASIA, AND MYELOPROLIFERATIVE DISORDERS (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL THERAPY, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **98**
Condition: UNDESCENDED TESTICLE (See Guideline Note 76)
Treatment: SURGICAL TREATMENT

Line: **99**
Condition: HEREDITARY IMMUNE DEFICIENCIES (See Guideline Notes 1,7,11,14,76)
Treatment: BONE MARROW TRANSPLANT

Line: **100**
Condition: DIABETIC AND OTHER RETINOPATHY (See Guideline Notes 64,65,76)
Treatment: LASER SURGERY

Line: **101**
Condition: BORDERLINE PERSONALITY DISORDER (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **102**
Condition: HEART FAILURE (See Guideline Notes 1,6,18,64,65,76)
Treatment: MEDICAL THERAPY

Line: **103**
Condition: CARDIOMYOPATHY (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **104**
Condition: END STAGE RENAL DISEASE (See Guideline Notes 1,76)
Treatment: RENAL TRANSPLANT

Line: **105**
Condition: CONGENITAL ANOMALIES OF DIGESTIVE SYSTEM AND ABDOMINAL WALL EXCLUDING NECROSIS; CHRONIC INTESTINAL PSEUDO-OBSTRUCTION (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **106**
Condition: HEMOLYTIC DISEASE DUE TO ISOIMMUNIZATION, ANEMIA DUE TO TRANSPLACENTAL HEMORRHAGE, AND FETAL AND NEONATAL JAUNDICE (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **107**
Condition: POISONING BY INGESTION, INJECTION, AND NON-MEDICINAL AGENTS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **108**
Condition: BOTULISM (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **109**
Condition: TETRALOGY OF FALLOT (TOF); CONGENITAL VENOUS ABNORMALITIES (See Guideline Notes 1,6,64,65,76)
Treatment: REPAIR

Line: **110**
Condition: CONGENITAL STENOSIS AND INSUFFICIENCY OF AORTIC VALVE (See Guideline Notes 6,64,65,76)
Treatment: SURGICAL VALVE REPLACEMENT/VALVULOPLASTY

Line: **111**
Condition: GIANT CELL ARTERITIS, KAWASAKI DISEASE, POLYMYALGIA RHEUMATICA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **112**
Condition: FRACTURE OF RIBS AND STERNUM, OPEN (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **113**
Condition: SUBACUTE MENINGITIS (EG. TUBERCULOSIS, CRYPTOCOCCOSIS) (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **114**
Condition: COAGULATION DEFECTS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **115**
Condition: CONGENITAL HEART BLOCK; OTHER OBSTRUCTIVE ANOMALIES OF HEART (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL THERAPY

Line: **116**
Condition: CANCER OF TESTIS (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **117**
Condition: CANCER OF EYE AND ORBIT (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES RADIATION THERAPY

Line: **118**
Condition: APLASTIC ANEMIAS; AGRANULOCYTOSIS
Treatment: BONE MARROW TRANSPLANT

Line: **119**
Condition: HODGKIN'S DISEASE (See Guideline Notes 7,11,12,14,19,76)
Treatment: BONE MARROW TRANSPLANT

Line: **120**
Condition: FOREIGN BODY IN PHARYNX, LARYNX, TRACHEA, BRONCHUS AND ESOPHAGUS (See Guideline Notes 64,65,76)
Treatment: REMOVAL OF FOREIGN BODY

Line: **121**
Condition: NUTRITIONAL ANEMIAS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **122**
Condition: ATRIAL SEPTAL DEFECT, SECUNDUM (See Guideline Notes 6,64,65,76)
Treatment: REPAIR SEPTAL DEFECT

Line: **123**
Condition: CHOANAL ATRESIA (See Guideline Notes 64,65,76)
Treatment: REPAIR OF CHOANAL ATRESIA

Line: **124**
Condition: OTHER SPECIFIED APLASTIC ANEMIAS (See Guideline Notes 7,11,14,76)
Treatment: BONE MARROW TRANSPLANT

Line: **125**
Condition: ABUSE AND NEGLECT (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **126**
Condition: ATTENTION DEFICIT DISORDERS WITH HYPERACTIVITY OR UNDIFFERENTIATED (See Guideline Notes 20,64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **127**
Condition: PYODERMA; MODERATE/SEVERE PSORIASIS (See Guideline Notes 1,21,64,65)
Treatment: MEDICAL THERAPY

Line: **128**
Condition: MALARIA, CHAGAS' DISEASE AND TRYPANOSOMIASIS (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **129**
Condition: ANAPHYLACTIC SHOCK; EDEMA OF LARYNX (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **130**
Condition: THYROTOXICOSIS WITH OR WITHOUT GOITER, ENDOCRINE EXOPHTHALMOS; CHRONIC THYROIDITIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, INCLUDING RADIATION THERAPY

Line: **131**
Condition: BENIGN NEOPLASM OF THE BRAIN AND SPINAL CORD (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL, SURGICAL, AND RADIATION THERAPY

Line: **132**
Condition: ACUTE KIDNEY INJURY (See Guideline Notes 1,7,64,65,76)
Treatment: MEDICAL THERAPY INCLUDING DIALYSIS

Line: **133**
Condition: COMMON TRUNCUS (See Guideline Notes 6,64,65,76)
Treatment: TOTAL REPAIR/REPLANT ARTERY

Line: **134**
Condition: GRANULOMATOSIS WITH POLYANGIITIS (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY AND RADIATION THERAPY

Line: **135**
Condition: TOTAL ANOMALOUS PULMONARY VENOUS CONNECTION (See Guideline Notes 1,6,64,65,76)
Treatment: COMPLETE REPAIR

Line: **136**
Condition: CRUSH INJURIES OTHER THAN DIGITS; COMPARTMENT SYNDROME (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **137**
Condition: OPEN FRACTURE/DISLOCATION OF EXTREMITIES (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **138**
Condition: CANCER OF CERVIX (See Guideline Notes 1,7,11,12,19,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY
ICD-10: C53.0-C53.9,Z51.0,Z51.11,Z85.41

Line: **139**
Condition: INTERRUPTED AORTIC ARCH (See Guideline Notes 6,64,65,76)
Treatment: TRANSVERSE ARCH GRAFT

Line: **140**
Condition: HODGKIN'S DISEASE (See Guideline Notes 1,7,11,12,14,19,64,65,76)
Treatment: MEDICAL THERAPY, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **141**
Condition: TRAUMATIC AMPUTATION OF LEG(S) (COMPLETE)(PARTIAL) WITH AND WITHOUT COMPLICATION (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **142**
Condition: OPPORTUNISTIC INFECTIONS IN IMMUNOCOMPROMISED HOSTS; CANDIDIASIS OF STOMA; PERSONS RECEIVING CONTINUOUS ANTIBIOTIC THERAPY (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **143**
Condition: EBSTEIN'S ANOMALY (See Guideline Notes 64,65,76)
Treatment: REPAIR SEPTAL DEFECT/VALVULOPLASTY/REPLACEMENT

Line: **144**
Condition: GLAUCOMA, OTHER THAN PRIMARY ANGLE-CLOSURE (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL,SURGICAL AND LASER TREATMENT

Line: **145**
Condition: MYASTHENIA GRAVIS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY, THYMECTOMY

Line: **146**
Condition: SYSTEMIC LUPUS ERYTHEMATOSUS, OTHER DIFFUSE DISEASES OF CONNECTIVE TISSUE (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **147**
Condition: CONDITIONS INVOLVING THE TEMPERATURE REGULATION OF NEWBORNS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **148**
Condition: PNEUMOTHORAX AND PLEURAL EFFUSION TUBE THORACOSTOMY (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL THERAPY

Line: **149**
Condition: HYPOTHERMIA (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY, EXTRACORPOREAL CIRCULATION

Line: **150**
Condition: ANEMIA OF PREMATURITY OR TRANSIENT NEONATAL NEUTROPENIA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **151**
Condition: ENTERIC INFECTIONS AND OTHER BACTERIAL FOOD POISONING (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **152**
Condition: GLYCOGENOSIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **153**
Condition: ACQUIRED HEMOLYTIC ANEMIAS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **154**
Condition: FEEDING AND EATING DISORDERS OF INFANCY OR CHILDHOOD
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **155**
Condition: CERVICAL VERTEBRAL DISLOCATIONS/FRACTURES, OPEN OR CLOSED; OTHER VERTEBRAL DISLOCATIONS/FRACTURES, OPEN; SPINAL CORD INJURIES WITH OR WITHOUT EVIDENCE OF VERTEBRAL INJURY (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **156**
Condition: DISORDERS OF MINERAL METABOLISM, OTHER THAN CALCIUM (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **157**
Condition: NON-PULMONARY TUBERCULOSIS
Treatment: MEDICAL THERAPY

Line: **158**
Condition: PYOGENIC ARTHRITIS (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **159**
Condition: VASCULAR INSUFFICIENCY OF INTESTINE (See Guideline Notes 64,65,76)
Treatment: SURGICAL TREATMENT

Line: **160**
Condition: HERPES ZOSTER; HERPES SIMPLEX AND WITH NEUROLOGICAL AND OPHTHALMOLOGICAL COMPLICATIONS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **161**
Condition: ACROMEGALY AND GIGANTISM
Treatment: MEDICAL THERAPY

Line: **162**
Condition: CANCER OF COLON, RECTUM, SMALL INTESTINE AND ANUS (See Guideline Notes 1,7,11,12,19,23,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **163**
Condition: NON-HODGKIN'S LYMPHOMAS (See Coding Specification Below) (See Guideline Notes 1,7,11,12,19,64,65,76)
Treatment: MEDICAL THERAPY, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **164**
Condition: TOXIC EPIDERMAL NECROLYSIS AND STAPHYLOCOCCAL SCALDED SKIN SYNDROME; STEVENS-JOHNSON SYNDROME; ERYTHEMA MULTIFORME MAJOR; ECZEMA HERPETICUM (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **165**
Condition: TRAUMATIC AMPUTATION OF ARM(S), HAND(S), THUMB(S), AND FINGER(S) (COMPLETE)(PARTIAL) WITH AND WITHOUT COMPLICATION (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **166**
Condition: GRANULOCYTE DISORDERS (See Guideline Notes 1,7,11,64,65)
Treatment: MEDICAL THERAPY

Line: **167**
Condition: BILIARY ATRESIA (See Guideline Notes 1,76)
Treatment: LIVER TRANSPLANT

