CONDITIONS

COVID Monoclonal Antibodies (REGEN-COV™) TREATMENT and POST-EXPOSURE PROPHYLAXIS

STATEWIDE DRUG THERAPY MANAGEMENT PROTOCOL for the OREGON PHARMACIST

AUTHORITY and PURPOSE: Per ORS 689.645, a pharmacist may provide patient care services pursuant to a statewide drug therapy management protocol.

- Following all elements outlined in OAR 855-020-0110, a pharmacist licensed and located in Oregon may prescribe and administer monoclonal antibodies casirivimab and imdevimab (REGEN-COV™).

- **STANDARDIZED PATIENT ASSESSMENT PROCESS ELEMENTS:**
  - Utilize the standardized COVID mAb Patient Intake Form (pg. 4-5)
  - Utilize the standardized COVID mAb Assessment and Treatment Care Pathway (pg. 6-21)
  - Utilize the standardized COVID mAb Patient Informational: Fact Sheet for Patients, Parents and Caregivers: EUA of REGEN-COV™ (pg. 23-27)
  - Utilize the standardized COVID mAb Provider Notification (pg. 28)

  PHARMACIST TRAINING/EDUCATION:
  - Completion of APhA Pharmacy-Based Immunization Delivery certificate (or equivalent)
  - Ensure Pharmacist is competent in pertinent physical assessment technique (ie. respiratory rate, pulse oximetry, blood pressure) and familiar with approved subcutaneous injection sites for REGEN-COV™.
  - Review REGEN-COV™ resources for healthcare providers, available at: https://www.regencov.com/hcp/resources
  - A minimum of 1 hour of training or continuing education (CE) on COVID monoclonal antibody treatment
    - CDC 8/12/2021 Webinar: CDC Therapeutic Options to Prevent Severe COVID-19 in Immunocompromised People
    - OHA 8/26/2021 Webinar: COVID-19 Monoclonal Antibody Webinar
    - CE: COVID-19 Monoclonal Antibody Assessment & Administration
    - CE: Pharmacists on the Frontline of COVID-19: From Testing to Treatment and Prevention

STATEWIDE DRUG THERAPY MANAGEMENT PROTOCOL for the OREGON PHARMACIST

REALD Data Collection Form

Date _____/_____/_____ Date of Birth _____/_____/_____ Age_____

Legal Name_____ Preferred Name _____

1. Which of the following describes your **Racial or Ethnic identity**? Please check **ALL** that apply.

Hispanic and Latino/a/x
□ Central American
□ Mexican
□ South American
□ Other Hispanic or Latino/a/x

Native Hawaiian and Pacific Islander
□ CHamoru (Chamorro)
□ Marshallese
□ Communities of the Micronesian Region
□ Native Hawaiian
□ Samoan
□ Other Pacific Islander

White
□ Eastern European
□ Slavic
□ Western European
□ Other White

American Indian and Alaska Native
□ American Indian
□ Alaska Native
□ Canadian Inuit, Metis, or First Nation
□ Indigenous Mexican, Central American, or South American

Black and African American
□ African American
□ Afro-Caribbean
□ Ethiopian
□ Somali
□ Other African (Black)
□ Other Black

Middle Eastern/North African
□ Middle Eastern
□ North African

Asian
□ Asian Indian
□ Cambodian
□ Chinese
□ Communities of Myanmar
□ Filipino/a
□ Hmong
□ Japanese
□ Korean
□ Laotian
□ South Asian
□ Vietnamese
□ Other Asian

Other Categories
□ Other (please list)
_____
□ Don't know
□ Don't want to answer

2. If you checked **more than one** category above, is there **<u>one</u>** you think of as your **primary** racial or ethnic identity?
   □ Yes. Please circle your primary racial or ethnic identity above.
   □ I do not have just one primary racial or ethnic identity.
   □ No. I identify as Biracial or Multiracial.
   □ N/A. I only checked one category above.
   □ Don't know
   □ Don't want to answer

Language (*Interpreters are available at no charge*)

3. What language or languages do you **use at home**? _____
   → Skip to question 9 if you indicated English only

4. In what language do you want us to communicate in **person, on the phone, or virtually** with you?

5. In what language do you want us to **write** to you? _____

6. Do you need or want an **interpreter** for us to communicate with you?
   □ Yes □ No □ Don't know □ Don't want to answer

7. If you need or want an interpreter, what type of interpreter is preferred?
□ Spanish language interpreter □ Deaf Interpreter for DeafBlind, additional barriers, or both
□ American Sign Language interpreter □ Contact sign language (PSE) interpreter
□ Other (**please list**): _____

→ Skip to question 9 if you do not use a language other than English or sign language

8. How well do you speak English?
□ Very Well □ Well □ Not Well □ Not at all □ Don't know □ Don't want to answer

	Disability Your answers will help us find health and service differences among people with and without functional difficulties. Your answers are confidential.	Yes	***If yes**, at what age did this condition begin?	No	Don't know	Don't want to answer	Don't know what this question is asking
9.	Are you deaf or do you have serious difficulty hearing?						
10.	Are you blind or do you have serious difficulty seeing, even when wearing glasses?						
11.	Do you have serious difficulty walking or climbing stairs?						
12.	Because of a physical, mental or emotional condition, do you have serious difficulty concentrating, remembering or making decisions?						
13.	Do you have difficulty dressing or bathing?						
14.	Do you have serious difficulty learning how to do things most people your age can learn?						
15.	Using your usual (customary) language, do you have serious difficulty communicating (for example understanding or being understood by others)?						
16.	Because of a physical, mental or emotional condition, do you have difficulty doing errands alone such as visiting a doctor's office or shopping?						
17.	Do you have serious difficulty with the following: mood, intense feelings, controlling your behavior, or experiencing delusions or hallucinations?						

All health care providers must begin collecting and reporting REALD data in accordance with current REALD standards and Oregon Disease Reporting rules starting October 1, 2021.

COVID Monoclonal Antibodies (REGEN-COV™) Self-Screening Patient Intake Form

(CONFIDENTIAL-Protected Health Information)

Date _____/_____/_____ Date of Birth _____/_____/_____ Age_____
Legal Name_____ Preferred Name _____
Sex Assigned at Birth (circle) M / F Gender Identification (circle) M / F / Other____
Preferred Pronouns (circle) She/Her/Hers, He/Him/His, They/Them/Their, Ze/Hir/Hirs, Other_____
Street Address _____
Phone ( ) _____ Email Address _____
Healthcare Provider Name _____ Phone ( ) _____ Fax ( ) _____
Do you have health insurance? Yes / No Insurance Provider Name _____
Any allergies to medications? Yes / No If yes, please list _____
Which of the following describes your racial or ethnic identity? Please check **ALL** that apply.
□ Black/African American □ Hispanic and Latino/a/x □ American Indian/Alaska Native □ Asian □ Other
□ Native Hawaiian/Pacific Islander □ Middle Eastern/North African □ White □ Not specified
Are you houseless? Yes / No
Do you live in a shelter, encampment or transitional housing? Yes / No
Do you have a disability? Yes / No

Background Information:

