

**OREGON HEALTH AUTHORITY
IMMUNIZING PHARMACIST PROTOCOL**

HEPATITIS B VACCINES AND COMBOS Heplisav-B [®] Twinrix [®] Engerix B [®] Recombivax HB [®] For Adult Formulations	
Last Reviewed	01 April 2019
Last Revised	02 April 2019
This order expires	31 July 2021

Revisions as of 04-02-2019 See table 1 on page 3.

- Updates from January 2018 MMWR⁵
 - Vaccination for persons with chronic liver disease (including, but not limited to, those with hepatitis C, cirrhosis, fatty liver disease, alcoholic liver disease, auto-immune hepatitis, and ALT or AST levels greater than twice the upper limit of normal)
 - Adults at risk for HBV infection, including universal vaccination of adults in settings in which a high proportion have risk factors for HBV infection and vaccination of adults requesting protection from HBV without acknowledgment of a specific risk factor
 - Guidance for post-exposure prophylaxis following occupational and other exposures listed in HepB immune globulin standing order
- Addition of Heplisav-B (HepB-CpG) vaccine⁶
- See separate orders for infants <2000 g and Pediatric Formulations.

I. OREGON IMMUNIZATION PHARMACY PROTOCOL:

1. Check the ALERT Immunization Information System (IIS) to determine whether the patient needs this vaccine and any other vaccines.
2. Screen clients years of age for contraindications.
3. Provide a current Vaccine Information Statement (VIS), and answer any questions.
4. Verify needle length for **IM** injection into the vastus lateralis or deltoid muscles.

5. Avoid injecting in the upper third of the deltoid muscle.
6. Both client and vaccinator must be seated for vaccine administration.⁷
7. Give hepatitis B vaccine to persons according to risk group, age, type of vaccine and vaccine status. See section II for schedule.
8. Record all required data elements in the client's permanent health record.
9. May be given with all ACIP-recommended child and adult vaccinations.
10. Ask client to remain seated on the premises for 15 minutes after vaccination to decrease the risk of injury should they faint.

Note: Give hepatitis B vaccine by IM injection only in the deltoid for adults.

Immunization Pharmacist

Date

II. Table 1. VACCINE SCHEDULE: Preferred age and dosage intervals for single and combination hepatitis B vaccines for Adult Formulations						
Vaccine & Dose	Dose Volume	Number of doses in series	Preferred age for first dose	Preferred spacing for second dose	Preferred spacing for third dose	Preferred spacing for fourth dose
Heplisav-B Adjuvanted¹	0.5 mL	2	≥18 years	28 days later		
Twinrix: 3-dose schedule as combined Hep A and Hep B vaccine²	1.0 mL	3	≥18 years	1 month	6 months after dose 1 and 5 months after dose 2	
Twinrix 4-dose (accelerated) schedule²	1.0 mL	4	≥18 years	7 days	21–30 days after dose 1	12 months after dose 1
Engerix-B for adults ≥20 years; *	1.0 mL (20 µg/mL)	3	≥20 years	1-2 month	6 months after dose 1 and 2-5 months after dose 2	
Engerix B: adults ≥20 years of age: accelerated schedule	1.0mL (20 µg)	4	≥20 years	1 month after dose 1	2 months after dose 1	12 months after dose 1
Engerix B Dialysis³◇	2.0 mL or 1mL x 2 (20 µg)	4	≥20 years	1 month	2 months after dose 1	6 months after dose 1
Recombivax HB⁴ (10 µg/mL)*	1.0 mL (10 µg)	3	≥20 years	1-2 months after dose 1	6 months after 1 and 2-5 months after dose 2	
Recombivax HB Dialysis⁴	1.0 mL (40 µg)	3	≥20 years	1 month	6 months after dose 1 and 2 months after dose 2	

***for 19-year-olds use a pediatric dose³**

◇Engerix B for dialysis patients: 4 doses are required, each given as a single 2-mL dose or as two 1-mL doses at 0, 1, 2, and 6 months.³

II. A. Table 2. Heplisav-B and Twinrix® Route: IM into the deltoid muscle⁵

Heplisav-B¹ Dose Volume: 0.5 mL		
Dose	Preferred Spacing	Preferred Age
1		≥18 years of age
2	28 days	
Twinrix® Usual Schedule² Dose Volume: 1.0 mL		
1		≥18 years of age
2	1 month after dose #1	
3	5 months after dose #2 and 6 months after dose #1	
Twinrix® Accelerated Schedule² Dose Volume: 1.0 mL		
1		≥18 years of age
2	7 days	
3	21–30 days	
4	11 months after dose 3 and 12 months after dose 1	

Because of the unique accelerated schedule for Twinrix, the 4-day grace period does not apply to the first 3 doses of this vaccine when administered on a 0-day, 7-day, 21–30-day, and 12-month schedule (new recommendation).⁵

II. B. VACCINE INTERCHANGEABILITY^{5,6}:

Although studies show that adults immunized with different formulations of the same monovalent vaccine respond similarly, ACIP recommends completion of any vaccination regimen with the same product whenever possible. However, if the originally used product is not available or known, vaccination with another monovalent product or with a combined vaccine is acceptable. The recommended intervals between doses for the hepatitis A, hepatitis B, Twinrix® and Heplisav-B® vaccines differ from each other and must still be observed.