Line: **168**
Condition: NON-HODGKIN'S LYMPHOMAS (See Guideline Notes 7,11,12,14,19,76)
Treatment: BONE MARROW TRANSPLANT

Line: **169**
Condition: LEUKOPLAKIA AND CARCINOMA IN SITU OF UPPER AIRWAY, INCLUDING ORAL CAVITY (See Guideline Notes 64,65,76)
Treatment: INCISION/EXCISION, MEDICAL THERAPY

Line: **170**
Condition: PREVENTIVE FOOT CARE IN HIGH RISK PATIENTS (See Guideline Note 76)
Treatment: MEDICAL AND SURGICAL TREATMENT OF TOENAILS AND HYPERKERATOSES OF FOOT

Line: **171**
Condition: ANAL, RECTAL AND COLONIC POLYPS (See Guideline Notes 1,76)
Treatment: EXCISION OF POLYP

Line: **172**
Condition: GONOCOCCAL AND CHLAMYDIAL INFECTIONS OF THE EYE; NEONATAL CONJUNCTIVITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **173**
Condition: COMPLICATED HERNIAS; UNCOMPLICATED INGUINAL HERNIA IN CHILDREN AGE 18 AND UNDER; PERSISTENT HYDROCELE (See Guideline Notes 24,63,64,65,76)
Treatment: REPAIR

Line: **174**
Condition: NON-DIABETIC HYPOGLYCEMIC COMA (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **175**
Condition: RUPTURED SPLEEN (See Guideline Note 76)
Treatment: REPAIR/SPLENECTOMY/INCISION

Line: **176**
Condition: ACUTE MASTOIDITIS (See Guideline Notes 64,65,76)
Treatment: MASTOIDECTOMY, MEDICAL THERAPY

Line: **177**
Condition: AMEBIASIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **178**
Condition: HYPERTENSIVE HEART AND RENAL DISEASE (See Guideline Notes 1,6,64,65)
Treatment: MEDICAL THERAPY

Line: **179**
Condition: POSTTRAUMATIC STRESS DISORDER (See Guideline Notes 25,64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **180**
Condition: GENERALIZED CONVULSIVE OR PARTIAL EPILEPSY WITHOUT MENTION OF IMPAIRMENT OF CONSCIOUSNESS (See Guideline Notes 1,19,76)
Treatment: SINGLE FOCAL SURGERY

Line: **181**
Condition: POLYARTERITIS NODOSA AND ALLIED CONDITIONS (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **182**
Condition: COMMON VENTRICLE (See Guideline Notes 6,64,65,76)
Treatment: TOTAL REPAIR

Line: **183**
Condition: DISORDERS OF AMINO-ACID TRANSPORT AND METABOLISM (NON PKU); HEREDITARY FRUCTOSE INTOLERANCE (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **184**
Condition: INTRACEREBRAL HEMORRHAGE (See Guideline Notes 1,6,64,65,90)
Treatment: MEDICAL THERAPY

Line: **185**
Condition: URETERAL STRICTURE OR OBSTRUCTION; HYDRONEPHROSIS; HYDROURETER (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **186**
Condition: CONDITIONS INVOLVING EXPOSURE TO NATURAL ELEMENTS (EG. LIGHTNING STRIKE, HEATSTROKE) (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY, BURN TREATMENT

Line: **187**
Condition: SEPTICEMIA (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **188**
Condition: FRACTURE OF PELVIS, OPEN AND CLOSED (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **189**
Condition: ACUTE OSTEOMYELITIS (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **190**
Condition: DIVERTICULITIS OF COLON (See Guideline Notes 1,64,65,76)
Treatment: COLON RESECTION, MEDICAL THERAPY

Line: **191**
Condition: RHEUMATIC MULTIPLE VALVULAR DISEASE (See Guideline Notes 6,64,65,76)
Treatment: SURGICAL TREATMENT

Line: **192**
Condition: CUSHING'S SYNDROME; HYPERALDOSTERONISM, OTHER CORTICOADRENAL OVERACTIVITY, MEDULLOADRENAL HYPERFUNCTION (See Guideline Notes 1,64,65,76,93)
Treatment: MEDICAL THERAPY/ADRENALECTOMY

Line: **193**
Condition: CONGENITAL TRICUSPID ATRESIA AND STENOSIS (See Guideline Notes 6,64,65,76)
Treatment: REPAIR

Line: **194**
Condition: CHRONIC ISCHEMIC HEART DISEASE (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **195**
Condition: NEOPLASMS OF ISLETS OF LANGERHANS (See Guideline Notes 1,76)
Treatment: EXCISION OF TUMOR

Line: **196**
Condition: CANCER OF BREAST (See Guideline Notes 1,3,7,11,12,26,64,65,76,79,88)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY, RADIATION THERAPY AND BREAST RECONSTRUCTION

Line: **197**
Condition: HEREDITARY ANGIOEDEMA (See Guideline Notes 1,7,11,12,33,64,65,76)
Treatment: MEDICAL THERAPY

Line: **198**
Condition: MULTIPLE MYELOMA (See Guideline Notes 7,11,12,14,76)
Treatment: BONE MARROW TRANSPLANT

Line: **199**
Condition: HEREDITARY ANEMIAS, HEMOGLOBINOPATHIES, AND DISORDERS OF THE SPLEEN (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **200**
Condition: ACUTE PANCREATITIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **201**
Condition: SUBARACHNOID AND INTRACEREBRAL HEMORRHAGE/HEMATOMA; CEREBRAL ANEURYSM; COMPRESSION OF BRAIN (See Guideline Notes 1,6,64,65,76,90)
Treatment: BURR HOLES, CRANIECTOMY/CRANIOTOMY

Line: **202**
Condition: BURN, PARTIAL THICKNESS WITHOUT VITAL SITE REQUIRING GRAFTING, UP TO 30% OF BODY SURFACE (See Guideline Notes 1,6,64,65,76)
Treatment: FREE SKIN GRAFT, MEDICAL THERAPY

Line: **203**
Condition: CONGENITAL LUNG ANOMALIES (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **204**
Condition: CHRONIC HEPATITIS; VIRAL HEPATITIS (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **205**
Condition: CONSTITUTIONAL APLASTIC ANEMIAS (See Guideline Notes 7,11,14,76)
Treatment: BONE MARROW TRANSPLANT

Line: **206**
Condition: CANCER OF SOFT TISSUE (See Guideline Notes 1,7,11,12,19,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **207**
Condition: CANCER OF BONES (See Guideline Notes 1,6,7,11,12,19,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **208**
Condition: CHRONIC ORGANIC MENTAL DISORDERS INCLUDING DEMENTIAS (See Guideline Notes 1,6,64,65,86,90)
Treatment: CONSULTATION/MEDICATION MANAGEMENT/LIMITED BEHAVIORAL MODIFICATION

Line: **209**
Condition: SLEEP APNEA AND NARCOLEPSY (See Guideline Notes 1,27,36,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **210**
Condition: DEPRESSION AND OTHER MOOD DISORDERS, MILD OR MODERATE (See Guideline Notes 28,64,65,92)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **211**
Condition: PNEUMOCOCCAL PNEUMONIA, OTHER BACTERIAL PNEUMONIA, BRONCHOPNEUMONIA (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **212**
Condition: SUPERFICIAL ABSCESSES AND CELLULITIS (See Coding Specification Below) (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **213**
Condition: ZOONOTIC BACTERIAL DISEASES (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **214**
Condition: DEEP OPEN WOUND, WITH OR WITHOUT TENDON OR NERVE INVOLVEMENT (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **215**
Condition: CANCER OF UTERUS (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **216**
Condition: RUPTURE OF LIVER (See Guideline Notes 64,65,76)
Treatment: SUTURE/REPAIR

Line: **217**
Condition: CANCER OF THYROID (See Guideline Notes 1,7,11,12,19,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **218**
Condition: NON-SUBSTANCE-RELATED ADDICTIVE BEHAVIORAL DISORDERS (See Guideline Notes 64,65) (Note: This line is not priced as part of the list as funding comes from non-OHP sources)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **219**
Condition: BULLOUS DERMATOSES OF THE SKIN (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **220**
Condition: ACUTE PULMONARY HEART DISEASE AND PULMONARY EMBOLI (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **221**
Condition: CANCER OF KIDNEY AND OTHER URINARY ORGANS (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **222**
Condition: CANCER OF STOMACH (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **223**
Condition: PORTAL VEIN THROMBOSIS (See Guideline Notes 64,65,76,77)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **224**
Condition: TESTICULAR CANCER (See Guideline Notes 7,11,12,14,30,76)
Treatment: BONE MARROW RESCUE AND TRANSPLANT

Line: **225**
Condition: DENTAL CONDITIONS (EG. PERIODONTAL DISEASE) (See Guideline Note 53)
Treatment: BASIC PERIODONTICS

Line: **226**
Condition: PULMONARY FIBROSIS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **227**
Condition: DYSLIPIDEMIAS
Treatment: MEDICAL THERAPY

Line: **228**
Condition: DISORDERS OF FLUID, ELECTROLYTE, AND ACID-BASE BALANCE (See Guideline Notes 1,7,64,65,76)
Treatment: MEDICAL THERAPY, DIALYSIS

Line: **229**
Condition: OCCUPATIONAL LUNG DISEASES (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **230**
Condition: DISEASES AND DISORDERS OF AORTIC VALVE (See Guideline Notes 1,6,64,65,76)
Treatment: AORTIC VALVE REPLACEMENT, VALVULOPLASTY, MEDICAL AND SURGICAL THERAPY

Line: **231**
Condition: DISORDERS OF PARATHYROID GLAND; BENIGN NEOPLASM OF PARATHYROID GLAND; DISORDERS OF CALCIUM METABOLISM (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **232**
Condition: ACUTE INFLAMMATION OF THE HEART DUE TO RHEUMATIC FEVER (See Guideline Notes 6,64,65)
Treatment: MEDICAL THERAPY

Line: **233**
Condition: RUPTURED VISCUS (See Guideline Notes 64,65,76)
Treatment: REPAIR

Line: **234**
Condition: INTESTINAL MALABSORPTION (See Coding Specification Below) (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **235**
Condition: FRACTURE OF FACE BONES; INJURY TO OPTIC AND OTHER CRANIAL NERVES (See Guideline Notes 64,65,76)
Treatment: SURGICAL TREATMENT

Line: **236**
Condition: MALIGNANT MELANOMA OF SKIN (See Guideline Notes 7,11,12,19,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **237**
Condition: URINARY FISTULA (See Guideline Notes 64,65,76)
Treatment: SURGICAL TREATMENT