1.	Are you under 12 years old?	□ Yes □ No
2.	Do you weigh under 88 lbs (40 kg)?	□ Yes □ No
3.	Have you had a positive COVID (SARS-CoV-2) antigen test within the past 14 days? If yes, please indicate the date of the positive test ___/___/_____.	□ Yes □ No
4.	In the past 10 days, have you experienced new or worsening of any of the following symptoms within the past 10 days? If yes, select any/all that apply: □ Fever □ Chills □ Cough □ Shortness of breath □ Difficulty breathing □ Fatigue □ Headache □ Muscle or body aches □ New loss of taste or smell □ Sore throat □ Congestion □ Runny nose □ Nausea □ Vomiting □ Diarrhea	□ Yes □ No
5.	Have you been in close contact of someone with COVID-19 disease within the last 96 hours (4 days), or living in a setting where risk of exposure is high? Note: Close contact with an infected individual is defined as: being within 6 feet for a total of 15 minutes or more, providing care at home to someone who is sick, having direct physical contact with the person (e.g., hugging or kissing), sharing eating or drinking utensils, or being exposed to respiratory droplets from an infected person (e.g., sneezing or coughing)	□ Yes □ No
6.	Are you fully vaccinated for COVID-19? If yes, indicate when Brand/Dose 1: _____ Brand/Dose 2: _____ Brand/Dose 3: _____	□ Yes □ No
7.	Do you have or have you had any of the following?	
	A. Age ≥65 years of age……	□ Yes □ No
	B. Cancer……	□ Yes □ No
	C. Chronic kidney disease……	□ Yes □ No
	D. Chronic lung diseases (e.g., chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)……	□ Yes □ No
	E. Dementia or other neurological conditions……	□ Yes □ No
	F. Diabetes (Type 1 or Type 2) ……	□ Yes □ No
	G. Heart conditions (such as heart failure, coronary artery disease, cardiomyopathies or hypertension) ……	□ Yes □ No
	H. HIV Infection……	□ Yes □ No
	I. Immunocompromised state (weakened immune system) ……	□ Yes □ No
	J. Liver Disease……	□ Yes □ No
	K. Medical-related technological dependence (e.g., tracheostomy, gastrostomy, or oxygen supplementation (not related to COVID 19)……	□ Yes □ No
	L. Neurodevelopmental disorders (e.g., cerebral palsy, intellectual or developmental disabilities including down syndrome) or other conditions that confer medical complexity (e.g., genetic or metabolic syndromes and severe congenital anomalies)……	□ Yes □ No

COVID Monoclonal Antibodies (REGEN-COV™) Self-Screening Patient Intake Form

(CONFIDENTIAL-Protected Health Information)

	M. Overweight or obese……	□ Yes □ No
	N. Pregnancy……	□ Yes □ No
	O. Sickle cell disease or thalassemia……	□ Yes □ No
	P. Smoking, current or former……	□ Yes □ No
	Q. Solid organ or blood stem cell transplant……	□ Yes □ No
	R. Stroke or cerebrovascular disease, which affects blood flow to the brain……	□ Yes □ No
	S. Substance use disorders……	□ Yes □ No
8.	Do you have any other medical problems? If yes, list them here: _____ _____	□ Yes □ No
9.	Are you allergic to casirivimab, imdevimab, histidine, histidine monohydrochloride monohydrate , polysorbate 80, or sucrose? If yes, please circle allergy.	□ Yes □ No
10.	Do you have any other allergies? If yes, list them here: _____ _____	□ Yes □ No
11.	Do you take any medications, including herbs or supplements? If yes, list them here: _____ _____	□ Yes □ No

Signature_____ Date ____/_____/_____

To Be Completed by a Pharmacist:

1. Weight _____ lbs. Height __ ft. ___ in. BMI _____
2. Oxygen Reading _____% SpO2, Respiratory Rate ____/min
3. Blood Pressure Reading _____/_____ mmHg, Pulse ____/min
4. Vaccination status in #6 should be confirmed via ALERT or CDC immunization card or self-reported (circle one)

If patient received therapy:

1. EUA Fact Sheet for Patients, Parents and Caregivers Provided: Version Date____/_____
2. Dose (check box and circle indication):
   - □ Casirivimab 600 mg and imdevimab 600 mg for treatment or post-exposure prophylaxis **-or-**
   - □ Casirivimab 300 mg and imdevimab 300 mg for ongoing exposure **-or-**
   - □ *Partial dose administered: Casirivimab _____mg and imdevimab _____mg due to: _____
3. Product/Lot: _____ Expiration: ___/___/_____ Product/Lot: _____ Expiration: ___/___/_____
4. Injection Sites:
   - □ R thigh □ R back of the upper arm □ Upper R quadrant of abdomen □ Lower R quadrant of abdomen
   - □ L thigh □ L back of the upper arm □ Upper L quadrant of abdomen □ Lower L quadrant of abdomen
5. Time Administration Began: ____:_____ AM/PM Time Administration Ended: ____:_____ AM/PM
6. Time Monitoring* Began: ____:_____ AM/PM Time Monitoring Ended: ____:_____ AM/PM
   *NOTE: 60 minutes of monitoring is still required even in patient received an incomplete dose.
7. Primary Care Provider (if known) contacted/notified of therapy Date _____/_____/_____
8. FDA MedWatch Report submitted (if adverse event occurred) Date _____/_____/_____

RPH Signature_____ Date ____/_____/_____

9. Follow-up with patient completed on Date ____/_____/_____

RPH Signature_____ Date ____/_____/_____

Standardized Assessment and Treatment Care Pathway
COVID Monoclonal Antibodies (REGEN-COV™)

1) COVID Monoclonal Antibody Screen (Form Qs: #1-2 and pharmacist physical assessment)

a. Age < 12 years old → **Refer to healthcare provider**
b. Weight < 88 lbs (40 kg) → **Refer to healthcare provider**
c. Clinical Factors:
    i. Oxygenation:
        i. SpO2 < 94% or if patient self-reports SpO2 is regularly 91-93% and SpO2 is lower than normal for the patient→ **Refer immediately to local Emergency Department or call 911**
        ii. If chronic oxygen supplementation required and, based on self-report, oxygen need has increased after positive COVID-19 test or exposure → **Refer to local Emergency Department or call 911**
        iii. If on oxygen supplementation due to current or previous COVID infection → **Refer for medical evaluation by a healthcare provider**
    ii. Respiratory rate >30/min → **Refer immediately to local Emergency Department or call 911**
    iii. Blood Pressure:
        i. Systolic Blood Pressure >180 mmHg or Diastolic Blood Pressure >120 mmHg → **Refer immediately to local Emergency Department or call 911**
        ii. Systolic Blood Pressure <90 mmHg or Diastolic Blood Pressure <60 mmHg → **Refer immediately to local Emergency Department or call 911**
        iii. Pulse <60 or >100 → **Refer for medical evaluation by a healthcare provider or call 911.**
    iv. Emergency warning signs:
        i. For COVID-19: Trouble breathing; persistent pain or pressure in the chest; new confusion; inability to wake or stay awake; pale, gray, or blue-colored skin, lips, or nail beds, depending on skin tone. → **Refer immediately to local Emergency Department or call 911**
        ii. For Hypoxia (<94% or <91% for those patients reporting lower baseline oxygen readings) Headache; shortness of breath; fast heartbeat; coughing; wheezing; confusion; bluish color in skin, fingernails, and lips → **Refer immediately to local Emergency Department or call 911**

The Pharmacist must document the physical assessment of the patient on the Patient Self-Screening Intake Form. The pharmacy must utilize medical grade devices for physical assessment of the patient.

If referral criteria not met, proceed to Step 2a.

2a) Treatment Screen (Form Qs: #3-4)

a. Positive SARS-CoV-2 molecular or antigen test within past 14 days associated with current symptoms?

    NOTE: Test results that are indeterminate or inconclusive results can suggest the presence of SARS-CoV2 in quantities insufficient for the molecular or antigen test to be positive. It is recommended to collect a new specimen and retest. If the results are still indeterminate or inconclusive, the patient should be referred to their healthcare provider for further evaluation.

AND

b. Onset of mild to moderate COVID-19 symptoms within past 10 days?

