

Immunization Protocol

Adult Hepatitis B Vaccines and Combinations: Engerix-B®, Heplisav-B®, Recombivax HB®, Twinrix®	
Last Reviewed	23 September 2024
Last Revised	16 December 2024
This order expires	30 September 2026

Table of contents

1. What's new	1
2. Oregon immunization protocol	2
3. Vaccine schedule for Hepatitis B	2
4. Licensed Hepatitis B vaccines	3
5. Recommendations for use	3
6. Contraindications	6
7. Warnings and precautions	6
8. Other considerations	6
9. Side effects and adverse reactions	9
10. Storage and handling	9
11. Adverse events reporting	9
12. References	9

1. What's new

- 12/16/2024: The CDC published an MMWR updating hepatitis B vaccination guidance to include Heplisav-B vaccine for pregnant patients. Providers can now administer Engerix-B, Heplisav-B, Recombivax HB, or Twinrix to pregnant people needing hepatitis B vaccination.
- 11/20/24: Prehevbrio has been discontinued and should not be used, effective immediately. Patients who previously received Prehevbrio should continue their hepatitis B vaccine series with another licensed product.
- 9/23/24: Added Twinrix as an option for vaccination during pregnancy. Removed latex precaution for Engerix-B and Twinrix.

2. Oregon immunization protocol

- A. Check the ALERT Immunization Information System (IIS) to determine whether the patient needs this vaccine and any other vaccines.
- B. Screen clients for contraindications and precautions.
- C. Provide a current Vaccine Information Statement (VIS), answering any questions.
- D. Record all required data elements in the client's permanent health record.
- E. Verify needle length for intramuscular (IM) injection into the deltoid muscle.
- F. To avoid injury related to vaccine administration, make sure staff who administer vaccines recognize the anatomic landmarks for identifying the deltoid muscle and use proper IM administration technique.
- G. Give hepatitis B vaccine IM to persons according to risk group, age, type of vaccine and vaccine status. See section 5 for schedules.
- H. Record all required data elements in the client's permanent health record.
- I. May be given with all ACIP-recommended child and adult vaccinations.
- J. Ensure epinephrine hydrochloride solution (1:1,000), oxygen and other appropriate agents and equipment are available for immediate use in case of anaphylactic or acute hypersensitivity reaction. Refer to [Guidelines for Managing Adverse Events Following Immunization](#).
- K. Ask client to remain seated on the premises for 15 minutes after vaccination to decrease the risk of injury should they faint.

Health Officer Signature

Date

Health Officer Signature

Date

3. Vaccine schedule for Hepatitis B

Minimum age and vaccine schedule varies by product. See section 5, below.

4. Licensed Hepatitis B vaccines¹⁻⁴

Product Name	Vaccine Components	Presentation	Acceptable Age Range
Engerix-B, adult formulation	Hepatitis B	1.0-mL single-dose vials and prefilled syringes	≥20 years
Heplisav-B		0.5-mL prefilled syringes	≥18 years
Recombivax HB, adult formulation		1.0-mL single-dose vials and prefilled syringes	≥20 years
Recombivax HB Dialysis		1.0-mL single-dose vials	≥20 years
Twinrix	Hepatitis A Hepatitis B	1.0-mL prefilled syringes	≥18 years

5. Recommendations for use

Routine Adult Hepatitis B Vaccine Schedules			
Engerix-B, Recombivax HB Vaccine Schedule ^{1,3}			
Dose	Preferred Age	Minimum Acceptable Age	Minimum Acceptable Spacing
1	≥20 years	≥20 years	
2			4 weeks dose 1 to 2
3			8 weeks dose 2 to 3 <u>and</u> 16 weeks after dose 1
Heplisav-B Vaccine Schedule ²			
Dose	Preferred Age	Minimum Acceptable Age	Minimum Acceptable Spacing
1	≥18 years	≥18 years	
2			1 month dose 1 to 2
Twinrix Vaccine Schedule ⁴			
Dose	Preferred Age	Minimum Acceptable Age	Minimum Acceptable Spacing
1	≥18 years	≥18 years	
2			1 month dose 1 to 2
3			5 months dose 2 to 3 <u>and</u> 6 months dose 1 to 3

Twinrix Accelerated Schedule⁴

Dose	Preferred Age	Minimum Acceptable Age	Minimum Acceptable Spacing
1	≥18 years	≥18 years	
2			7 days dose 1 to 2
3			14 days dose 2 to 3
4			11 months dose 3 to 4 <u>and</u> 12 months after dose 1

Engerix-B Accelerated Schedule¹

Dose	Preferred Age	Minimum Acceptable Age	Minimum Acceptable Spacing
1	≥20 years	≥20 years	
2			1 month dose 1 to 2
3			1 month dose 2 to 3
4			10 months dose 3 to 4 <u>and</u> 12 months after dose 1