Line: **238**
Condition: MYCOBACTERIA, FUNGAL INFECTIONS, TOXOPLASMOSIS, AND OTHER OPPORTUNISTIC INFECTIONS (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **239**
Condition: HYPOPLASTIC LEFT HEART SYNDROME (See Guideline Note 76)
Treatment: REPAIR

Line: **240**
Condition: ADULT RESPIRATORY DISTRESS SYNDROME; ACUTE RESPIRATORY FAILURE; RESPIRATORY CONDITIONS DUE TO PHYSICAL AND CHEMICAL AGENTS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **241**
Condition: ACUTE LYMPHOCYTIC LEUKEMIAS (ADULT) AND MULTIPLE MYELOMA (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL THERAPY, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **242**
Condition: LIMB THREATENING VASCULAR DISEASE, INFECTIONS, AND VASCULAR COMPLICATIONS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **243**
Condition: TETANUS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **244**
Condition: CANCER OF OVARY (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **245**
Condition: SHORT BOWEL SYNDROME - AGE 5 OR UNDER (See Guideline Notes 1,76)
Treatment: INTESTINE AND INTESTINE/LIVER TRANSPLANT

Line: **246**
Condition: CONDITIONS REQUIRING HEART-LUNG AND LUNG TRANSPLANTATION (See Guideline Notes 1,76)
Treatment: HEART-LUNG AND LUNG TRANSPLANT

Line: **247**
Condition: ACUTE AND SUBACUTE NECROSIS OF LIVER; SPECIFIED INBORN ERRORS OF METABOLISM (EG. MAPLE SYRUP URINE DISEASE, TYROSINEMIA) (See Guideline Notes 1,76)
Treatment: LIVER TRANSPLANT

Line: **248**
Condition: DERMATOLOGICAL PREMALIGNANT LESIONS AND CARCINOMA IN SITU (See Guideline Notes 64,65,76)
Treatment: DESTRUCT/EXCISION/MEDICAL THERAPY

Line: **249**
Condition: PRIMARY ANGLE-CLOSURE GLAUCOMA (See Guideline Notes 64,65,76)
Treatment: MEDICAL, SURGICAL AND LASER SURGERY

Line: **250**
Condition: CORNEAL ULCER; SUPERFICIAL INJURY OF EYE AND ADNEXA (See Guideline Notes 64,65,76)
Treatment: CONJUNCTIVAL FLAP; MEDICAL THERAPY

Line: **251**
Condition: TORSION OF TESTIS (See Guideline Notes 64,65,76)
Treatment: ORCHIECTOMY, REPAIR

Line: **252**
Condition: LIFE-THREATENING EPISTAXIS (See Guideline Notes 64,65,76)
Treatment: SEPTOPLASTY/REPAIR/CONTROL HEMORRHAGE

Line: **253**
Condition: RETAINED INTRAOCULAR FOREIGN BODY, MAGNETIC AND NONMAGNETIC (See Guideline Notes 64,65,76)
Treatment: FOREIGN BODY REMOVAL

Line: **254**
Condition: METABOLIC BONE DISEASE (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **255**
Condition: PARKINSON'S DISEASE (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **256**
Condition: CHRONIC PANCREATITIS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **257**
Condition: MULTIPLE SCLEROSIS AND OTHER DEMYELINATING DISEASES OF CENTRAL NERVOUS SYSTEM (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **258**
Condition: PSYCHOLOGICAL FACTORS AGGRAVATING PHYSICAL CONDITION (EG. ASTHMA, CHRONIC GI CONDITIONS, HYPERTENSION) (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **259**
Condition: ARTERIAL EMBOLISM/THROMBOSIS: ABDOMINAL AORTA, THORACIC AORTA (See Guideline Notes 6,76)
Treatment: SURGICAL TREATMENT

Line: **260**
Condition: CHRONIC OSTEOMYELITIS (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **261**
Condition: MULTIPLE ENDOCRINE NEOPLASIA (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **262**
Condition: DEFORMITIES OF HEAD (See Guideline Notes 1,6,64,65,76,81)
Treatment: CRANIOTOMY/CRANIECTOMY

Line: **263**
Condition: DISEASES OF MITRAL, TRICUSPID, AND PULMONARY VALVES (See Guideline Notes 1,6,64,65,76)
Treatment: VALVULOPLASTY, VALVE REPLACEMENT, MEDICAL THERAPY

Line: **264**
Condition: CANCER OF PENIS AND OTHER MALE GENITAL ORGANS (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **265**
Condition: CANCER OF ENDOCRINE SYSTEM, EXCLUDING THYROID; CARCINOID SYNDROME (See Guideline Notes 1,7,11,12,19,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **266**
Condition: CANCER OF RETROPERITONEUM, PERITONEUM, OMENTUM AND MESENTERY (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **267**
Condition: CANCER OF LUNG, BRONCHUS, PLEURA, TRACHEA, MEDIASTINUM AND OTHER RESPIRATORY ORGANS (See Coding Specification Below) (See Guideline Notes 1,7,11,12,19,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **268**
Condition: CONGESTIVE HEART FAILURE, CARDIOMYOPATHY, MALIGNANT ARRHYTHMIAS, AND COMPLEX CONGENITAL HEART DISEASE (See Guideline Notes 1,6,18,64,65,70,76)
Treatment: CARDIAC TRANSPLANT; HEART/KIDNEY TRANSPLANT

Line: **269**
Condition: TRACHOMA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **270**
Condition: ACUTE, SUBACUTE, CHRONIC AND OTHER TYPES OF IRIDOCYCLITIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **271**
Condition: DENTAL CONDITIONS (TIME SENSITIVE EVENTS)
Treatment: URGENT DENTAL SERVICES

Line: **272**
Condition: RICKETTSIAL AND OTHER ARTHROPOD-BORNE DISEASES (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **273**
Condition: DIABETES INSIPIDUS (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **274**
Condition: ADVANCED DEGENERATIVE DISORDERS AND CONDITIONS OF GLOBE (See Guideline Notes 64,65,76)
Treatment: ENUCLEATION

Line: **275**
Condition: CANCER OF BLADDER AND URETER (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **276**
Condition: TRAUMATIC AMPUTATION OF FOOT/FEET (COMPLETE)(PARTIAL) WITH AND WITHOUT COMPLICATION (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **277**
Condition: LEPROSY, YAWS, PINTA (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **278**
Condition: RETINOPATHY OF PREMATURITY (See Guideline Note 76)
Treatment: CRYOSURGERY

Line: **279**
Condition: UROLOGIC INFECTIONS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **280**
Condition: CANCER OF SKIN, EXCLUDING MALIGNANT MELANOMA (See Guideline Notes 1,7,11,12,19,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **281**
Condition: INJURY TO BLOOD VESSELS OF THE THORACIC CAVITY (See Guideline Notes 1,6,64,65,76)
Treatment: REPAIR

Line: **282**
Condition: OTHER PSYCHOTIC DISORDERS (See Guideline Notes 64,65,82)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **283**
Condition: HYDROPS FETALIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **284**
Condition: DEFORMITY/CLOSED DISLOCATION OF JOINT (See Guideline Notes 6,64,65,76)
Treatment: SURGICAL TREATMENT

Line: **285**
Condition: SENSORINEURAL HEARING LOSS - AGE 5 OR UNDER (See Guideline Notes 31,76)
Treatment: COCHLEAR IMPLANT

Line: **286**
Condition: RETINAL DETACHMENT AND OTHER RETINAL DISORDERS (See Guideline Notes 64,65,76)
Treatment: RETINAL REPAIR, VITRECTOMY

Line: **287**
Condition: HYPOPLASIA AND DYSPLASIA OF LUNG (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **288**
Condition: BUDD-CHIARI SYNDROME, AND OTHER VENOUS EMBOLISM AND THROMBOSIS (See Guideline Notes 64,65,76,77)
Treatment: THROMBECTOMY/LIGATION

Line: **289**
Condition: LIFE-THREATENING CARDIAC ARRHYTHMIAS (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **290**
Condition: ANOREXIA NERVOSA (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **291**
Condition: CHRONIC OBSTRUCTIVE PULMONARY DISEASE; CHRONIC RESPIRATORY FAILURE (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **292**
Condition: DISSECTING OR RUPTURED AORTIC ANEURYSM (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL THERAPY

Line: **293**
Condition: COMPLICATIONS OF A PROCEDURE ALWAYS REQUIRING TREATMENT (See Coding Specification Below) (See Guideline Notes 6,64,65,76,90)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **294**
Condition: CHRONIC LEUKEMIAS; POLYCYTHEMIA RUBRA VERA (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL THERAPY, WHICH INCLUDES CHEMOTHERAPY, RADIATION AND RADIONUCLEIDE THERAPY

Line: **295**
Condition: CANCER OF VAGINA, VULVA, AND OTHER FEMALE GENITAL ORGANS (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **296**
Condition: CANCER OF ORAL CAVITY, PHARYNX, NOSE AND LARYNX (See Coding Specification Below) (See Guideline Notes 1,7,11,12,19,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **297**
Condition: CONSTITUTIONAL APLASTIC ANEMIA (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **298**
Condition: OSTEOPETROSIS (See Guideline Notes 1,7,11,14,76)
Treatment: BONE MARROW TRANSPLANT

Line: **299**
Condition: CLOSED INJURIES OF DIGITS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **300**
Condition: ACUTE STRESS DISORDER (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **301**
Condition: ADRENAL OR CUTANEOUS HEMORRHAGE OF FETUS OR NEONATE (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **302**
Condition: NEUROLOGICAL DYSFUNCTION IN POSTURE AND MOVEMENT CAUSED BY CHRONIC CONDITIONS (See Coding Specification Below) (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT (EG. DURABLE MEDICAL EQUIPMENT AND ORTHOPEDIC PROCEDURE)

Line: **303**
Condition: ANOMALIES OF GALLBLADDER, BILE DUCTS, AND LIVER (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **304**
Condition: CANCER OF BRAIN AND NERVOUS SYSTEM (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: LINEAR ACCELERATOR, MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **305**
Condition: APLASTIC ANEMIAS
Treatment: MEDICAL THERAPY

Line: **306**
Condition: CATARACT (See Guideline Notes 32,64,65,76)
Treatment: EXTRACTION OF CATARACT

Line: **307**
Condition: AFTER CATARACT (See Guideline Note 76)
Treatment: DISCISSION, LENS CAPSULE

Line: **308**
Condition: FISTULA INVOLVING FEMALE GENITAL TRACT (See Guideline Notes 64,65,76)
Treatment: CLOSURE OF FISTULA