NOTE: fever or chills; cough; shortness of breath or difficulty breathing; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; and/or diarrhea)

If YES to BOTH questions above, proceed to Step 3.
If NO to EITHER question above, proceed to Step 2b.

2b) Post-Exposure Prophylaxis Screen (Form Qs: #5-6, 7I)

a. Has the patient been in close contact of someone with COVID-19 disease within the last 96 hours, or living in a setting where risk of exposure is high?

NOTE: Close contact with an infected individual is defined as: being within 6 feet for a total of 15 minutes or more, providing care at home to someone who is sick, having direct physical contact with the person (e.g., hugging or kissing), sharing eating or drinking utensils, or being exposed to respiratory droplets from an infected person (e.g., sneezing or coughing)

AND

b. Is the patient:
   i. Unvaccinated OR
   ii. Partially vaccinated OR
   iii. Vaccinated but not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals with immunocompromising conditions including those taking immunosuppressive medications)?

NOTE: The CDC defines moderate to severe immunocompromised as the following:
- Been receiving active cancer treatment for tumors or cancers of the blood
- Received an organ transplant and are taking medicine to suppress the immune system
- Received a stem cell transplant within the last 2 years or are taking medicine to suppress the immune system
- Moderate or severe primary immunodeficiency (such as DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection
- Active treatment with high-dose corticosteroids or other drugs that may suppress your immune response

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html

The pharmacist must check the ALERT Immunization Information System (IIS) to determine whether the patient is fully vaccinated. If ALERT IIS is unavailable, use available documentation and patient statement. The patient should not be vaccinated until 90 days after last receipt of COVID-19 Monoclonal Antibodies (REGEN-COV™).

NOTE: Individuals are considered to be fully vaccinated 2 weeks after their final dose of a multi-dose series, or 2 weeks after a single-dose vaccine. For additional information visit- https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html

If YES to BOTH questions above, proceed to Step 3.

If NO to EITHER question above, COVID monoclonal antibody (mAb) therapy is not indicated at this time and pharmacists are not authorized to prescribe or administer COVID mAb treatment in accordance with this RPH protocol. → ***Refer*** *the patient for further evaluation and management by the patient's primary care provider. If patient has not had a SARS-CoV-2 molecular or antigen test, obtain test and repeat question #2a once results are available.*

3) Risk of Progression Screen (Form Qs: #7, demographics and REALD)

a. Does the patient have at least one of the conditions or factors met in #7 of the Self-Screening Patient Intake Form which places an individual at high risk of progression to severe COVID-19?

b. Does the patient identify as Black, African American, Latina/o/x, American Indian/Alaska Native, Asian, Asian American, or Pacific Islander on the Self-Screening Patient Intake Form which places an individual at high risk of progression to severe COVID-19?

NOTE: Other factors, such as race, ethnicity, disability or houselessness place individual patients at high risk for progression to severe COVID-19. Data indicates that:

- Patients of color or from tribal communities are most harmed by health inequities and the risk of hospitalization and death for these groups is greater than that of white patients. These patients may face higher risk than white patients, due to longstanding societal injustices including racism, discrimination, colonization, etc., which have and continue to negatively impact health outcomes. For this reason, people who identify as Black/African American, Latino/a/x, American Indian/Alaska Native, Asian or Pacific Islander are eligible for REGEN-COV™ under this protocol.
- Patients with the following disabilities might be at increased risk of becoming infected or having unrecognized illness or progression to severe disease.
  - People who have limited mobility or who cannot avoid coming into close contact with others who may be infected, such as direct support providers and family members
  - People who have trouble understanding information or practicing preventive measures, such as hand washing and social distancing
  - People who may not be able to communicate symptoms of illness

  https://www.cdc.gov/ncbddd/humandevelopment/covid-19/people-with-disabilities.html
- There is increased transmission of virus in congregate settings and outdoor settings that do not provide protection from the environment, adequate access to hygiene and sanitation facilities, or connection to services and healthcare. These settings include houselessness, sleeping outdoors or in an encampment setting.

Pharmacist must obtain patient weight, height, and calculate BMI to verify condition of overweight/obese in #7M on the Patient Intake Form.
https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm

If YES to either question above, proceed to Step 4.
If NO, COVID monoclonal antibody (mAb) treatment is not indicated at this time and pharmacists are not authorized to prescribe or administer COVID mAb treatment in accordance with this RPH protocol. → ***Refer*** *the patient for further evaluation and management by the patient's primary care provider.*

4) Allergy Screen (Form Qs: 9)

a. Does the patient have a known hypersensitivity to any ingredient of REGEN-COV™?

If YES → ***Refer***
If NO, proceed to Step 5.

5) Document the Patient Education per Section X (pg. 11)

Document that you communicated to your patient or parent/caregiver, as age appropriate, information consistent with the "Fact Sheet for Patients, Parents, and Caregivers- Emergency Use Authorization (EUA) of REGEN-COV™" and provided a copy of the Fact Sheet to the patient or parent/caregiver prior to the patient receiving REGEN-COV™ (casirivimab and imdevimab), including:

a. FDA has authorized the emergency use of REGEN-COV™ (casirivimab and imdevimab) for the two indications described in this protocol (**see Indications**).
b. The patient or parent/caregiver has the option to accept or refuse REGEN-COV™.
c. The significant known and potential risks and benefits of REGEN-COV™, and the extent to which such risks and benefits are unknown.
d. Information on available alternative treatments and the risks and benefits of those alternatives, including clinical trials*.
   NOTE: **Intravenous monoclonal antibody therapy is preferred for *treatment* of COVID-19 unless it would result in a delay of therapy**. Refer to Fact sheet for Healthcare Providers- Emergency Use Authorization (EUA) of REGEN-COV™ for other alternatives. For information on clinical trials that are testing the use of REGEN-COV™ related to COVID-19, please see www.clinicaltrials.gov.
e. Patients treated with REGEN-COV™
   i. should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines.
   ii. may not be vaccinated for COVID-19 until 90 days after treatment with REGEN-COV™.

6) Administer therapy per Section VI, VII and VIII (pg. 8-10)
If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, Pharmacists must immediately discontinue administration and follow the Oregon Immunization Program's Guidelines for Managing Severe Adverse Events Following Immunization.
NOTE: Patients administered partial/incomplete therapy may not be vaccinated for COVID-19 until 90 days after treatment with REGEN-COV™.

7) Monitor patient per Section IX (pg. 10-11) and report any witnessed or known serious advents potentially related to treatment per Section XI (pg. 11)
Ask patient to remain seated in the clinic for 60 minutes after administering therapy to decrease the risk of injury should they faint, and for the Pharmacist must monitor for visible signs of drug reactions and for anaphylaxis.
NOTE: Patients administered partial/incomplete therapy must be observed for 60 minutes.

If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, Pharmacists must follow the Oregon Immunization Program's Guidelines for Managing Severe Adverse Events Following Immunization and report to FDA Medwatch.

8) Notify primary care provider (if known) within 5 days of receipt of therapy, fax form required

9) Document follow-up with patient within 7 days, phone consultation permitted

Oregon licensed pharmacist must adhere to the EUA when prescribing/administering REGEN-COV™

Standardized Assessment and Treatment Care Pathway
COVID Monoclonal Antibodies (REGEN-COV™)

REGEN-COV™ (casirivimab and imdevimab)

I. INDICATIONS:

1. **Treatment:** The U.S. Food and Drug Administration (FDA) has issued an EUA to permit the emergency use of the unapproved product REGEN-COV™ for the treatment of mild to moderate COVID-19 within 10 days of symptom* onset in adult and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

   *Mild or moderate COVID-19 symptoms may include: fever or chills; cough; shortness of breath or difficulty breathing; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; and/or diarrhea.