- 1. HEPLISAV-B:**⁵ The 2-dose HepB vaccine series only applies when both doses in the series consist of Heplisav-B. Series consisting of a combination of 1 dose of Heplisav-B and a different vaccine should consist of a total of 3 vaccine doses and should adhere to the 3-dose schedule minimum intervals of 4 weeks between doses 1 and 2, 8 weeks between doses 2 and 3, and 16 weeks between doses 1 and 3. Doses administered at less than the minimum interval should be repeated. However, a series containing 2 doses of Heplisav-B administered at least 4 weeks apart is valid, even if the patient received a single earlier dose from another manufacturer.
- 2. TWINRIX:**⁵ Twinrix is approved for persons ≥ 18 years of age and can be administered to persons in this age group for whom either hepatitis A or hepatitis B vaccine is recommended. Because the hepatitis B component of Twinrix is equivalent to a standard adult dose of hepatitis B vaccine, the schedule is the same whether Twinrix or single-antigen hepatitis B vaccine is used. Single-antigen hepatitis A vaccine can be used to complete a series begun with Twinrix or vice versa; however, a total of 3 doses are required.⁸

II C. Table 3. HEMODIALYSIS and other IMMUNOCOMPROMISED PERSONS

Age	SINGLE-ANTIGEN VACCINE						Post vaccine serology testing
	Recombivax HB ⁴			Engerix-B ³			
	# of doses	Dose (µg)	Volume (mL)	# of doses	Dose (µg)	Volume (mL)	
<20 years*	3	5	0.5	3	10	0.5 mL	annually‡
≥20 years	3	40 [◇]	1.0	4	40 [§]	2.0 mL	

* Higher doses might be more immunogenic, but no specific recommendations have been made.

◇ Dialysis formulation administered on a 3-dose schedule at 0, 1, and 6 months.

§ One 2.0-mL dose or two 1.0-mL doses administered on a 4-dose schedule at 0, 1, 2, and 6 months

‡ Booster doses should be provided when antibody levels decline below 10 mIU/mL.

Hemodialysis patients. For hemodialysis patients treated in outpatient centers, the need for booster doses should be assessed by annual anti-HBs testing. A booster dose should be administered when anti-HBs levels decline to <10 mIU/mL. Anti-HBs testing 1–2 months following the booster dose to assess response is **not** recommended.

Other immunocompromised persons. For other immunocompromised persons (e.g., HIV-infected persons, hematopoietic stem-cell transplant recipients, and persons receiving chemotherapy), the need for booster doses has not been determined. Annual anti-HBs testing and **booster doses should be considered** for persons with an ongoing risk for exposure.

III A. TABLE 4. LICENSED MONOVALENT HEPATITIS B VACCINES

PRODUCT NAME	VACCINE COMPONENTS	LATEX
Heplisav B^{®1} (HepB-CpG)	20 µg HBsAg, 3 mg CpG-1028	None
Engerix-B³	20 µg HBsAg, 0.5 mg aluminum	Latex
Recombivax HB (10 µg/mL)	10 µg HBsAg, 0.5 mg aluminum	
Recombivax HB Dialysis	40 µg HBsAg, 0.5 mg aluminum	

III B TABLE 5. LICENSED COMBINATION HEPATITIS B VACCINE

PRODUCT NAME	VACCINE COMPONENTS	LATEX
Twinrix^{®2}	720 ELISA Units Hepatitis A 20 µg HBsAg 0.45 mg aluminum 20 ng neomycin sulfate	Latex

IV. RECOMMENDATIONS FOR USE:⁵**IV A. Pre-Exposure Prophylaxis**

- Persons at risk for infection through sexual exposure
 - Sex partners of hepatitis B surface antigen (HBsAg)-positive persons
 - Sexually active persons not in a long-term, mutually monogamous relationship
 - Persons seeking evaluation or treatment for a sexually transmitted infection
 - Men who have sex with men
 - Recent or current injection drug use
- Persons at risk for infection by percutaneous or mucosal exposure to blood
 - Household contacts of HBsAg-positive persons