Line: **309**
Condition: VITREOUS DISORDERS (See Guideline Notes 64,65,76)
Treatment: VITRECTOMY

Line: **310**
Condition: CLEFT PALATE AND/OR CLEFT LIP (See Guideline Notes 64,65,76,80)
Treatment: EXCISION AND REPAIR VESTIBULE OF MOUTH, ORTHODONTICS

Line: **311**
Condition: GOUT (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **312**
Condition: PERTUSSIS AND DIPTHERIA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **313**
Condition: THROMBOCYTOPENIA (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **314**
Condition: VIRAL PNEUMONIA (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **315**
Condition: DISORDERS OF ARTERIES, OTHER THAN CAROTID OR CORONARY (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **316**
Condition: PARALYTIC ILEUS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **317**
Condition: CIRRHOSIS OF LIVER OR BILIARY TRACT; BUDD-CHIARI SYNDROME; HEPATIC VEIN THROMBOSIS; INTRAHEPATIC VASCULAR MALFORMATIONS; CAROLI'S DISEASE (See Coding Specification Below) (See Guideline Notes 1,76)
Treatment: LIVER TRANSPLANT, LIVER-KIDNEY TRANSPLANT

Line: **318**
Condition: PERVASIVE DEVELOPMENTAL DISORDERS, INCLUDING AUTISM SPECTRUM DISORDERS (See Guideline Notes 1,64,65,75)
Treatment: CONSULTATION/MEDICATION MANAGEMENT/LIMITED BEHAVIORAL MODIFICATION

Line: **319**
Condition: CHRONIC INFLAMMATORY DISORDER OF ORBIT (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **320**
Condition: CONGENITAL DISLOCATION OF HIP; COXA VARA AND VALGA (See Guideline Notes 6,64,65,76)
Treatment: SURGICAL TREATMENT

Line: **321**
Condition: CORNEAL OPACITY AND OTHER DISORDERS OF CORNEA (See Guideline Notes 64,65,76)
Treatment: KERATOPLASTY

Line: **322**
Condition: HEARING LOSS - AGE 5 OR UNDER (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY INCLUDING HEARING AIDS

Line: **323**
Condition: DISORDERS INVOLVING THE IMMUNE SYSTEM (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **324**
Condition: CANCER OF ESOPHAGUS (See Guideline Notes 1,7,11,12,19,33,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **325**
Condition: CANCER OF LIVER (See Guideline Notes 1,7,11,12,33,64,65,76,78)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **326**
Condition: CANCER OF PANCREAS (See Guideline Notes 1,7,11,12,33,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **327**
Condition: STROKE (See Guideline Notes 1,6,64,65,76,90)
Treatment: MEDICAL THERAPY

Line: **328**
Condition: PURULENT ENDOPHTHALMITIS (See Guideline Notes 64,65,76)
Treatment: VITRECTOMY

Line: **329**
Condition: FOREIGN BODY IN CORNEA AND CONJUNCTIVAL SAC (See Guideline Notes 64,65,76)
Treatment: REMOVAL CONJUNCTIVAL FOREIGN BODY

Line: **330**
Condition: OBESITY (ADULT BMI ≥ 30, CHILDHOOD BMI ≥ 95 PERCENTILE)
Treatment: INTENSIVE NUTRITIONAL/PHYSICAL ACTIVITY COUNSELING AND BEHAVIORAL INTERVENTIONS

Line: **331**
Condition: HEMANGIOMAS, COMPLICATED
Treatment: MEDICAL THERAPY

Line: **332**
Condition: OTHER ANEURYSM OF PERIPHERAL ARTERY (See Guideline Note 76)
Treatment: SURGICAL TREATMENT

Line: **333**
Condition: SIALOADENITIS, ABSCESS, FISTULA OF SALIVARY GLANDS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **334**
Condition: CYSTICERCOSIS, OTHER CESTODE INFECTION, TRICHINOSIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **335**
Condition: NON-DISSECTING ANEURYSM WITHOUT RUPTURE (See Guideline Notes 6,64,65,76)
Treatment: SURGICAL TREATMENT

Line: **336**
Condition: FUNCTIONAL AND MECHANICAL DISORDERS OF THE GENITOURINARY SYSTEM INCLUDING BLADDER OUTLET OBSTRUCTION (See Coding Specification Below) (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **337**
Condition: DISSEMINATED INTRAVASCULAR COAGULATION (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **338**
Condition: CANCER OF PROSTATE GLAND (See Guideline Notes 1,7,11,12,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **339**
Condition: SYSTEMIC SCLEROSIS; SJOGREN'S SYNDROME (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **340**
Condition: ANAEROBIC INFECTIONS REQUIRING HYPERBARIC OXYGEN
Treatment: HYPERBARIC OXYGEN

Line: **341**
Condition: BENIGN CEREBRAL CYSTS (See Guideline Note 76)
Treatment: DRAINAGE

Line: **342**
Condition: ALCOHOLIC FATTY LIVER OR ALCOHOLIC HEPATITIS, CIRRHOSIS OF LIVER (See Guideline Notes 1,64,65,76,77)
Treatment: MEDICAL THERAPY

Line: **343**
Condition: SCLERITIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **344**
Condition: RUBEOSIS AND OTHER DISORDERS OF THE IRIS (See Guideline Notes 64,65,76)
Treatment: LASER SURGERY

Line: **345**
Condition: WOUND OF EYE GLOBE (See Guideline Notes 64,65,76)
Treatment: SURGICAL REPAIR

Line: **346**
Condition: ACUTE NECROSIS OF LIVER (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **347**
Condition: CHRONIC KIDNEY DISEASE (See Guideline Notes 1,7,64,65,76)
Treatment: MEDICAL THERAPY INCLUDING DIALYSIS

Line: **348**
Condition: HEREDITARY HEMORRHAGIC TELANGIECTASIA (See Guideline Note 76)
Treatment: EXCISION

Line: **349**
Condition: RHEUMATIC FEVER (See Guideline Notes 6,64,65)
Treatment: MEDICAL THERAPY

Line: **350**
Condition: INTESTINAL DISACCHARIDASE AND OTHER DEFICIENCIES (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **351**
Condition: OTHER AND UNSPECIFIED ANTERIOR PITUITARY HYPERFUNCTION, BENIGN NEOPLASM OF THYROID GLAND AND OTHER ENDOCRINE GLANDS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES RADIATION THERAPY

Line: **352**
Condition: DENTAL CONDITIONS (EG. CARIES, FRACTURED TOOTH) (See Guideline Note 91)
Treatment: BASIC RESTORATIVE (E.G. COMPOSITE RESTORATIONS FOR ANTERIOR TEETH, AMALGAM RESTORATIONS FOR POSTERIOR TEETH)

Line: **353**
Condition: DENTAL CONDITIONS (EG. SEVERE CARIES, INFECTION) (See Guideline Notes 34,48)
Treatment: ORAL SURGERY (I.E. EXTRACTIONS AND OTHER INTRAORAL SURGICAL PROCEDURES)

Line: **354**
Condition: NEUROLOGICAL DYSFUNCTION IN COMMUNICATION CAUSED BY CHRONIC CONDITIONS (See Guideline Notes 6,64,65,76,90)
Treatment: MEDICAL THERAPY

Line: **355**
Condition: CARDIAC ARRHYTHMIAS (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL THERAPY, PACEMAKER

Line: **356**
Condition: MILD/MODERATE BIRTH TRAUMA FOR BABY (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **357**
Condition: NON-LIMB THREATENING PERIPHERAL VASCULAR DISEASE (See Guideline Notes 6,64,65,76)
Treatment: SURGICAL TREATMENT

Line: **358**
Condition: SARCOIDOSIS (See Guideline Notes 1,64,65)
Treatment: MEDICAL THERAPY

Line: **359**
Condition: STRABISMUS DUE TO NEUROLOGIC DISORDER
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **360**
Condition: URINARY SYSTEM CALCULUS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **361**
Condition: STRUCTURAL CAUSES OF AMENORRHEA (See Guideline Note 76)
Treatment: SURGICAL TREATMENT

Line: **362**
Condition: PENETRATING WOUND OF ORBIT (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **363**
Condition: CLOSED FRACTURE OF EXTREMITIES (EXCEPT TOES) (See Guideline Notes 6,64,65,76)
Treatment: OPEN OR CLOSED REDUCTION

Condition: RHEUMATOID ARTHRITIS, OSTEOARTHRITIS, OSTEOCHONDRITIS DISSECANS, AND ASEPTIC NECROSIS OF BONE (See Guideline Notes 6,15,64,65,71,76,83)
Treatment: ARTHROPLASTY/RECONSTRUCTION

Line: **365**
Condition: DISEASES OF PULMONARY ARTERY (See Guideline Notes 6,64,65,76)
Treatment: SURGICAL TREATMENT

Line: 366
Condition: BODY INFESTATIONS (EG. LICE, SCABIES) (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: 367
Condition: CHORIORETINAL INFLAMMATION
Treatment: MEDICAL, SURGICAL, AND LASER TREATMENT

Line: 368
Condition: DYSTONIA (UNCONTROLLABLE); LARYNGEAL SPASM AND STENOSIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: 369
Condition: CYST AND PSEUDOCYST OF PANCREAS (See Guideline Notes 64,65,76)
Treatment: DRAINAGE OF PANCREATIC CYST

Line: 370
Condition: ACUTE SINUSITIS (See Guideline Notes 35,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: 371
Condition: HYPHEMA (See Guideline Note 76)
Treatment: REMOVAL OF BLOOD CLOT

Line: 372
Condition: ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: 373
Condition: ENTROPION AND TRICHIASIS OF EYELID (See Guideline Note 76)
Treatment: REPAIR

Line: 374
Condition: STREPTOCOCCAL SORE THROAT AND SCARLET FEVER; VINCENT'S DISEASE; ULCER OF TONSIL; UNILATERAL HYPERTROPHY OF TONSIL (See Guideline Notes 36,64,65,76)
Treatment: MEDICAL THERAPY, TONSILLECTOMY/ADENOIDECTOMY

Line: 375
Condition: INTESTINAL PARASITES (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: 376
Condition: AMBLYOPIA (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: 377
Condition: TOXIC EFFECT OF GASES, FUMES, AND VAPORS REQUIRING HYPERBARIC OXYGEN
Treatment: HYPERBARIC OXYGEN