   Limitations of Authorized Use as Treatment:

   - REGEN-COV™ is not authorized for use in patients:
     - who are hospitalized due to COVID-19, OR
     - who require oxygen therapy due to COVID-19, OR
     - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related co-morbidity.

2. **Post-exposure Prophylaxis:** The FDA also issued an EUA to permit the emergency use of the unapproved product REGEN-COV™ in adult and pediatric individuals (12 years of age and older weighing at least 40 kg) for post-exposure prophylaxis of COVID-19 in individuals who are at high risk for progression to severe COVID-19, including hospitalization or death, and are:
   a. not fully vaccinated* or who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals with immunocompromising conditions including those taking immunosuppressive medications**) AND
      i. Who have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention (CDC)*** OR
      ii. Who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (e.g., nursing homes, prisons)

   * Individuals are considered to be fully vaccinated 2 weeks after their final dose of a multi-dose series, or 2 weeks after a single-dose vaccine.

   **See this website for more details: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html

   ***Close contact with an infected individual is defined as: being within 6 feet for a total of 15 minutes or more, providing care at home to someone who is sick, having direct physical contact with the person (e.g., hugging or kissing), sharing eating or drinking utensils, or being exposed to respiratory droplets from an infected person (e.g., sneezing or coughing). See this website for additional details: https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html

Limitations of Authorized Use as Post-exposure Prophylaxis:

- Post-exposure prophylaxis with REGEN-COV™ is not a substitute for vaccination against COVID-19. Patients may not be vaccinated for COVID-19 until 90 days after treatment with REGEN-COV™.
- REGEN-COV™ is not authorized for pre-exposure prophylaxis for prevention of COVID-19.

II. PATIENT ELIGIBILITY:

An eligible patient must meet the criteria within one of the two authorized indications. For both indications, a patient must be at high risk for progression to severe COVID-19, including hospitalization or death. Patients at high risk include, but are not limited to, individuals with at least one of the following risk factors:

- Older age (age ≥65 years of age)
- Obesity or being overweight (BMI >25 kg/m^2, or if age 12-17 years, have BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm)
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung disease (e.g., chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorders (e.g., cerebral palsy) or other conditions that confer medical complexity (e.g., genetic or metabolic syndromes and severe congenital anomalies)
- Have a medical-related technological dependence (e.g., tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID 19)

Authorization of REGEN-COV™ under the EUA is not limited to the medical conditions or factors listed above. Other factors, such as race or ethnicity may also place individual patients at high risk for progression to severe COVID-19. For example, data show that patients of color or from tribal communities are most harmed by health inequities and the risk of hospitalization and death for these groups is greater than that of white patients. These patients may face higher risk than white patients, due to longstanding societal injustices including racism, discrimination, colonization, etc., which have and continue to negatively impact health outcomes. For this reason, people who identify as Black, African American, Latina/o/x, American Indian/Alaska Native, Asian, Asian American or Pacific Islander are eligible for REGEN-COV™ under this protocol.

If a patient requesting monoclonal antibody treatment does not fall into one of the categories specified above, pharmacists should refer the patient to a medical provider for risk-benefit consideration.

For additional information on medical conditions and factors associated with increased risk for progression to severe COVID, see the CDC website: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.

III. CONTRAINDICATIONS:

REGEN-COV™ is contraindicated in individuals with previous severe hypersensitivity reactions, including anaphylaxis, to REGEN-COV™.

IV. AVAILABLE DOSAGE FORMS:

REGEN-COV™ is available as:

1. A single-dose vial co-formulated in a 1:1 ratio of casirivimab and imdevimab

Antibody	Concentration
REGEN-COV™ (casirivimab and imdevimab)	600 mg/600 mg per 10 mL (60 mg/60 mg per mL)

OR

2. Individual antibody solutions in separate single-dose vials, which may be supplied in separate cartons or in a dose pack.

Antibody	Concentration
Casirivimab REGN10933	1,332 mg/11.1 mL (120 mg/mL)
	300 mg/2.5 mL (120 mg/mL)
Imdevimab REGN10987	1,332 mg/11.1 mL (120 mg/mL)
	300 mg/2.5 mL (120 mg/mL)

The REGEN-COV™ dose packs contain individual vials of casirivimab and imdevimab. Configurations of 2, 5 and 8 cartons may vary in vial size, strength, and appearance. Dose packs are sufficient to prepare up to two treatment doses:

Dose Pack Size	Dose Pack Components	Concentration
2 Cartons	1 casirivimab REGN10933	1,332 mg/11.1 mL (120 mg/mL)
	1 imdevimab REGN10987	1,332 mg/11.1 mL (120 mg/mL)
8 Cartons	4 casirivimab REGN10933	300 mg/2.5 mL (120 mg/mL)
	4 imdevimab REGN10987	300 mg/2.5 mL (120 mg/mL)
5 Cartons	1 casirivimab REGN10933	1,332 mg/11.1 mL (120 mg/mL)
	4 imdevimab REGN10987	300 mg/2.5 mL (120 mg/mL)
5 Cartons	4 casirivimab REGN10933	300 mg/2.5 mL (120 mg/mL)
	1 imdevimab REGN10987	1,332 mg/11.1 mL (120 mg/mL)

The 11.1 mL vials may be used to prepare multiple doses simultaneously as appropriate. Immediately discard any product remaining in the vial.

The vial stoppers for all dosage forms are not made with natural rubber latex.

V. STORAGE AND HANDLING:

Refrigerate unopened vials at 2 °C to 8 °C (36 °F to 46 °F) in the individual original carton to protect from light.

Remove the casirivimab and imdevimab vial(s) from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. Do not expose to direct heat. Do not shake the vials.

DO NOT FREEZE. DO NOT EXPOSE TO DIRECT LIGHT. DO NOT SHAKE. DO NOT EXPOSE TO DIRECT HEAT.

Casirivimab is preservative-free. Discard any unused portion.

Imdevimab is preservative-free. Discard any unused portion.

VI. DOSAGE:

Treatment Dosage:

Casirivimab 600 mg and imdevimab 600 mg administered together by subcutaneous injection as soon as possible after positive SARS-CoV-2 viral testing and within 10 days of mild or moderate symptom* onset.

*Mild or moderate COVID-19 symptoms may include: fever or chills; cough; shortness of breath or difficulty breathing; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; and/or diarrhea.

Post-exposure Prophylaxis Dosage:

Casirivimab 600 mg and imdevimab 600 mg administered together by subcutaneous injection as soon as possible after exposure to SARS-CoV-2. The clinical trial leading to authorization studied patients that were dosed within 96 hours of exposure.

Repeat Dosing Dosage:

The pharmacist may prescribe repeat dosing for individuals with ongoing exposure* to SARS-CoV-2 for longer than 4 weeks and who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination. Following the initial subcutaneous dose of casirivimab 600 mg and imdevimab 600 mg, dosing of casirivimab 300 mg and imdevimab 300 mg by subcutaneous injection is repeated once every 4 weeks for the duration of the ongoing exposure.

*Ongoing exposure is any resident in a congregate care setting with active exposure or repeated exposure to household contact with COVID.

Dosage Adjustments:

No dosage adjustment is recommended in pregnant or lactating women and in patients with renal impairment.

VII. PREPARATION OF SUBCUTANEOUS INJECTION:

Remove the casirivimab and imdevimab vial(s) from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation**. Do not expose to direct heat. Do not shake the vials**.

Inspect casirivimab and imdevimab vial(s) visually for particulate matter and discoloration prior to administration. Should either be observed, the vial must be discarded and replaced with a new vial. The solution for each vial should be clear to slightly opalescent, colorless to pale yellow.