- Residents and staff of facilities for developmentally disabled persons
 - Health-care and public-safety personnel with reasonably anticipated risk for exposure to blood or blood-contaminated body fluids
 - Hemodialysis patients and predialysis, peritoneal dialysis, and home dialysis patients
 - Persons with diabetes mellitus aged <60 years; and persons with diabetes mellitus aged ≥60 years at the discretion of the treating clinician
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- Travelers to countries with high or intermediate levels of endemic HBV infection (HBsAg prevalence ≥2%)
 - Persons with hepatitis C virus infection, persons with chronic liver disease (including, but not limited to, those with cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an alanine aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice the upper limit of normal)
 - Persons with human immunodeficiency virus infection
 - Incarcerated persons
 - Immigrants, refugees, or adoptees from countries where HBV infection is endemic and their household members.
 - Other persons seeking protection from hepatitis B virus infection (even without acknowledgment of a specific risk factor)

IV B. Prevacination Testing^{5*}:

Prevaccination testing is recommended for the following persons:

- Household, sexual, or needle contacts of hepatitis B surface antigen (HBsAg)–positive persons
- HIV-positive persons
- Persons with elevated alanine aminotransferase/aspartate aminotransferase of unknown etiology

- Hemodialysis patients
- Men who have sex with men
- Persons who currently inject or previously injected drugs
- Persons born in countries of high and intermediate hepatitis B virus (HBV) endemicity (HBsAg prevalence $\geq 2\%$)
- U.S.-born persons not vaccinated as infants whose parents were born in countries with high HBV endemicity ($\geq 8\%$)
- Persons needing immunosuppressive therapy, including chemotherapy, immunosuppression related to organ transplantation, and immunosuppression for rheumatologic or gastroenterologic disorders
- Donors of blood, plasma, organs, tissues, or semen

*Serologic testing comprises testing for hepatitis B surface antigen (HBsAg), antibody to HBsAg, and antibody to hepatitis B core antigen.

IV C. Post-Exposure Prophylaxis and Occupational Health Recommendations

See separate Hepatitis B Immune Globulin (HBIG) Oregon Model Standing Order

IV D. Postvaccination Serologic Testing⁵

Postvaccination serologic testing includes serological screening for different markers, each for a specific reason:

- a. **HBsAg**: to determine whether they have become infected with the hepatitis B virus;
- b. **HBsAb (Anti-HBs)**: to determine whether the vaccine induced a protective immune response in the recipient.
- c. **HBeAg (Hepatitis B e-antigen)**: This is a viral protein that is secreted by hepatitis B infected cells. It is associated with chronic hepatitis B infections and is used as a marker of active viral disease and a patient's degree of infectiousness.

- A **positive result** indicates that the person has high levels of virus and greater infectiousness.
- A **negative result** indicates low to zero levels of virus in the blood and that the person is less infectious to others.⁵

Postvaccination serologic testing following a complete series of HepB vaccination⁵:

Postvaccination serologic testing 1–2 months after the final dose of vaccine is recommended for certain persons following vaccination.

- hemodialysis patients and others who might require outpatient hemodialysis (e.g., predialysis, peritoneal dialysis, and home dialysis)
- HIV-infected and other immunocompromised persons
- other immunocompromised persons (e.g., hematopoietic stem-cell transplant recipients or persons receiving chemotherapy)
- health-care personnel and public-safety workers
- sex partners of HBsAg-positive persons.

Postvaccination serologic testing should be performed using a method that allows determination of the protective level of anti-HBs (≥ 10 mIU/mL).

Persons with anti-HBs < 10 mIU/mL following receipt of 2 doses of HepB-CpG (Heplisav-B) should be revaccinated with a second complete HepB-CpG series or any 3-dose hepatitis B series, followed by anti-HBs testing 1–2 months after the final dose.

Alternatively, revaccination may consist of administration of an additional single HepB vaccine dose followed by anti-HBs testing 1–2 months later (and, if anti-HBs remains < 10 mIU/mL, completion of the second HepB vaccine series followed again by anti-HBs testing 1–2 months after the final dose).

Administration of more than two complete HepB vaccine series is generally not recommended, except for hemodialysis, and potentially immunocompromised patients.

HepB-CpG may be used for revaccination following an initial HepB vaccine series that consisted of doses of HepB-CpG or doses from a different manufacturer.

HepB-CpG may also be used to revaccinate new health-care personnel (including the challenge dose) initially vaccinated with a vaccine from a different manufacturer in the distant past who have anti-HBs <10 mIU/mL upon hire or matriculation.

IV. D. Services Available at the Oregon State Public Health Laboratory (OSPHL)

OSPHL offers serologic testing for HBsAg, anti-HBs, hepatitis B core antibody (anti-HBc), and IgM anti-HBc. HBe antigen testing is not routinely available but may be arranged under special circumstances; consult with the Acute and Communicable Disease Prevention section at 971-673-1111. For more information regarding proper specimen submission, refer to the Lab Test Menu at www.healthoregon.org/labtests. As of January 2017, OSPHL does not provide PCR testing for hepatitis B virus.