Line: 378
Condition: DISORDERS OF SPINE WITH NEUROLOGIC IMPAIRMENT (See Guideline Notes 1,6,37,64,65,72,76,94)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: 379
Condition: ENCEPHALOCELE (See Guideline Note 76)
Treatment: SURGICAL TREATMENT

Line: 380
Condition: BENIGN NEOPLASM OF RESPIRATORY AND INTRATHORACIC ORGANS (See Guideline Notes 64,65,76)
Treatment: LOBECTOMY, MEDICAL THERAPY, WHICH INCLUDES RADIATION THERAPY

Line: 381
Condition: RETINAL TEAR (See Guideline Notes 64,65,76)
Treatment: LASER PROPHYLAXIS

Line: 382
Condition: CHOLESTEATOMA; INFECTIONS OF THE PINNA (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **383**
Condition: DISRUPTIONS OF THE LIGAMENTS AND TENDONS OF THE ARMS AND LEGS, EXCLUDING THE KNEE, RESULTING IN SIGNIFICANT INJURY/IMPAIRMENT (See Guideline Notes 6,64,65,76)
Treatment: REPAIR

Line: **384**
Condition: DYSFUNCTION RESULTING IN LOSS OF ABILITY TO MAXIMIZE LEVEL OF INDEPENDENCE IN SELF-DIRECTED CARE CAUSED BY CHRONIC CONDITIONS THAT CAUSE NEUROLOGICAL DYSFUNCTION (See Guideline Notes 1,6,38,64,65,76,90)
Treatment: MEDICAL THERAPY (SHORT TERM REHABILITATION WITH DEFINED GOALS)

Line: **385**
Condition: ANEMIAS DUE TO DISEASE OR TREATMENT AND OTHER APLASTIC ANEMIAS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **386**
Condition: ESOPHAGEAL STRICTURE; ACHALASIA (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **387**
Condition: CHRONIC ULCER OF SKIN (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **388**
Condition: ESOPHAGITIS; ESOPHAGEAL AND INTRAESOPHAGEAL HERNIAS (See Guideline Note 76)
Treatment: SURGICAL TREATMENT

Line: **389**
Condition: BULIMIA NERVOSA (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **390**
Condition: LATE SYPHILIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **391**
Condition: CENTRAL SEROUS RETINOPATHY (See Guideline Note 10)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **392**
Condition: DENTAL CONDITIONS (E.G. PULPAL PATHOLOGY, PERMANENT ANTERIOR TOOTH)
Treatment: BASIC ENDODONTICS (I.E. ROOT CANAL THERAPY)

Line: **393**
Condition: SUPERFICIAL INJURIES WITH INFECTION (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **394**
Condition: PITUITARY DWARFISM (See Guideline Notes 64,65,74)
Treatment: MEDICAL THERAPY

Line: **395**
Condition: SEPARATION ANXIETY DISORDER (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **396**
Condition: ACUTE OTITIS MEDIA (See Guideline Notes 29,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **397**
Condition: PANIC DISORDER; AGORAPHOBIA (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **398**
Condition: CROUP SYNDROME, EPIGLOTTITIS, ACUTE LARYNGOTRACHEITIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY, INTUBATION, TRACHEOTOMY

Line: **399**
Condition: STRABISMUS; CONGENITAL ANOMALIES OF EYE; LACRIMAL DUCT OBSTRUCTION IN CHILDREN (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **400**
Condition: ACHALASIA, NON-NEONATAL (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **401**
Condition: ENDOMETRIOSIS AND ADENOMYOSIS (See Guideline Notes 1,39,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **402**
Condition: MYELOID DISORDERS
Treatment: MEDICAL THERAPY, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **403**
Condition: INFLUENZA (See Guideline Note 87)
Treatment: MEDICAL THERAPY

Line: **404**
Condition: THROMBOTIC DISORDERS
Treatment: MEDICAL THERAPY

Line: **405**
Condition: GENDER DYSPHORIA
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **406**
Condition: ANOGENITAL VIRAL WARTS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL THERAPY

Line: **407**
Condition: LYMPHADENITIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **408**
Condition: UTERINE LEIOMYOMA AND POLYPS (See Guideline Notes 40,64,65,76)
Treatment: TOTAL HYSTERECTOMY OR MYOMECTOMY

Line: **409**
Condition: APHAKIA AND OTHER DISORDERS OF LENS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL THERAPY

Line: **410**
Condition: BILATERAL ANOMALIES OF EXTERNAL EAR WITH IMPAIRMENT OF HEARING (See Guideline Notes 64,65,76)
Treatment: RECONSTRUCT OF EAR CANAL

Line: **411**
Condition: DISSOCIATIVE DISORDERS (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **412**
Condition: EPIDERMOLYSIS BULLOSA (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY

Line: **413**
Condition: DELIRIUM DUE TO MEDICAL CAUSES (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **414**
Condition: SPINAL DEFORMITY, CLINICALLY SIGNIFICANT (See Guideline Notes 1,6,41,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **415**
Condition: MIGRAINE HEADACHES (See Guideline Notes 1,64,65,92)
Treatment: MEDICAL THERAPY

Line: **416**
Condition: DENTAL CONDITIONS (EG. PULPAL PATHOLOGY, PERMANENT BICUSPID/PREMOLAR TOOTH)
Treatment: BASIC ENDODONTICS (I.E. ROOT CANAL THERAPY)

Line: **417**
Condition: SCHIZOTYPAL PERSONALITY DISORDERS (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **418**
Condition: BALANOPOSTHITIS AND OTHER DISORDERS OF PENIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **419**
Condition: OVERANXIOUS DISORDER; GENERALIZED ANXIETY DISORDER; ANXIETY DISORDER, UNSPECIFIED (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **420**
Condition: TRANSIENT CEREBRAL ISCHEMIA; OCCLUSION/STENOSIS OF PRECEREBRAL ARTERIES WITHOUT OCCLUSION (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY; THROMBOENDARTERECTOMY

Line: **421**
Condition: PERIPHERAL NERVE ENTRAPMENT; PALMAR FASCIAL FIBROMATOSIS (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **422**
Condition: MENIERE'S DISEASE (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **423**
Condition: DISORDERS OF SHOULDER, INCLUDING SPRAINS/STRAINS GRADE 3 THROUGH 6 (See Guideline Notes 6,64,65,76)
Treatment: REPAIR/RECONSTRUCTION, MEDICAL THERAPY

Line: **424**
Condition: INCONTINENCE OF FECES; FECAL IMPACTION (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **425**
Condition: SENSORINEURAL HEARING LOSS - OVER AGE OF FIVE (See Guideline Notes 1,49,76)
Treatment: COCHLEAR IMPLANT

Line: **426**
Condition: OPPOSITIONAL DEFIANT DISORDER (See Guideline Notes 42,64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **427**
Condition: MENSTRUAL BLEEDING DISORDERS (See Guideline Notes 1,44,64,65,76,88)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **428**
Condition: COMPLICATIONS OF A PROCEDURE USUALLY REQUIRING TREATMENT (See Guideline Notes 6,43,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **429**
Condition: ADRENOGENITAL DISORDERS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **430**
Condition: ACUTE PERIPHERAL MOTOR AND DIGITAL NERVE INJURY
Treatment: SURGICAL THERAPY

Line: **431**
Condition: ANGIOEDEMA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **432**
Condition: NON-MALIGNANT OTITIS EXTERNA (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **433**
Condition: VAGINITIS AND CERVICITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **434**
Condition: NONINFLAMMATORY DISORDERS AND BENIGN NEOPLASMS OF OVARY, FALLOPIAN TUBES AND UTERUS; OVARIAN CYSTS; GONADAL DYSGENISIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **435**
Condition: URETHRAL FISTULA (See Guideline Notes 64,65,76)
Treatment: EXCISION, MEDICAL THERAPY

Line: **436**
Condition: INTERNAL DERANGEMENT OF KNEE AND LIGAMENTOUS DISRUPTIONS OF THE KNEE, RESULTING IN SIGNIFICANT INJURY/IMPAIRMENT (See Guideline Notes 6,64,65,76)
Treatment: REPAIR, MEDICAL THERAPY

Line: **437**
Condition: OPEN WOUND OF EAR DRUM (See Guideline Note 76)
Treatment: TYMPANOPLASTY

Line: **438**
Condition: CHRONIC DEPRESSION (DYSTHYMIA) (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **439**
Condition: HYPOSPADIAS AND EPISPADIAS (See Guideline Notes 64,65,73,76,89)
Treatment: REPAIR

Line: **440**
Condition: CANCER OF GALLBLADDER AND OTHER BILIARY (See Guideline Notes 1,7,11,12,33,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY

Line: **441**
Condition: PRECANCEROUS VULVAR CONDITIONS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **442**
Condition: RECURRENT EROSION OF THE CORNEA (See Guideline Notes 64,65,76)
Treatment: ANTERIAL STROMAL PUNCTURE, REMOVAL OF CORNEAL EPITHELIUM; WITH OR WITHOUT CHEMOCAUTERIZATION

Line: **443**
Condition: STEREOTYPY/HABIT DISORDER AND SELF-ABUSIVE BEHAVIOR DUE TO NEUROLOGICAL DYSFUNCTION (See Guideline Notes 1,64,65)
Treatment: CONSULTATION/MEDICATION MANAGEMENT/LIMITED BEHAVIORAL MODIFICATION

Line: **444**
Condition: FOREIGN BODY IN UTERUS, VULVA AND VAGINA (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **445**
Condition: RESIDUAL FOREIGN BODY IN SOFT TISSUE (See Guideline Note 76)
Treatment: REMOVAL

Line: **446**
Condition: VENOUS TRIBUTARY (BRANCH) OCCLUSION; CENTRAL RETINAL VEIN OCCLUSION (See Guideline Notes 64,65,76)
Treatment: LASER SURGERY, MEDICAL THERAPY INCLUDING INJECTION

Line: **447**
Condition: TRIGEMINAL AND OTHER NERVE DISORDERS (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT, RADIATION THERAPY

Line: **448**
Condition: MALUNION AND NONUNION OF FRACTURE (See Guideline Notes 6,64,65,76)
Treatment: SURGICAL TREATMENT

Line: **449**
Condition: DENTAL CONDITIONS (EG. PULPAL PATHOLOGY, PERMANENT MOLAR TOOTH)
Treatment: BASIC ENDODONTICS (I.E. ROOT CANAL THERAPY)

Line: **450**
Condition: ADJUSTMENT DISORDERS (See Coding Specification Below) (See Guideline Notes 45,64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **451**
Condition: HEARING LOSS - OVER AGE OF FIVE (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL THERAPY INCLUDING HEARING AIDS