1. Casirivimab and imdevimab should be prepared using the appropriate number of syringes (see Table 1). Obtain 3 mL or 5 mL polypropylene Luer Lock syringes with luer connection and 21-gauge 1½ inch transfer needles.
2. Withdraw the appropriate amount of solution into each syringe (see Table 1). Prepare all syringes at the same time.
3. Replace the 21-gauge transfer needle with a 25-gauge or 27-gauge needle for subcutaneous injection.
4. This product is preservative-free and therefore, the prepared syringes should be administered immediately. If immediate administration is not possible, store the prepared casirivimab and imdevimab syringes in the refrigerator between 2 °C to 8 °C (36 °F to 46 °F) for no more than 4 hours or at room temperature up to 25°C (77 °F) for no more than 4 total hours. If refrigerated, allow the syringes to equilibrate to room temperature for approximately 20 minutes prior to administration.

Preparation of 600 mg of Casirivimab and 600 mg of Imdevimab for Subcutaneous Injections.

Prepare 600 mg of Casirivimab and 600 mg of Imdevimab	Preparation of **4 Syringes**
Using Casirivimab and Imdevimab *Co-formulated Vial*	Withdraw 2.5 mL solution per syringe into FOUR separate syringes.
Using Casirivimab *individual vial* and Imdevimab *individual vial*	• Casirivimab: Withdraw 2.5 mL solution per syringe into TWO separate syringes. • Imdevimab: Withdraw 2.5 mL solution per syringe into TWO separate syringes. For total of 4 syringes.

Preparation of 300 mg of Casirivimab and 300 mg of Imdevimab for Subcutaneous Injections for Repeat Dosing*.

Prepare 300 mg of Casirivimab and 300 mg of Imdevimab	Preparation of **2 Syringes**
Using Casirivimab and Imdevimab *Co-formulated Vial*	Withdraw 2.5 mL solution per syringe into TWO separate syringes.
Using Casirivimab *individual vial* and Imdevimab *individual vial*	• Casirivimab: Withdraw 2.5 mL solution per syringe into ONE syringe. • Imdevimab: Withdraw 2.5 mL solution per syringe into ONE syringe. For total of 2 syringes.

* Subsequent repeat dosing every 4 weeks for the duration of ongoing exposure after the initial 600 mg casirivimab and 600 mg imdevimab doses.

VIII. ADMINISTRATION OF SUBCUTANEOUS INJECTION:

Administer the subcutaneous injections consecutively, each at a different injection site, into the thigh, back of the upper arm, or abdomen, except for 2 inches (5 cm) around the navel. The waistline should be avoided.

When administering the subcutaneous injections, it is recommended that providers use different quadrants of the abdomen or upper thighs or back of the upper arms to space apart each 2.5 mL subcutaneous injection of casirivimab and imdevimab. DO NOT inject into skin that is tender, damaged, bruised, or scarred.

IX. POST-TREATMENT MONITORING:

Ask patient to remain seated in the clinic for 60 minutes after administering therapy to decrease the risk of injury should they faint and for the Pharmacist to monitor for visible signs of drug reactions and for anaphylaxis.

Pharmacists must submit a report on all medication errors and any witnessed or known SERIOUS ADVERSE EVENTS potentially related to REGEN-COV™. See Section **Adverse Reactions and Medication Errors Reporting Requirements and Instructions**.

Hypersensitivity Reactions Including Anaphylaxis:

REGEN-COV™ may only be administered in settings in which pharmacists have immediate access to medications to treat severe hypersensitivity reactions, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, Pharmacists must immediately discontinue administration and follow the Oregon Immunization Program's Guidelines for Managing Severe Adverse Events Following Immunization.

Clinical Worsening After Administration:

Clinical worsening of COVID-19 after administration of REGEN-COV™ has been reported and may include signs or symptoms of fever, hypoxia or increased respiratory difficulty, arrhythmia (e.g., atrial fibrillation, tachycardia, bradycardia), fatigue, and altered mental status. Some of these events required hospitalization. It is not known if these events were related to REGEN-COV™ use or were due to progression of COVID-19.

Adverse Effects:

See Clinical Summary in Appendix 1 for a summary of adverse effects noted in clinical trials. Additional adverse events associated with REGEN-COV™, some of which may be serious, may become apparent with more widespread use.

X. PATIENT EDUCATION:

As the health care provider, you must communicate to your patient or parent/caregiver, as age appropriate, information consistent with the "Fact Sheet for Patients, Parents and Caregivers" (and provide a copy of the Fact Sheet) prior to the patient receiving REGEN-COV™ (see References), including:

- FDA has authorized the emergency use of REGEN-COV™ for the two indications described in this protocol (**see Indications**).
- The patient or parent/caregiver has the option to accept or refuse REGEN-COV™.
- The significant known and potential risks and benefits of REGEN-COV™, and the extent to which such risks and benefits are unknown.
- Information on available alternative treatments and the risks and benefits of those alternatives, including clinical trials*.

  * *NOTE:* **Intravenous monoclonal antibody therapy is preferred for *treatment* of COVID-19 unless it would result in a delay of therapy**. Refer to Fact sheet for Healthcare Providers- Emergency Use Authorization (EUA) of REGEN-COV™ for other alternatives. For information on clinical trials that are testing the use of REGEN-COV™ related to COVID-19, please see www.clinicaltrials.gov.

- Patients treated with REGEN-COV™:
  - **should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines**.
  - may not be vaccinated for COVID-19 until 90 days after treatment with REGEN-COV™.

XI. REQUIRED DOCUMENTATION:

Pharmacists must review the Patient Self-Assessment Intake form, utilize this Patient Assessment and Treatment Care pathway and document required elements of the pathway in the patient's medical record and record that the patient/caregiver has been:

1. Given the "Fact Sheet for Patients, Parents, and Caregivers- Emergency Use Authorization (EUA) of Regen-COV™" (see References),
2. Informed of alternatives to receiving REGEN-COV™, and
3. Informed that REGEN-COV™ is an unapproved drug that is authorized for use under this Emergency Use Authorization.

XII. ADVERSE REACTIONS AND MEDICATION ERRORS REPORTING REQUIREMENTS:

The prescribing pharmacist a is responsible for mandatory reporting of all medication errors and any witnessed or known serious adverse events* potentially related to treatment within 7 calendar days from the onset of the event to both the patient's primary care provider (if known) and FDA MedWatch. The reports should include unique identifiers and the words "REGEN-COV™ use for COVID-19 under Emergency Use Authorization (EUA)" in the description section of the report.

- Submit adverse event reports to FDA MedWatch using one of the following methods:
  - Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
  - Complete and submit a postage-paid FDA Form 3500 (https://www.fda.gov/media/76299/download) and return by:
    - Mail to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787, or
    - Fax (1-800-FDA-0178), or
  - Call 1-800-FDA-1088 to request a reporting form
  - Submitted reports should include in the field name, "Describe Event, Problem, or Product Use/Medication Error" a statement "REGEN-COV™ use for COVID-19 under Emergency Use Authorization (EUA)."

*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

The prescribing pharmacist is responsible for mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of REGEN-COV™.

IMPORTANT: When reporting adverse events or medication errors to MedWatch, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:

- Patient demographics (e.g., patient initials, date of birth)
- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of REGEN-COV™
- Pertinent laboratory and virology information

- Outcome of the event and any additional follow-up information if it is available at the time of the MedWatch report. Subsequent reporting of follow-up information should be completed if additional details become available.

In addition, please provide a copy of all FDA MedWatch forms to:

- Regeneron Pharmaceuticals, Inc
  - Fax: 1-888-876-2736
  - E-mail: medical.information@regeneron.com
  - Or call Regeneron Pharmaceuticals at 1-844-734-6643 to report adverse events.