Note: As of January 2017, testing is available to LHDs through the Oregon State Public Health Laboratory at no charge. This will be maintained if funding is available to support this testing. There is a charge for testing ordered by private providers.

V. CONTRAINDICATIONS

A. RecombivaxHB^{®4}

- Hypersensitivity to baker's yeast
- Hypersensitivity to soy peptones

B. Engerix-B^{®3}

- Hypersensitivity to baker's yeast

C. Twinrix^{®2}

- Hypersensitivity to baker's yeast
- Hypersensitivity to neomycin, polysorbate 80, polymyxin B
- **Severe allergic reaction** or anaphylactic response after a previous dose
- **Moderate or severe acute illness** with or without fever: defer

vaccination until illness resolves

D. Heplisav-B®¹

- Severe allergic reaction, such as anaphylaxis, after a previous dose of any hepatitis B vaccine or to any component of Heplisav-B, including yeast.
- Pregnancy
- Breastfeeding

VI. WARNINGS AND PRECAUTIONS

RecombivaxHB®⁴ Engerix-B®³ Twinrix®²: Dry natural rubber **latex** is used in the vial stopper, the **syringe plunger stopper and tip cap** which may cause allergic reactions in latex-sensitive individuals.

VII. TABLE 6. SIDE EFFECTS AND ADVERSE EVENTS

Event	Adults
Pain at injection site	13%–29%
Mild systemic complaints (fatigue, headache)	11%–17%
Temperature up to 37.7 C (≤99.9°F)	1%
Severe systemic reactions	Rare

VIII. OTHER CONSIDERATIONS

1. **Adverse Events:** epinephrine hydrochloride solution (1:1,000) and other appropriate agents and equipment must be available for immediate use in case of anaphylactic or acute hypersensitivity reaction.⁵
2. **Lactation:** Breast feeding is not a contraindication to vaccination for mother or infant. HBsAg-positive women should be encouraged to breast feed; breast-feeding does not pose any additional risk of exposure to the infant.⁹
3. **DO NOT RESTART A SERIES.** Count the number of doses the recipient has had, and give the next dose due, observing client age and minimum spacing.⁵
4. **Vaccination of Pregnant Women**⁵

- Pregnant women who are identified as being at risk for HBV infection during pregnancy (e.g., having more than one sex partner during the previous 6 months, been evaluated or treated for an STI, recent or current injection-drug use, or having had an HBsAg-positive sex partner) should be vaccinated with Recombivax HB or Engerix-B. Do not use Heplisav-B.
- Pregnant women at risk for HBV infection during pregnancy should be counseled concerning other methods to prevent HBV infection.

IX. STORAGE AND HANDLING

All clinics and pharmacies enrolled with the Vaccines for Children (VFC) Program must immediately report any storage and handling deviations to the Oregon Immunization Program at 971-673-4VFC (4823).

Table 7. Hepatitis B vaccines¹⁻⁴

Vaccine	Latex	Temp	Storage Issues	Notes
Heplisav-B [®]	No	Store at 2°–8°C	Do not use if vaccine has been frozen	Do not dilute
Engerix-B [®]	Yes: syringe			
Recombivax HB [®]	Yes: syringe			
Twinrix [®]	Yes: syringe			

X. ADVERSE EVENTS REPORTING

Private providers are to report events directly to VAERS and can read about options on how to do so at <https://vaers.hhs.gov/reportevent.html>

A pharmacist who administers any vaccine must report the following elements to the OHA ALERT Immunization Information System in a manner prescribed by OHA within 15 days of administration. This replaces the former requirement to notify the primary health care provider. A pharmacist is not required to notify the primary health care provider. Oregon Administrative Rule 855-019-0290-(2)(3).¹¹

TABLE C. Table 8. Events Reportable to VAERS¹⁰

Event and interval from vaccination
A. Anaphylaxis or anaphylactic shock (7 days)
B. Shoulder injury related to vaccine administration (7 days)
C. Vasovagal syncope (7 days)
D. Any acute complications or sequelae (including death) of the above event (interval - not applicable)
E. Events described in manufacturer's package insert as contraindications to additional doses of vaccine (interval - see package insert)

To request this material in an alternative format (e.g., Braille) or to clarify any part of the above order, contact the Oregon Health Authority Immunization Program at 971-673-0300 and 711 for TTY. For other questions, consult with the vaccine recipient's primary health care provider or a consulting physician.

Electronic copy of this standing order is available at:

[1.usa.gov/PharmacyImmunizationProtocols](https://www.usa.gov/PharmacyImmunizationProtocols)

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