Line: **452**
Condition: TOURETTE'S DISORDER AND TIC DISORDERS (See Guideline Notes 1,64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **453**
Condition: ATHEROSCLEROSIS, AORTIC AND RENAL (See Guideline Notes 1,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **454**
Condition: DEGENERATION OF MACULA AND POSTERIOR POLE (See Guideline Notes 46,64,65,76)
Treatment: MEDICAL, SURGICAL AND LASER THERAPY

Line: **455**
Condition: REACTIVE ATTACHMENT DISORDER OF INFANCY OR EARLY CHILDHOOD (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **456**
Condition: DISORDERS OF REFRACTION AND ACCOMMODATION (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **457**
Condition: EXOPHTHALMOS AND CYSTS OF THE EYE AND ORBIT (See Guideline Notes 64,65,76)
Treatment: SURGICAL TREATMENT

Line: **458**
Condition: DENTAL CONDITIONS (EG. MISSING TEETH, PROSTHESIS FAILURE) (See Guideline Note 62)
Treatment: REMOVABLE PROSTHODONTICS (E.G. FULL AND PARTIAL DENTURES, RELINES)

Line: **459**
Condition: URINARY INCONTINENCE (See Guideline Notes 1,6,47,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **460**
Condition: DISORDERS OF PLASMA PROTEIN METABOLISM (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **461**
Condition: DENTAL CONDITIONS (E.G. PULPAL PATHOLOGY, PERMANENT ANTERIOR TOOTH)
Treatment: ADVANCED ENDODONTICS (E.G. RETREATMENT OF PREVIOUS ROOT CANAL THERAPY)

Line: **462**
Condition: FACTITIOUS DISORDERS (See Guideline Notes 64,65)
Treatment: CONSULTATION

Line: **463**
Condition: SIMPLE AND SOCIAL PHOBIAS (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **464**
Condition: ACUTE BRONCHITIS AND BRONCHIOLITIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **465**
Condition: CENTRAL PTERYGIUM AFFECTING VISION (See Guideline Notes 64,65,76)
Treatment: EXCISION OR TRANSPOSITION OF PTERYGIUM WITHOUT GRAFT, RADIATION THERAPY

Line: **466**
Condition: BRANCHIAL CLEFT CYST; THYROGLOSSAL DUCT CYST; CYST OF PHARYNX OR NASOPHARYNX (See Guideline Notes 64,65,76)
Treatment: EXCISION, MEDICAL THERAPY

Line: **467**
Condition: OBSESSIVE-COMPULSIVE DISORDERS (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **468**
Condition: OSTEOARTHRITIS AND ALLIED DISORDERS (See Guideline Notes 1,6,64,65,76)
Treatment: MEDICAL THERAPY, INJECTIONS

Line: **469**
Condition: ATELECTASIS (COLLAPSE OF LUNG) (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **470**
Condition: CHRONIC SINUSITIS (See Guideline Notes 35,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **471**
Condition: UTERINE PROLAPSE; CYSTOCELE (See Guideline Notes 50,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **472**
Condition: BRACHIAL PLEXUS LESIONS (See Guideline Notes 64,65,76)
Treatment: MEDICAL THERAPY

Line: **473**
Condition: DENTAL CONDITIONS (EG. CARIES, FRACTURED TOOTH)
Treatment: ADVANCED RESTORATIVE (I.E. BASIC CROWNS)

Line: **474**
Condition: GONADAL DYSFUNCTION, MENOPAUSAL MANAGEMENT (See Guideline Notes 64,65,74,76,88)
Treatment: OOPHORECTOMY, ORCHIECTOMY, HORMONAL REPLACEMENT FOR PURPOSES OTHER THAN INFERTILITY

Line: **475**
Condition: ENCOPRESIS NOT DUE TO A PHYSIOLOGICAL CONDITION (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **476**
Condition: ACQUIRED PTOSIS AND OTHER EYELID DISORDERS WITH VISION IMPAIRMENT (See Guideline Notes 64,65,76)
Treatment: PTOSIS REPAIR

Line: **477**
Condition: KERATOCONJUNCTIVITS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **478**
Condition: USE OF ADDICTIVE SUBSTANCES
Treatment: MEDICAL THERAPY

Line: **479**
Condition: SELECTIVE MUTISM (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **480**
Condition: THROMBOSED AND COMPLICATED HEMORRHOIDS (See Guideline Notes 64,65,76)
Treatment: HEMORRHOIDECTOMY, INCISION

Line: **481**
Condition: CHRONIC OTITIS MEDIA (See Guideline Notes 51,64,65,76)
Treatment: PE TUBES/ADENOIDECTOMY/TYMPANOPLASTY, MEDICAL THERAPY

Line: **482**
Condition: RECTAL PROLAPSE (See Guideline Notes 64,65,76)
Treatment: SURGICAL TREATMENT

Line: **483**
Condition: OTOSCLEROSIS (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **484**
Condition: FOREIGN BODY IN EAR AND NOSE (See Guideline Notes 64,65,76)
Treatment: REMOVAL OF FOREIGN BODY

Line: **485**
Condition: ANAL FISTULA; CHRONIC ANAL FISSURE (See Guideline Notes 1,52,64,65,76)
Treatment: SPHINCTEROTOMY, FISSURECTOMY, FISTULECTOMY, MEDICAL THERAPY

Line: **486**
Condition: CLOSED DISLOCATIONS/FRACTURES OF NON-CERVICAL VERTEBRAL COLUMN WITHOUT SPINAL CORD INJURY (See Guideline Notes 6,64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **487**
Condition: CONDUCT DISORDER, AGE 18 OR UNDER (See Guideline Notes 54,64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **488**
Condition: BREAST CYSTS AND OTHER DISORDERS OF THE BREAST (See Guideline Notes 64,65,76)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **489**
Condition: CYSTS OF BARTHOLIN'S GLAND AND VULVA (See Guideline Notes 64,65,76)
Treatment: INCISION AND DRAINAGE, MEDICAL THERAPY

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Line: **490**
Condition: LICHEN PLANUS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **491**
Condition: RUPTURE OF SYNOVIUM
Treatment: REMOVAL OF BAKER'S CYST

Line: **492**
Condition: ENOPHTHALMOS (See Guideline Notes 64,65)
Treatment: ORBITAL IMPLANT

Line: **493**
Condition: BELL'S PALSY, EXPOSURE KERATOCONJUNCTIVITIS (See Guideline Notes 64,65)
Treatment: TARSORRHAPHY

Line: **494**
Condition: PERIPHERAL ENTHESOPATHIES (See Guideline Notes 6,64,65)
Treatment: MEDICAL THERAPY

Line: **495**
Condition: DERMATOPHYTOSIS OF NAIL, GROIN, AND FOOT AND OTHER DERMATOMYCOSIS (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **496**
Condition: CLOSED FRACTURES OF RIBS, STERNUM AND COCCYX (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **497**
Condition: SOMATIZATION DISORDER, SOMATOFORM PAIN DISORDER, CONVERSION DISORDER
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **498**
Condition: SPASTIC DIPLEGIA
Treatment: RHIZOTOMY

Line: **499**
Condition: DENTAL CONDITIONS (EG. PERIODONTAL DISEASE)
Treatment: ADVANCED PERIODONTICS (E.G. SURGICAL PROCEDURES AND SPLINTING)

Line: **500**
Condition: HEPATORENAL SYNDROME (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **501**
Condition: PARAPHILIAS AND OTHER PSYCHOSEXUAL DISORDERS (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **502**
Condition: ECTROPION AND BENIGN NEOPLASM OF EYE
Treatment: ECTROPION REPAIR

Line: **503**
Condition: RAYNAUD'S SYNDROME (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **504**
Condition: CALCIUM PYROPHOSPHATE DEPOSITION DISEASE (CPPD) AND HYDROXYAPETITE DEPOSITION DISEASE
Treatment: MEDICAL THERAPY

Line: **505**
Condition: PHIMOSIS
Treatment: SURGICAL TREATMENT

Line: **506**
Condition: CERUMEN IMPACTION (See Guideline Notes 64,65)
Treatment: REMOVAL OF EAR WAX

Line: **507**
Condition: SIALOLITHIASIS, MUCOCELE, DISTURBANCE OF SALIVARY SECRETION, OTHER AND UNSPECIFIED DISEASES OF SALIVARY GLANDS (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **508**
Condition: CHRONIC CONJUNCTIVITIS, BLEPHAROCONJUNCTIVITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **509**
Condition: OTHER DISORDERS OF SYNOVIUM, TENDON AND BURSA, COSTOCHONDRITIS, AND CHONDRODYSTROPHY (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **510**
Condition: ERYTHEMATOUS CONDITIONS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **511**
Condition: PERIPHERAL ENTHESOPATHIES
Treatment: SURGICAL TREATMENT

Line: **512**
Condition: NASAL POLYPS, OTHER DISORDERS OF NASAL CAVITY AND SINUSES (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **513**
Condition: DENTAL CONDITIONS (E.G. PULPAL PATHOLOGY, PERMANENT BICUSPID/PREMOLAR TOOTH)
Treatment: ADVANCED ENDODONTICS (E.G. RETREATMENT OF PREVIOUS ROOT CANAL THERAPY)

Line: **514**
Condition: CIRCUMSCRIBED SCLERODERMA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **515**
Condition: PERIPHERAL NERVE DISORDERS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **516**
Condition: CLOSED FRACTURE OF GREAT TOE (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **517**
Condition: DYSFUNCTION OF NASOLACRIMAL SYSTEM IN ADULTS; LACRIMAL SYSTEM LACERATION (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **518**
Condition: BENIGN NEOPLASM OF KIDNEY AND OTHER URINARY ORGANS (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **519**
Condition: VERTIGINOUS SYNDROMES AND OTHER DISORDERS OF VESTIBULAR SYSTEM (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **520**
Condition: ESOPHAGITIS AND GERD; ESOPHAGEAL SPASM
Treatment: MEDICAL THERAPY

Line: **521**
Condition: CLOSED FRACTURE OF ONE OR MORE PHALANGES OF THE FOOT, NOT INCLUDING THE GREAT TOE
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **522**
Condition: HYDRADENITIS SUPPURATIVA; DISSECTING CELLULITIS OF THE SCALP
Treatment: MEDICAL THERAPY