XIII. OTHER REPORTING REQUIREMENTS:

Healthcare facilities and providers must report therapeutics information and utilization data through HHS Protect, Teletracking or National Healthcare Safety Network (NHSN) as directed by the U.S. Department of Health and Human Services.

XIV. REFERENCES:

REGEN-COV™ (casirivimab and imdevimab) [Emergency Use Authorization Fact Sheet for Health Care Providers]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc. July 2021. Available at https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf

REGEN-COV™ (casirivimab and imdevimab) [Emergency Use Authorization Fact Sheet for Patients, Parents and Caregivers]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc. July 2021. Available at https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-patient.pdf. Spanish edition available https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-patient-spanish.pdf.

Standardized Assessment and Treatment Care Pathway
COVID Monoclonal Antibodies (REGEN-COV™)

APPENDIX 1. Clinical Summary

Reference: REGEN-COV™ (casirivimab and imdevimab) [Emergency Use Authorization Fact Sheet for Health Care Providers]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc. July 2021. Available at https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf

Overall, approximately 16,000 subjects have been exposed to REGEN-COV™ (casirivimab and imdevimab) in clinical trials in hospitalized and non-hospitalized subjects. Approximately 13,500 subjects received intravenous infusions and 2,500 subjects received subcutaneous injections.

The safety of REGEN-COV™ (casirivimab and imdevimab) is based on analyses from:

- COV-2067, a Phase 1/2/3 trial of ambulatory (non-hospitalized) subjects with COVID-19;
- COV-2069, a Phase 3 post-exposure prophylaxis trial for prevention of COVID-19; and
- COV-2093, a Phase 1 trial evaluating the safety and pharmacokinetics of REGEN-COV™ repeat subcutaneous dosing every 4 weeks for 24 weeks.

COV-2067 :

This is a randomized, double-blind, placebo-controlled clinical trial (NCT04425629) in subjects with mild to moderate COVID-19. In the phase 3 portion of the trial, subjects were treated with a single intravenous infusion of 600 mg of casirivimab and 600 mg of imdevimab (n=827), or 1,200 mg of casirivimab and 1,200 mg of imdevimab (n=1,849) (unauthorized dose under EUA), or 4,000 mg of casirivimab and 4,000 mg of imdevimab (n=1,012) (unauthorized dose under EUA), or placebo (n=1,843).

At baseline, in all randomized subjects with at least one risk factor, the median age was 50 years (with 13% of subjects ages 65 years or older), 52% of the subjects were female, 84% were White, 36% were Hispanic or Latino, and only 5% were Black or African American. In subjects with available baseline symptom data, 15% had mild symptoms, 42% had moderate, 42% had severe symptoms, and 2% reported no symptoms at baseline; the median duration of symptoms was 3 days.

The primary endpoint was the proportion of subjects with ≥1 COVID-19-related hospitalization or all-cause death through Day 29. The results for subjects treated with 600 mg of casirivumab and 600 mg of imdevimab compared to placebo are outlined in **Table 1**.

Table 1. Total Events (COVID-19-related hospitalization or all-cause death) through Day 29.

	Casirivumab 600 mg and Imdevimab 600 mg (IV) (n=736)	Placebo (n=748)
COVID-19-related hospitalization or all-cause death	7 (1.0%)	24 (3.2%)
Relative Risk Reduction	70% (p=0.0024)	
Absolute Difference	2.2%, NNT = 46	

Abbreviations: IV = intravenous; NNT = number needed-to-treat to prevent one event COVID-19-related hospitalization or all-cause death.

In pooled phase 1/2/3 analysis, infusion-related reactions (adverse event assessed as causally related by the investigator) of grade 2 or higher severity have been observed in 10/4,206 (0.2%) of those who received REGEN-COV™ at the authorized dose or a higher dose. The infusion was permanently discontinued in 4 subjects who developed infusion-related reactions (urticaria, pruritus, flushing,

pyrexia, shortness of breath, chest tightness, nausea, vomiting, rash) but each received doses higher than what is authorized under EUA.

Anaphylactic reactions have been reported in subjects receiving REGEN-COV™. The events began within 1 hour of completion of the infusion, and in at least one case required treatment including epinephrine. The events resolved.

COV-2069:

This is a Phase 3, randomized, double-blind, placebo-controlled clinical trial (NCT04452318) that assessed the efficacy and safety of REGEN-COV™ (casirivimab and imdevimab) for post-exposure prophylaxis of COVID-19 in household contacts of individuals infected with SARS-CoV-2. The trial enrolled subjects who were asymptomatic and who lived in the same household with a SARS-CoV-2 infected patient. Subjects who were SARS-CoV-2 negative (PCR negative and seronegative) at baseline were enrolled and received a single dose of 600 mg of casirivimab and 600 mg of imdevimab subcutaneously (n=751) or placebo (n=752). Subjects who were SARS-CoV-2 positive at baseline were enrolled in Cohort B and received a single dose of 600 mg of casirivimab and 600 mg of imdevimab subcutaneously or placebo.

Cohort A:

At baseline, the median age was 44 years (with 9% of subjects ages 65 years or older), 54% of the subjects were female, 86% were White, 41% were Hispanic or Latino, and 9% were Black or African American. The primary efficacy endpoint was the proportion of subjects who developed PCR-confirmed COVID-19 through Day 29. The results for subjects treated with 600 mg of casirivumab and 600 mg of imdevimab compared to placebo are outlined in **Table 2**. In a post-hoc analysis in a subgroup of subjects who met the criteria for high risk for progression to severe COVID-19, there was a 76% relative risk reduction in COVID-19 with REGEN-COV™ treatment versus placebo [10/570 (2%) vs. 42/567 (7%); adjusted odds ratio 0.22; p<0.0001].

Table 2. Total PCR-confirmed Positive COVID-19 Test through Day 29.

	Casirivumab 600 mg and Imdevimab 600 mg SC (n=753)	Placebo (n=752)
PCR-confirmed Positive COVID-19 Test	11 (1.5%)	59 (7.8%)
Relative Risk Reduction	81% (Adjust OR = 0.17; p<0.0001)	
Absolute Difference	6.3%, NNT = 16	

Abbreviations: NNT = number needed-to-treat to prevent one positive COVID-19 infection; SC = subcutaneous.

Adverse events were reported in 265 subjects (20%) in the REGEN-COV™ group and 379 subjects (29%) in the placebo group. Injection site reactions (all grade 1 and 2) occurred in 55 subjects (4%) in the REGEN-COV™ group and 19 subjects (2%) in the placebo group. The most common signs and symptoms of injection site reactions which occurred in at least 1% of subjects in the REGEN-COV™ group were erythema and pruritus. Hypersensitivity reactions occurred in 2 subjects (0.2%) in the REGEN-COV™ group and all hypersensitivity reactions were grade 1 in severity. There were no cases of anaphylaxis.

Cohort B:

In a post-hoc analysis of the overall combined Cohort A and Cohort B (regardless of serology status at baseline), there was a 62% risk reduction in COVID-19 with REGEN-COV™ treatment versus placebo [46/1201 (4%) vs. 119/1177 (10%); adjusted odds ratio 0.35; p<0.0001].

Adverse events were reported in 52 subjects (34%) in the REGEN-COV™ group and 75 subjects (48%) in the placebo group. Injection site reactions, all of which were grade 1 or 2, occurred in 6 subjects (4%) in the REGEN-COV™ group and 1 subject (1%) in the placebo group. The most common signs and symptoms of injection site reactions which occurred in at least 1% of subjects in the REGEN-COV™ group were ecchymosis and erythema. There were no cases of hypersensitivity reaction or anaphylaxis.