Adult Hepatitis B Vaccine Schedules for Special Situations **Engerix-B Dialysis and Immunocompromised Schedule^{1,5}**

Dose	Minimum Acceptable Age	Dose Volume	Minimum Acceptable Spacing
1	≥20 years	One 2.0-mL dose or two 1.0-mL doses	
2			1 month dose 1 to 2
3			1 month dose 2 to 3
4			4 months dose 3 to 4

Recombivax HB Dialysis and Immunocompromised Schedule^{3,5}

Dose	Minimum Acceptable Age	Dose Volume	Minimum Acceptable Spacing
1	≥20 years	1.0 mL (40-μg formulation)	
2			4 weeks dose 1 to 2
3			8 weeks dose 2 to 3 <u>and</u> 16 weeks after dose 1

Pre-Exposure Prophylaxis^{5,6}

- A. Hepatitis B vaccination is recommended for all adults 19–59 years of age.
- B. Adults ≥60 years of age with risk factors for hepatitis B infection.
- C. Persons at risk for infection through sexual exposure:
 - Sexual partners of hepatitis B positive persons;
 - Persons seeking evaluation or treatment for a sexually transmitted infection;
 - Sexually active persons not in a monogamous relationship;
 - Men who have sex with men.
- D. Persons at risk for infection by percutaneous or mucosal exposure to blood:
 - Recent or current injection-drug use;
 - Household contacts of HBsAg-positive persons;
 - Residents and staff of facilities for developmentally disabled persons;
 - Healthcare and public-safety personnel with reasonably anticipated risk for exposure to blood or blood-contaminated body fluids;
 - Hemodialysis patients and pre-dialysis, peritoneal dialysis, and home dialysis patients;
 - Persons with diabetes mellitus aged ≥60 years at the discretion of the treating clinician.⁵
- E. Persons with:
 - Hepatitis C virus infection;
 - Human immunodeficiency virus;
 - 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).
- F. Others:
 - Travelers to countries with high or intermediate levels of endemic hepatitis B virus (HBV) infection (HBsAg prevalence ≥2%);
 - Incarcerated persons.

6. Contraindications¹⁻⁴

- A. All: Severe allergic reaction to a previous dose of any hepatitis B-containing vaccine or to a vaccine component.
- B. Engerix B, Heplisav-B, Recombivax HB, Twinrix: Hypersensitivity to yeast
- C. Twinrix: Hypersensitivity to neomycin

Vaccine	Vaccine Excipient Summary ⁹
Engerix-B	aluminum hydroxide, yeast protein, sodium chloride, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate
Heplisav- B	yeast protein, yeast DNA, deoxycholate, phosphorothioate-linked oligodeoxynucleotide, sodium phosphate, dibasic dodecahydrate, sodium chloride monobasic dehydrate, polysorbate 80
Recombivax HB	formaldehyde, potassium aluminum sulfate, amorphous aluminum hydroxyphosphate sulfate, yeast protein
Twinrix	MRC-5 cellular proteins, formalin, aluminum phosphate, aluminum hydroxide, amino acids, sodium chloride, phosphate buffer, polysorbate 20, neomycin sulfate, yeast protein

7. Warnings and precautions¹⁻⁴

Recombivax HB: Dry natural rubber latex is used in the vial stopper, the syringe plunger stopper and tip cap.

8. Other considerations

- A. Vaccine Interchangeability:
 - **Heplisav-B²**: A 2-dose 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. 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.
 - **Twinrix⁴**: Recommended for persons at risk for hepatitis A or hepatitis B. The hepatitis B component of Twinrix is equivalent to a standard adult dose of hepatitis B vaccine, the hepatitis A component has 50% of the adult standard dose. A total of 3 Twinrix doses are required to complete the series. If Twinrix is unavailable or not used to complete the Twinrix series,

administer single-antigen vaccine as follows: If 1 dose of Twinrix was given, complete the series with 2 adult doses of hepatitis B vaccine and 2 adult doses of hepatitis A vaccine. If 2 doses of Twinrix were given, complete the schedule with 1 adult dose of hepatitis A vaccine and 1 adult dose of hepatitis B vaccine.

B. Booster Doses

- Hemodialysis patients: Post vaccination serology testing is recommended annually. Booster doses should be provided when anti-HBs levels decline to <10 mIU/mL.⁶ Anti-HBs testing 1–2 months following the booster dose to assess response is not recommended.
- Other immunocompromised persons: In 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.

C. Lactation and Pregnancy^{6,9}

- Universal hepatitis B vaccination is recommended for adults 19–59 years of age, including pregnant persons. Pregnant people can be vaccinated with Recombivax HB, Engerix-B, Heplisav-B or Twinrix.⁹
- Lactation: Breast feeding is not a contraindication to vaccination for mother or infant.