Line: **523**
Condition: CHRONIC PROSTATITIS, OTHER DISORDERS OF PROSTATE (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **524**
Condition: PHLEBITIS AND THROMBOPHLEBITIS, SUPERFICIAL (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **525**
Condition: DISORDERS OF SWEAT GLANDS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **526**
Condition: PARALYSIS OF VOCAL CORDS OR LARYNX (See Guideline Notes 64,65)
Treatment: INCISION/EXCISION/ENDOSCOPY

Line: **527**
Condition: POSTTHROMBOTIC SYNDROME
Treatment: MEDICAL THERAPY

Line: **528**
Condition: FOREIGN BODY IN GASTROINTESTINAL TRACT
Treatment: MEDICAL THERAPY

Line: **529**
Condition: PANNICULITIS
Treatment: MEDICAL THERAPY

Line: **530**
Condition: ROSACEA; ACNE (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **531**
Condition: SEXUAL DYSFUNCTION (See Guideline Notes 64,65)
Treatment: PSYCHOTHERAPY, MEDICAL AND SURGICAL TREATMENT

Line: **532**
Condition: UNCOMPLICATED HERNIA (OTHER THAN INGUINAL HERNIA IN CHILDREN AGE 18 AND UNDER OR DIAPHRAGMATIC HERNIA) (See Guideline Notes 64,65)
Treatment: REPAIR

Line: **533**
Condition: BENIGN NEOPLASM OF NASAL CAVITIES, MIDDLE EAR AND ACCESSORY SINUSES
Treatment: EXCISION, RECONSTRUCTION

Line: **534**
Condition: BENIGN NEOPLASM BONE AND ARTICULAR CARTILAGE INCLUDING OSTEOID OSTEOMAS; BENIGN NEOPLASM OF CONNECTIVE AND OTHER SOFT TISSUE (See Guideline Notes 6,64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT, RADIATION THERAPY

Line: **535**
Condition: DEFORMITIES OF UPPER BODY AND ALL LIMBS (See Guideline Notes 64,65)
Treatment: REPAIR/REVISION/RECONSTRUCTION/RELOCATION/MEDICAL THERAPY

Line: **536**
Condition: DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **537**
Condition: PELVIC PAIN SYNDROME, DYSPAREUNIA (See Guideline Notes 55,64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **538**
Condition: ATOPIC DERMATITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **539**
Condition: CONTACT DERMATITIS AND OTHER ECZEMA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **540**
Condition: HYPOTENSION (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **541**
Condition: VIRAL, SELF-LIMITING ENCEPHALITIS, MYELITIS AND ENCEPHALOMYELITIS (See Guideline Notes 61,64,65)
Treatment: MEDICAL THERAPY

Line: **542**
Condition: PERIPHERAL NERVE DISORDERS
Treatment: SURGICAL TREATMENT

Line: **543**
Condition: DENTAL CONDITIONS (E.G. PULPAL PATHOLOGY, PERMANENT MOLAR TOOTH)
Treatment: ADVANCED ENDODONTICS (E.G. RETREATMENT OF PREVIOUS ROOT CANAL THERAPY)

Line: **542**
Condition: ICHTHYOSIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **545**
Condition: LESION OF PLANTAR NERVE; PLANTAR FASCIAL FIBROMATOSIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY, EXCISION

Line: **546**
Condition: ACUTE AND CHRONIC DISORDERS OF SPINE WITHOUT NEUROLOGIC IMPAIRMENT (See Guideline Notes 6,56,64,65,72,94)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **547**
Condition: TENSION HEADACHES (See Guideline Notes 64,65,92)
Treatment: MEDICAL THERAPY

Line: **548**
Condition: MILD PSORIASIS ; DERMATOPHYTOSIS: SCALP, HAND, BODY, DEEP-SEATED (See Guideline Notes 57,64,65)
Treatment: MEDICAL THERAPY

Line: **549**
Condition: DEFORMITIES OF FOOT (See Guideline Notes 64,65)
Treatment: FASCIOTOMY/INCISION/REPAIR/ARTHRODESIS

Line: **550**
Condition: FOREIGN BODY GRANULOMA OF MUSCLE, SKIN AND SUBCUTANEOUS TISSUE (See Guideline Notes 64,65,76)
Treatment: REMOVAL OF GRANULOMA

Line: **551**
Condition: HYDROCELE (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY, EXCISION

Line: **552**
Condition: SYMPTOMATIC URTICARIA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **553**
Condition: IMPULSE DISORDERS (See Guideline Notes 58,64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **554**
Condition: SUBLINGUAL, SCROTAL, AND PELVIC VARICES (See Guideline Notes 64,65)
Treatment: VENOUS INJECTION, VASCULAR SURGERY

Line: **555**
Condition: ASEPTIC MENINGITIS (See Guideline Notes 61,64,65)
Treatment: MEDICAL THERAPY

Line: **556**
Condition: TMJ DISORDER (See Guideline Notes 64,65)
Treatment: TMJ SPLINTS

Line: **557**
Condition: CHRONIC DISEASE OF TONSILS AND ADENOIDS (See Guideline Notes 36,64,65)
Treatment: TONSILLECTOMY AND ADENOIDECTOMY

Line: **558**
Condition: OTHER NONINFECTIOUS GASTROENTERITIS AND COLITIS (See Guideline Notes 61,64,65)
Treatment: MEDICAL THERAPY

Line: **559**
Condition: HEMATOMA OF AURICLE OR PINNA AND HEMATOMA OF EXTERNAL EAR (See Guideline Notes 64,65)
Treatment: DRAINAGE

Line: **560**
Condition: MILD ECZEMATOUS AND OTHER HYPERTROPHIC OR ATROPHIC CONDITIONS OF SKIN (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **561**
Condition: CHONDROMALACIA (See Guideline Notes 6,64,65)
Treatment: MEDICAL THERAPY

Line: **562**
Condition: DYSMENORRHEA (See Guideline Notes 59,64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **563**
Condition: OPEN WOUND OF EAR DRUM (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **564**
Condition: SPASTIC DYSPHONIA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **565**
Condition: MACROMASTIA
Treatment: BREAST REDUCTION

Line: **566**
Condition: ALLERGIC RHINITIS AND CONJUNCTIVITIS, CHRONIC RHINITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **567**
Condition: CANCER OF LIVER AND INTRAHEPATIC BILE DUCTS (See Guideline Note 12)
Treatment: LIVER TRANSPLANT

Line: **568**
Condition: BENIGN NEOPLASM AND CONDITIONS OF EXTERNAL FEMALE GENITAL ORGANS
Treatment: EXCISION

Line: **569**
Condition: HORDEOLUM AND OTHER DEEP INFLAMMATION OF EYELID; CHALAZION (See Guideline Notes 64,65)
Treatment: INCISION AND DRAINAGE, MEDICAL THERAPY

Line: **570**
Condition: CONDUCTIVE HEARING LOSS
Treatment: AUDIANT BONE CONDUCTORS

Line: **571**
Condition: ACUTE ANAL FISSURE (See Guideline Notes 64,65)
Treatment: FISSURECTOMY, MEDICAL THERAPY

Line: **572**
Condition: PLEURISY (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **573**
Condition: PERITONEAL ADHESION
Treatment: SURGICAL TREATMENT

Line: **574**
Condition: DERMATITIS DUE TO SUBSTANCES TAKEN INTERNALLY (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **575**
Condition: BLEPHARITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **576**
Condition: UNSPECIFIED URINARY OBSTRUCTION AND BENIGN PROSTATIC HYPERPLASIA WITHOUT OBSTRUCTION (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **577**
Condition: OTHER COMPLICATIONS OF A PROCEDURE (See Guideline Notes 6,43,64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **578**
Condition: LYMPHEDEMA (See Guideline Notes 43,64,65)
Treatment: MEDICAL THERAPY, OTHER OPERATION ON LYMPH CHANNEL

Line: **579**
Condition: PERSONALITY DISORDERS EXCLUDING BORDERLINE AND SCHIZOTYPAL
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **580**
Condition: ACUTE NON-SUPPURATIVE LABYRINTHITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **581**
Condition: DEVIATED NASAL SEPTUM, ACQUIRED DEFORMITY OF NOSE, OTHER DISEASES OF UPPER RESPIRATORY TRACT (See Guideline Notes 64,65)
Treatment: EXCISION OF CYST/RHINECTOMY/PROSTHESIS

Line: **582**
Condition: STOMATITIS AND OTHER DISEASES OF ORAL SOFT TISSUES (See Guideline Notes 64,65)
Treatment: INCISION AND DRAINAGE, MEDICAL THERAPY

Line: **583**
Condition: CAVUS DEFORMITY OF FOOT; FLAT FOOT; POLYDACTYLY AND SYNDACTYLY OF TOES (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY, ORTHOTIC

Line: **584**
Condition: INFECTIOUS MONONUCLEOSIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **585**
Condition: URETHRITIS, NON-SEXUALLY TRANSMITTED (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **586**
Condition: CONGENITAL ANOMALIES OF FEMALE GENITAL ORGANS EXCLUDING VAGINA (See Guideline Notes 64,65)
Treatment: SURGICAL TREATMENT

Line: **587**
Condition: SPINAL DEFORMITY, NOT CLINICALLY SIGNIFICANT (See Guideline Notes 60,64,65)
Treatment: ARTHRODESIS/REPAIR/RECONSTRUCTION, MEDICAL THERAPY

Line: **588**
Condition: CANDIDIASIS OF MOUTH, SKIN AND NAILS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **589**
Condition: BENIGN NEOPLASM OF MALE GENITAL ORGANS: TESTIS, PROSTATE, EPIDIDYMIS (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **590**
Condition: ATROPHY OF EDENTULOUS ALVEOLAR RIDGE
Treatment: VESTIBULOPLASTY, GRAFTS, IMPLANTS

Line: **591**
Condition: DISEASE OF NAILS, HAIR AND HAIR FOLLICLES (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **592**
Condition: OBESITY (ADULT BMI ≥ 30, CHILDHOOD BMI ≥ 95 PERCENTILE) (See Guideline Notes 8,64,65)
Treatment: NON-INTENSIVE NUTRITIONAL/PHYSICAL ACTIVITY COUNSELING AND BEHAVIORAL INTERVENTIONS; BARIATRIC SURGERY FOR OBESITY WITH A SIGNIFICANT COMORBIDITY OTHER THAN TYPE II DIABETES & BMI >=35 OR BMI>=40 WITHOUT A SIGNIFICANT COMORBIDITY

Line: **593**
Condition: ACUTE TONSILLITIS OTHER THAN BETA-STREPTOCOCCAL (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **594**
Condition: CORNS AND CALLUSES (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **595**
Condition: SYNOVITIS AND TENOSYNOVITIS (See Guideline Notes 6,64,65)
Treatment: MEDICAL THERAPY