COV-2093:

This is a randomized double-blind, placebo-controlled Phase 1 trial evaluating the safety, pharmacokinetic and immunogenicity of repeated doses of 600 mg of casirivimab and 600 mg of imdevimab administered subcutaneously in healthy adult subjects. Subjects were randomized 3:1 to REGEN-COV™ (n=729) or placebo (n=240) administered every 4 weeks for 24 weeks. Adverse events were reported in 380 subjects (52%) in the REGEN-COV™ group and 111 subjects (46%) in the placebo group. Injection site reactions occurred in 12% and 4% of subjects following single dose administration in the REGEN-COV™ and placebo groups, respectively.

With repeat dosing, injection site reactions occurred in 252 subjects (35%) in the REGEN-COV™ group and 38 subjects (16%) in the placebo group; all injection site reactions were grade 1 or 2 in severity. Hypersensitivity reactions occurred in 8 subjects (1%) in the REGEN-COV™ group; and all hypersensitivity reactions were grade 1 or 2 in severity. There were no cases of anaphylaxis.

COVID Monoclonal Antibodies (REGEN-COV™) Prescription

Optional-May be used by pharmacy if desired

Patient Name:	Date of birth:
Address:	
City/State/Zip Code:	Phone number:

☐ Verified DOB with valid photo ID

Rx

☐ Drug: Casirivimab 600 mg and imdevimab 600 mg (REGEN-COV™) administered subcutaneously by Pharmacist for ☐ initial treatment or ☐ post-exposure prophylaxis of SARS-CoV-2.

- Sig: Inject according to protocol
- Quantity: #10mL
- Refills: none

☐ Drug: Casirivimab 300 mg and imdevimab 300 mg (REGEN-COV™) administered subcutaneously by Pharmacist for ongoing exposure to SARS-CoV-2 lasting longer than 4 weeks

- Sig: Inject according to protocol
- Quantity: #5mL
- Refills: none

Written Date: _____

Prescriber Name: _____Prescriber Signature: _____

Pharmacy Address: _____ Pharmacy Phone: _____

-or-

☐ Patient Referred

Notes:_____
_____
_____
_____

FACT SHEET FOR PATIENTS, PARENTS AND CAREGIVERS
EMERGENCY USE AUTHORIZATION (EUA) OF REGEN-COV™
(casirivimab and imdevimab) FOR CORONAVIRUS DISEASE 2019 (COVID-19)

You are being given a medicine called **REGEN-COV (casirivimab and imdevimab)** for the treatment or post-exposure prevention of coronavirus disease 2019 (COVID-19). SARS-CoV-2 is the virus that causes COVID-19. This Fact Sheet contains information to help you understand the potential risks and potential benefits of taking REGEN-COV.

Receiving REGEN-COV may benefit certain people with COVID-19 and may help prevent certain people who have been exposed to someone who is infected with SARS-CoV-2 from getting SARS-CoV-2 infection, or may prevent certain people who are at high risk of exposure to someone who is infected with SARS-CoV-2 from getting SARS-CoV-2 infection.

Read this Fact Sheet for information about REGEN-COV. Talk to your healthcare provider if you have questions. It is your choice to receive REGEN-COV or stop at any time.

WHAT IS COVID-19?

COVID-19 is caused by a virus called a coronavirus, SARS-CoV-2. People can get COVID-19 through contact with another person who has the virus.

COVID-19 illnesses have ranged from very mild (including some with no reported symptoms) to severe, including illness resulting in death. While information so far suggests that most COVID-19 illness is mild, serious illness can happen and may cause some of your other medical conditions to become worse. People of all ages with severe, long-lasting (chronic) medical conditions like heart disease, lung disease, and diabetes, for example, and other conditions including obesity, seem to be at higher risk of being hospitalized for COVID-19. Older age, with or without other conditions, also places people at higher risk of being hospitalized for COVID-19.

WHAT ARE THE SYMPTOMS OF COVID-19?

The symptoms of COVID-19 include fever, cough, and shortness of breath, which may appear 2 to 14 days after exposure. Serious illness including breathing problems can occur and may cause your other medical conditions to become worse.

WHAT IS REGEN-COV (casirivimab and imdevimab)?

REGEN-COV is an investigational medicine used in adults and adolescents (12 years of age and older who weigh at least 88 pounds (40 kg)) who are at high risk for severe COVID-19, including hospitalization or death for:

- treatment of mild to moderate symptoms of COVID-19
- post-exposure prevention of COVID-19 in persons who are:
    - not fully vaccinated against COVID-19 (Individuals are considered to be fully vaccinated 2 weeks after their second vaccine dose in a 2-dose series [such as the Pfizer or Moderna vaccines], or 2 weeks after a single-dose vaccine [such as Johnson & Johnson's Janssen vaccine]), **or**,
    - are not expected to build up enough of an immune response to the complete COVID-19 vaccination (for example, someone with immunocompromising

conditions, including someone who is taking immunosuppressive medications), **and**

- have been exposed to someone who is infected with SARS-CoV-2. Close contact with someone who is infected with SARS-CoV-2 is defined as being within 6 feet for a total of 15 minutes or more, providing care at home to someone who is sick, having direct physical contact with the person (hugging or kissing, for example), sharing eating or drinking utensils, or being exposed to respiratory droplets from an infected person (sneezing or coughing, for example). For additional details, go to https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html, **or**
- someone who is at high risk of being exposed to someone who is infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (for example, as nursing homes, prisons,).

REGEN-COV is investigational because it is still being studied. There is limited information known about the safety and effectiveness of using REGEN-COV to treat people with COVID-19 or to prevent COVID-19 in people who are at high risk of being exposed to someone who is infected with SARS-CoV-2. REGEN-COV is not authorized for pre-exposure prophylaxis for prevention of COVID-19.

The FDA has authorized the emergency use of REGEN-COV for the treatment of COVID-19 and the post-exposure prevention of COVID-19 under an Emergency Use Authorization (EUA). For more information on EUA, see the **"What is an Emergency Use Authorization (EUA)?"** section at the end of this Fact Sheet.

WHO SHOULD NOT TAKE REGEN-COV?

Do not take REGEN-COV if you have had a severe allergic reaction to REGEN-COV.

WHAT SHOULD I TELL MY HEALTH CARE PROVIDER BEFORE I RECEIVE REGEN-COV?

Tell your healthcare provider about all of your medical conditions, including if you:

- Have any allergies
- Have had a severe allergic reaction including anaphylaxis to REGEN-COV previously
- Have received a COVID-19 vaccine.
- Have any serious illnesses
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Are taking any medications (prescription, over-the-counter, vitamins, and herbal products)

HOW WILL I RECEIVE REGEN-COV (casirivimab and imdevimab)?

- REGEN-COV consists of two investigational medicines, casirivimab and imdevimab, given together at the same time through a vein (intravenous or IV) or injected in the

tissue just under the skin (subcutaneous injections). **Your healthcare provider will determine the most appropriate way for you to be given REGEN-COV.**

- Treatment: If you are receiving an intravenous infusion, the infusion will take 20 to 50 minutes or longer. Your healthcare provider will determine the duration of your infusion.
    - If your healthcare provider determines that you are unable to receive REGEN-COV as an intravenous infusion which would lead to a delay in treatment, then as an alternative, REGEN-COV can be given in the form of subcutaneous injections. If you are receiving subcutaneous injections, your dose will be provided as multiple injections given in separate locations around the same time.
- Post-exposure prevention: If you are receiving subcutaneous injections, your dose will be provided as multiple injections given in separate locations around the same time. If you are receiving an intravenous infusion, the infusion will take 20 to 50 minutes or longer.
    - After the initial dose, if your healthcare provider determines that you need to receive additional doses of REGEN-COV for ongoing protection, the additional intravenous or subcutaneous doses would be administered monthly.