D. Prevaccination serological testing* is recommended for⁶:

- Persons born in countries of high and intermediate hepatitis B virus (HBV) endemicity (HBsAg prevalence $\geq 2\%$);
- HIV positive persons;
- Household, sex, and needle-sharing contacts of HBsAg-positive persons;
- Men who have sex with men;
- Past or current injection drug users.

Hepatitis B vaccine should be administered immediately after collection of blood for testing.

Pre-vaccination testing is not required and should not delay vaccination if not readily available.

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

E. Postvaccination serologic testing⁶

- Postvaccination serologic testing 1–2 months after the final dose of the complete vaccine series is recommended for:
 - Health-care personnel and public-safety workers;
 - Hemodialysis patients and others who might require outpatient hemodialysis (e.g., pre-dialysis, 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);
 - 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).

F. Revaccination for non-responders^{6,7}:

- Persons with anti-HBs < 10 mIU/mL following receipt of 2 doses of Heplisav-B (HepB-CpG) should be revaccinated with a second complete Heplisav-B 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 hepatitis B vaccine dose (challenge dose) followed by anti-HBs testing 1–2 months later.
- If anti-HBs remains < 10 mIU/mL, completion of a second hepatitis B vaccine series followed again by anti-HBs testing 1–2 months after the final dose.
- Administration of more than two complete hepatitis B vaccine series is generally not recommended, except for hemodialysis, and potentially immunocompromised patients.
- Heplisav-B (HepB-CpG) may be used for revaccination following an initial hepatitis B vaccine series that consisted of doses of HepB-CpG or doses from a different manufacturer.
- Healthcare personnel who do not respond to a challenge dose should complete revaccination and retesting for anti-HBs.

See separate Hepatitis B Immune Globulin (HBIG) Oregon Model Standing Order for post-exposure prophylaxis and occupational health recommendations.

9. Side effects and adverse reactions¹⁻⁴

Event	Adults
Pain at the injection site	Up to 52%
Mild systemic complaints (fatigue, headache)	Up to 25%
Temperature up to 37.7 C (≤99.9°F)	Less than 2%
Any severe reaction	Rare

10. Storage and handling¹⁻⁴

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).

Vaccine	Temp	Storage Issues
Engerix-B, Heplisav B, Recombivax HB, Twinrix	Store at 2°–8° C	Do not use if vaccine has been frozen.

11. Adverse events reporting

Public providers are to complete the Vaccine Adverse Events Reporting System (VAERS) report online at <https://vaers.hhs.gov/reportevent.html>.

VAERS Reporting Table:

https://vaers.hhs.gov/docs/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf

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).

12. References

1. Engerix-B®. [Package insert]. 2023. Available at: www.fda.gov/media/119403/download. Accessed 16 Dec 2024.
2. Heplisav-B®. [Package insert]. 2024. Available

at:www.fda.gov/media/108745/download. Accessed 16 Dec 2024.

3. Recombivax® HB. [Package insert]. 2018. Available at:
www.fda.gov/media/74274/download. Accessed 16 Dec 2024.
4. Twinrix®. [Package insert]. 2023. Available at:
www.fda.gov/media/119351/download. Accessed 16 Dec 2024.
5. Weng MK, Doshani M, Khan MA, et al. Universal hepatitis B vaccination in adults aged 19–59 Years: Updated recommendations of the Advisory Committee on Immunization Practices—United States, 2022. MMWR 2022; 71:477–83. Available at: www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7113a1-H.pdf. Accessed 16 Dec 2024.
6. Schillie S, Vellozzi C, Reingold A, et al. Prevention of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices. MMWR 2018; 67(RR-1):1–31. Available at www.cdc.gov/mmwr/volumes/67/rr/rr6701a1.htm#B7_down. Accessed 16 Dec 2024.
7. Schillie S, Harris A, Link-Gelles R, Romero J, Ward J, Nelson N. Recommendations of the Advisory Committee on Immunization Practices for use of a hepatitis B vaccine with a novel adjuvant. MMWR 2018;67:455–8. Available at: <http://dx.doi.org/10.15585/mmwr.mm6715a5>. Accessed 16 Dec 2024.
8. Centers for Disease Control and Prevention. Vaccine Excipient Summary. Available at: www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf. Accessed 16 Dec 2024.
9. Sandul A, Rapposelli K, Nyendak M, Kim M. Updated recommendation for universal hepatitis B vaccination in adults aged 19–59 Years—United States, 2024. MMWR 2024;73:1106. Available at: <http://www.cdc.gov/mmwr/volumes/73/wr/mm7348a3.htm>. Accessed 16 Dec 2024.

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 immunization protocol is available at:
www.oregon.gov/standing-protocols.