Line: **596**
Condition: PROLAPSED URETHRAL MUCOSA (See Guideline Notes 64,65)
Treatment: SURGICAL TREATMENT

Line: **597**
Condition: DENTAL CONDITIONS (EG. CARIES, FRACTURED TOOTH)
Treatment: ADVANCED RESTORATIVE-ELECTIVE (INLAYS,ONLAYS,GOLD FOIL AND HIGH NOBLE METAL RESTORATIONS)

Line: **598**
Condition: SECONDARY AND ILL-DEFINED MALIGNANT NEOPLASMS (See Guideline Notes 7,11,12,64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **599**
Condition: GANGLION (See Guideline Notes 64,65)
Treatment: EXCISION

Line: **600**
Condition: EPISCLERITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **601**
Condition: DIAPER RASH (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **602**
Condition: TONGUE TIE AND OTHER ANOMALIES OF TONGUE
Treatment: FRENOTOMY, TONGUE TIE

Line: **603**
Condition: INCONSEQUENTIAL CYSTS OF ORAL SOFT TISSUES (See Guideline Notes 64,65)
Treatment: INCISION AND DRAINAGE

Line: **604**
Condition: CONGENITAL DEFORMITIES OF KNEE (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **605**
Condition: CHRONIC PANCREATITIS
Treatment: SURGICAL TREATMENT

Line: **606**
Condition: HERPES SIMPLEX WITHOUT COMPLICATIONS, EXCLUDING GENITAL HERPES (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **607**
Condition: DENTAL CONDITIONS (EG. MISSING TEETH)
Treatment: COMPLEX PROSTHODONTICS (I.E. FIXED BRIDGES, OVERDENTURES)

Line: **608**
Condition: CONGENITAL ANOMALIES OF THE EAR WITHOUT IMPAIRMENT OF HEARING; UNILATERAL ANOMALIES OF THE EAR
Treatment: OTOPLASTY, REPAIR AND AMPUTATION

Line: **609**
Condition: KELOID SCAR; OTHER ABNORMAL GRANULATION TISSUE
Treatment: INTRALESIONAL INJECTIONS/DESTRUCTION/EXCISION, RADIATION THERAPY

Line: **610**
Condition: DISORDERS OF SOFT TISSUE (See Guideline Notes 64,65,72)
Treatment: MEDICAL THERAPY

Line: **611**
Condition: MINOR BURNS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **612**
Condition: DISORDERS OF SLEEP WITHOUT SLEEP APNEA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **613**
Condition: ORAL APHTHAE (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **614**
Condition: SPRAINS AND STRAINS OF ADJACENT MUSCLES AND JOINTS, MINOR (See Guideline Notes 6,64,65)
Treatment: MEDICAL THERAPY

Line: **615**
Condition: ASYMPTOMATIC URTICARIA (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **616**
Condition: FINGERTIP AVULSION
Treatment: REPAIR WITHOUT PEDICLE GRAFT

Line: **617**
Condition: ABUSE OF NONADDICTIVE SUBSTANCES
Treatment: MEDICAL THERAPY

Line: **618**
Condition: MINOR HEAD INJURY: HEMATOMA/EDEMA WITH NO LOSS OF CONSCIOUSNESS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **619**
Condition: VIRAL WARTS EXCLUDING VENEREAL WARTS (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT, CRYOSURGERY

Line: **620**
Condition: ACUTE UPPER RESPIRATORY INFECTIONS AND COMMON COLD (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **621**
Condition: OTHER VIRAL INFECTIONS (See Guideline Notes 61,64,65,69)
Treatment: MEDICAL THERAPY

Line: **622**
Condition: PHARYNGITIS AND LARYNGITIS AND OTHER DISEASES OF VOCAL CORDS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **623**
Condition: ANOMALIES OF RELATIONSHIP OF JAW TO CRANIAL BASE, MAJOR ANOMALIES OF JAW SIZE, OTHER SPECIFIED AND UNSPECIFIED DENTOFACIAL ANOMALIES (See Guideline Notes 64,65)
Treatment: OSTEOPLASTY, MAXILLA/MANDIBLE

Line: **624**
Condition: DENTAL CONDITIONS (EG. MALOCCLUSION)
Treatment: ORTHODONTIA (I.E. FIXED AND REMOVABLE APPLIANCES AND ASSOCIATED SURGICAL PROCEDURES)

Line: **625**
Condition: DENTAL CONDITIONS (EG. MISSING TEETH)
Treatment: IMPLANTS (I.E. IMPLANT PLACEMENT AND ASSOCIATED CROWN OR PROSTHESIS)

Line: **626**
Condition: BENIGN LESIONS OF TONGUE (See Guideline Notes 64,65)
Treatment: EXCISION

Line: **627**
Condition: UNCOMPLICATED HEMORRHOIDS (See Guideline Notes 64,65)
Treatment: HEMORRHOIDECTOMY, MEDICAL THERAPY

Line: **628**
Condition: PREVENTIVE SERVICES WITH LIMITED OR NO EVIDENCE OF EFFECTIVENESS
Treatment: MEDICAL THERAPY

Line: **629**
Condition: OPEN WOUND OF INTERNAL STRUCTURES OF MOUTH WITHOUT COMPLICATION (See Guideline Notes 64,65)
Treatment: REPAIR SOFT TISSUES

Line: **630**
Condition: SEBACEOUS CYST (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **631**
Condition: SEBORRHEIC KERATOSIS, DYSCHROMIA, AND VASCULAR DISORDERS, SCAR CONDITIONS, AND FIBROSIS OF SKIN (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **632**
Condition: REDUNDANT PREPUCE (See Guideline Notes 64,65)
Treatment: ELECTIVE CIRCUMCISION

Line: **633**
Condition: CONJUNCTIVAL CYST (See Guideline Notes 64,65)
Treatment: EXCISION OF CONJUNCTIVAL CYST

Line: **634**
Condition: BENIGN NEOPLASMS OF SKIN AND OTHER SOFT TISSUES (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **635**
Condition: DISEASE OF CAPILLARIES
Treatment: EXCISION

Line: **636**
Condition: BENIGN CERVICAL CONDITIONS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **637**
Condition: CYST, HEMORRHAGE, AND INFARCTION OF THYROID (See Guideline Notes 64,65)
Treatment: SURGICAL TREATMENT

Line: **638**
Condition: PICA (See Guideline Notes 64,65)
Treatment: MEDICAL/PSYCHOTHERAPY

Line: **639**
Condition: ACUTE VIRAL CONJUNCTIVITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY
ICD-10: B30.0-B30.9,H10.30-H10.33

Line: **640**
Condition: MUSCULAR CALCIFICATION AND OSSIFICATION (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY
ICD-10: M61.00,M61.011-M61.9

Line: **641**
Condition: SUPERFICIAL WOUNDS WITHOUT INFECTION AND CONTUSIONS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **642**
Condition: CHRONIC BRONCHITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **643**
Condition: GALACTORRHEA, MASTODYNIA, ATROPHY, BENIGN NEOPLASMS AND UNSPECIFIED DISORDERS OF THE BREAST (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **644**
Condition: BENIGN POLYPS OF VOCAL CORDS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY, STRIPPING

Line: **645**
Condition: BENIGN NEOPLASMS OF DIGESTIVE SYSTEM (See Guideline Notes 64,65)
Treatment: SURGICAL TREATMENT

Line: **646**
Condition: VARICOSE VEINS OF LOWER EXTREMITIES WITHOUT ULCER OR INFLAMMATION (See Guideline Notes 64,65)
Treatment: STRIPPING/SCLEROTHERAPY, MEDICAL THERAPY

Line: **647**
Condition: CYST OF KIDNEY, ACQUIRED (See Guideline Notes 64,65)
Treatment: MEDICAL AND SURGICAL TREATMENT

Line: **648**
Condition: HYPERTELORISM OF ORBIT (See Guideline Notes 64,65)
Treatment: ORBITOTOMY

Line: **649**
Condition: GALLSTONES WITHOUT CHOLECYSTITIS (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY, CHOLECYSTECTOMY

Line: **650**
Condition: GYNECOMASTIA
Treatment: MASTECTOMY

Line: **651**
Condition: TMJ DISORDERS (See Guideline Notes 64,65)
Treatment: TMJ SURGERY

Line: **652**
Condition: EDEMA AND OTHER CONDITIONS INVOLVING THE SKIN OF THE FETUS AND NEWBORN (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **653**
Condition: DENTAL CONDITIONS WHERE TREATMENT IS CHOSEN PRIMARILY FOR AESTHETIC CONSIDERATIONS
Treatment: COSMETIC DENTAL SERVICES

Line: **654**
Condition: DENTAL CONDITIONS WHERE TREATMENT RESULTS IN MARGINAL IMPROVEMENT
Treatment: ELECTIVE DENTAL SERVICES

Line: **655**
Condition: AGENESIS OF LUNG (See Guideline Notes 64,65)
Treatment: MEDICAL THERAPY

Line: **656**
Condition: CENTRAL RETINAL ARTERY OCCLUSION
Treatment: PARACENTESIS OF AQUEOUS

Line: **657**
Condition: MENTAL DISORDERS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65)
Treatment: EVALUATION

Line: **658**
Condition: INTRACRANIAL CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65)
Treatment: EVALUATION

Line: **659**
Condition: INFECTIOUS DISEASES WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65)
Treatment: EVALUATION

Line: **660**
Condition: ENDOCRINE AND METABOLIC CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65,67)
Treatment: EVALUATION

Line: **661**
Condition: CARDIOVASCULAR CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65)
Treatment: EVALUATION

Line: **662**
Condition: SENSORY ORGAN CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65)
Treatment: EVALUATION

Line: **663**
Condition: NEUROLOGIC CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65)
Treatment: EVALUATION

Line: **664**
Condition: DERMATOLOGICAL CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65)
Treatment: EVALUATION

Line: **665**
Condition: RESPIRATORY CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65)
Treatment: EVALUATION

Line: **666**
Condition: GENITOURINARY CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65,73)
Treatment: EVALUATION

Line: **667**
Condition: MUSCULOSKELETAL CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65)
Treatment: EVALUATION

Line: **668**
Condition: GASTROINTESTINAL CONDITIONS WITH NO OR MINIMALLY EFFECTIVE TREATMENTS OR NO TREATMENT NECESSARY (See Guideline Notes 64,65)
Treatment: EVALUATION