WHAT ARE THE IMPORTANT POSSIBLE SIDE EFFECTS OF REGEN-COV (casirivimab and imdevimab)?

Possible side effects of REGEN-COV are:

- Allergic reactions. Allergic reactions can happen during and after infusion or injection of REGEN-COV. Tell your healthcare provider right away or seek immediate medical attention if you get any of the following signs and symptoms of allergic reactions: fever, chills, nausea, headache, shortness of breath, low or high blood pressure, rapid or slow heart rate, chest discomfort or pain, weakness, confusion, feeling tired, wheezing, swelling of your lips, face, or throat, rash including hives, itching, muscle aches, feeling faint, dizziness and sweating. These reactions may be severe or life threatening.
- Worsening symptoms after treatment: You may experience new or worsening symptoms after infusion or injection, including fever, difficulty breathing, rapid or slow heart rate, tiredness, weakness or confusion. If these symptoms occur, contact your healthcare provider or seek immediate medical attention as some of these symptoms have required hospitalization. It is unknown if these symptoms are related to treatment or are due to the progression of COVID-19.

The side effects of getting any medicine by vein may include brief pain, bleeding, bruising of the skin, soreness, swelling, and possible infection at the infusion site. The side effects of getting any medicine by subcutaneous injection may include pain, bruising of the skin, soreness, swelling, and possible infection at the injection site.

These are not all the possible side effects of REGEN-COV. Not a lot of people have been given REGEN-COV. Serious and unexpected side effects may happen. REGEN-COV is still being studied so it is possible that all of the risks are not known at this time.

It is possible that REGEN-COV could interfere with your body's own ability to fight off a future infection of SARS-CoV-2. Similarly, REGEN-COV may reduce your body’s immune response to a vaccine for SARS-CoV-2. Specific studies have not been conducted to address these possible risks. Talk to your healthcare provider if you have any questions.

WHAT OTHER TREATMENT CHOICES ARE THERE?
Like REGEN-COV (casirivimab and imdevimab), FDA may allow for the emergency use of other medicines to treat people with COVID-19. Go to https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization for information on the emergency use of other medicines that are not approved by FDA that are used to treat people with COVID-19. Your healthcare provider may talk with you about clinical trials you may be eligible for.

It is your choice to be treated or not to be treated with REGEN-COV. Should you decide not to receive REGEN-COV or stop it at any time, it will not change your standard medical care.

WHAT OTHER PREVENTION CHOICES ARE THERE?
Vaccines to prevent COVID-19 are also available under Emergency Use Authorization. Use of REGEN-COV does not replace vaccination against COVID-19. REGEN-COV is not authorized for pre-exposure prophylaxis for prevention of COVID-19.

WHAT IF I AM PREGNANT OR BREASTFEEDING?
There is limited experience using REGEN-COV (casirivimab and imdevimab) in pregnant women or breastfeeding mothers. For a mother and unborn baby, the benefit of receiving REGEN-COV may be greater than the risk of using the product. If you are pregnant or breastfeeding, discuss your options and specific situation with your healthcare provider.

HOW DO I REPORT SIDE EFFECTS WITH REGEN-COV (casirivimab and imdevimab)?
Tell your healthcare provider right away if you have any side effect that bothers you or does not go away.

Report side effects to **FDA MedWatch** at www.fda.gov/medwatch or call 1-800-FDA-1088 or call 1-844-734-6643.

HOW CAN I LEARN MORE?
- Ask your health care provider.
- Visit www.REGENCOV.com
- Visit https://www.covid19treatmentguidelines.nih.gov/
- Contact your local or state public health department.

WHAT IS AN EMERGENCY USE AUTHORIZATION (EUA)?
The United States FDA has made REGEN-COV (casirivimab and imdevimab) available under an emergency access mechanism called an EUA. The EUA is supported by a Secretary of Health and Human Service (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic.

REGEN-COV has not undergone the same type of review as an FDA-approved product. In issuing an EUA under the COVID-19 public health emergency, the FDA must determine, among other things, that based on the totality of scientific evidence available, it is reasonable to believe that the product may be effective for diagnosing, treating, or preventing COVID-19, or a serious or life-threatening disease or condition caused by COVID-19; that the known and potential benefits of the product, when used to diagnose, treat, or prevent such disease or condition, outweigh the known and potential risks of such product; and that there are no adequate, approved and available alternatives. All of these criteria must be met to allow for the medicine to be used in the treatment of COVID-19 or prevention of COVID-19 during the COVID-19 pandemic.

The EUA for REGEN-COV is in effect for the duration of the COVID-19 declaration justifying emergency use of these products, unless terminated or revoked (after which the products may no longer be used).

REGENERON

Manufactured by:
Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, NY 10591-6707

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Provider Notification
COVID Monoclonal Antibodies (REGEN-COV™) Administration

Pharmacy Name:_____

Pharmacy Address:_____

Pharmacy Phone: _____ Pharmacy Fax: _____

Dear Provider_____ (name), (____) _____ -_____ (FAX)

Your patient _____(name) _____/_____/_____ (DOB) was:

☐ **Prescribed and administered COVID Monoclonal Antibodies** (REGEN-COV™) at our Pharmacy noted above. The prescription issued and administered consisted of:

- ☐ Treatment of COVID-19: Casirivimab 600 mg and imdevimab 600 mg (REGEN-COV™) administered subcutaneously by the Pharmacist for initial treatment of SARS-CoV-2. Prior to prescribing and administration of COVID Monoclonal Antibodies (REGEN-COV™) for treatment of COVID-19, your patient was tested for and/or indicated the following:

Test Name	Date of Test	Result
SARS-CoV-2 (molecular or antigen)	1) _____/_____/_____	□ reactive □ *indeterminate/inconclusive* □ negative
	2*) _____/_____/_____	□ reactive □ *indeterminate/inconclusive* □ negative

*2nd test only required if 1st test is *indeterminate/inconclusive*

- ☐ Post-Exposure Prophylaxis of COVID-19: Casirivimab 600 mg and imdevimab 600 mg (REGEN-COV™) administered subcutaneously by the Pharmacist as soon as possible after exposure to SARS-CoV-2.
- ☐ Ongoing Exposure: Casirivimab 300 mg and imdevimab 300 mg (REGEN-COV™) administered subcutaneously by the Pharmacist for ongoing exposure to SARS-CoV-2 lasting longer than 4 weeks.

Your patient was:

- Provided with the FDA EUA REGEN-COV™ Fact Sheet for Patients, Parents, & Caregivers https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-patient.pdf
- Informed that an office visit with you or another provider on your team is recommended after monoclonal antibody administration.
- For treatment or post-exposure prevention of COVID-19, the patient was also advised that they should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines.
- For post-exposure prophylaxis, the patient was also informed that REGEN-COV™ does not replace vaccination against COVID-19 and, if applicable, they may not be vaccinated for COVID-19 until 90 days after treatment with REGEN-COV™.

☐ **Tested for SARS-CoV-2 (molecular or antigen) twice, both results were *indeterminate or inconclusive* and therefore the patient is being referred to you for follow-up**. COVID monoclonal antibodies were not prescribed or administered to your patient.

If you have further questions: Please contact the prescribing pharmacy or call Regeneron Medical Information Department at 1-844-REGN-MID (1-844-734-6643). Clinicians can review the NIH COVID-19 Treatment Guidelines as well as the FDA EUA for the therapy.

- NIH COVID-19 Treatment Guidelines: https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/
- FDA EUA for REGEN-COV™: https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf