

**Protocol for Hepatitis B Containing Vaccines
(ENGERIX-B®, HEPLISAV-B®, PREHEVBRIOTM, RECOMBIVAX HB®, TWINRIX®)**

1. What's New

A. PreHevbrio® has been removed from the market, for further information view this [link](#).

2. Immunization Protocol

A. Administer an IM dose of Hepatitis B vaccine appropriate for the person's age, risk group, and the formulation being used.

B. May be given with all ACIP-recommended child and adult vaccinations.

3. Vaccine Schedule (see prescribing information for “Recommended Spacing”)

Routine Schedules

Pediatric Hepatitis B Vaccine^{1,4,9} (Engerix-B®, Recombivax-HB®) Dose and Route – 0.5-mL, IM		
Dose	Acceptable Age Range	Minimum Acceptable Spacing
1	7 through 19 years	
2		4 weeks
3		8 weeks after dose 2 and 16 weeks after dose 1

Adult Hepatitis B Vaccine^{2,9} (HEPLISAV-B®) Dose and Route – 0.5-mL, IM		
Dose	Acceptable Age Range	Minimum Acceptable Spacing
1	≥18 years	
2		4 weeks

Adult Hepatitis B Vaccine^{3,9} (PREHEVBRIOTM) Dose and Route – 1.0-mL, IM		
Dose	Acceptable Age Range	Minimum Acceptable Spacing
1	≥18 years	
2		4 weeks
3		8 weeks after dose 2 and 16 weeks after dose 1

Adult Hepatitis A – Hepatitis B Combination Vaccine^{5,9} (TWINRIX®) Dose and Route – 1.0-mL, IM		
Dose	Acceptable Age Range	Minimum Acceptable Spacing
1	≥18 years	
2		4 weeks
3		5 months after dose 2 and 6 months after dose 1

Adult Hepatitis B Vaccine^{1,4,9} (Engerix-B®, Recombivax-HB®) Dose and Route – 1.0-mL, IM		
Dose	Acceptable Age Range	Minimum Acceptable Spacing
1	≥20 years	
2		4 weeks
3		8 weeks after dose 2 and 16 weeks after dose 1

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Additional Schedules (e.g., Catch-up, Alternative, Accelerated, and Dialysis)

Catch-up Pediatric Hepatitis B Vaccine Schedule		
Dose	Preferred Spacing	Minimum Spacing After Previous Dose
1		
2	8 weeks after dose 1	4 weeks after dose 1
3	4 months after dose 2 and 6 months after dose 1	8 weeks after dose 2 and 16 weeks after dose 1

Alternative Pediatric Hepatitis B Vaccine Schedules ^{1,4}							
Vaccine and Formulation	Dose Volume	Number of Doses in Series	Age at First Dose	Interval from 1 to 2	Interval from 2 to 3	Interval from 1 to 3	Interval from 1 to 4
Engerix-B® (20 mcg/mL)	0.5 mL	4	1 through 10 years	4 weeks	4 weeks	8 weeks	12 months
		3	5 through 16 years	12 months	12 months	24 months	
	1.0 mL*	4	11 through 18 years	4 weeks	4 weeks	8 weeks	12 months
		3		4 weeks	8 weeks	6 months	
Recombivax HB® (10 mcg/mL)	1.0 mL	2	11 through 15 years◊	4 to 6 months			

* 1.0-mL dose recommended for persons who travel to endemic areas, sexual exposure, and children born to Hepatitis B surface antigen positive (HBsAg+) mothers.

◊ Both doses must be 1.0 mL of Recombivax HB®. Series must be completed prior to 16th birthday, or an additional dose is required.

TWINRIX® Accelerated Schedule ⁵		
Dose	Acceptable Age Range	Minimum Acceptable Spacing
1	≥18 years	
2		7 days after dose 1
3		14 to 23 days after dose 2
4		12 months from dose 1
ENGERIX-B® Accelerated Schedule ¹		
Dose	Acceptable Age Range	Minimum Acceptable Spacing
1	≥20 years	
2		4 weeks after dose 1
3		4 weeks after dose 2
4		10 months after dose 3 and 12 months from dose 1

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ENGERIX-B® Dialysis Schedule¹			
Dose	Acceptable Age Range	Dose Volume	Minimum Acceptable Spacing
1	≥ 20 years	One 2.0-mL dose or Two 1.0-mL doses	
2			4 weeks after dose 1
3			4 weeks after dose 2
4			4 months after dose 3

RECOMBIVAX HB® Dialysis Schedule⁴			
Dose	Acceptable Age Range	Dose Volume	Minimum Acceptable Spacing
1	≥ 20 years	1.0 mL (40-mcg formulation)	
2			4 weeks after dose 1
3			8 weeks after dose 2 and 16 weeks from dose 1

4) Additional Considerations for Use

- A) Hepatitis B vaccination is recommended for all adults 19 through 59 years of age.
- B) Hepatitis B vaccination is recommended for Adults ≥ 60 years of age with risk factors for hepatitis B infection.

C) Determining Patient Risk

- i) 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 long-term, mutually monogamous relationship
 - Men who have sex with men (MSM)
- ii) Persons at risk for infection by percutaneous or mucosal exposure to blood⁷:
 - Recent or current injection-drug use
 - Household contacts of Hepatitis B surface antigen (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; and persons with diabetes mellitus aged ≥ 60 years at the discretion of the treating clinician
- iii) Persons with⁷:
 - Hepatitis C virus infection
 - Human immunodeficiency virus

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- 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)

iv) Others⁷:

- Travelers to countries with high or intermediate levels of endemic hepatitis B virus (HBV) infection (HBsAg prevalence $\geq 2\%$)
- 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

D) **Vaccine Interchangeability**^{2,5}

- i) Heplisav-B^{®2}: 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.
- ii) Twinrix^{®5}: 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.

E) **Booster Doses**

- i) Hemodialysis patients: Post vaccination serology testing is recommended annually. Booster doses should be provided when anti-HBs levels decline to <10 milli-international units/mL.⁷ Anti-HBs testing 1 to 2 months following the booster dose to assess response is not recommended.
- ii) 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.

F) **Prevaccination Serological Testing**⁷

- i) Pre-vaccination serological testing* is recommended for⁷:
 - Persons born in countries of high and intermediate hepatitis B virus endemicity (HBsAg prevalence $\geq 2\%$)

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- HIV positive persons
- Household, sex, and needle-sharing contacts of HbsAg-positive persons
- Men who have sex with men (MSM)
- Past or current injection drug users
- Adoptees born in Asia, the Pacific Islands, Africa, and other regions of high or intermediate hepatitis B endemicity should undergo serologic testing for HbsAg regardless of vaccination status. Adoptees born in countries other than those mentioned above whose records indicate receipt of ≥ 3 doses of vaccine can be considered protected if ≥ 1 dose was administered at age ≥ 6 months.
- *Hepatitis B vaccine should be administered immediately after collection of blood for testing. Serologic testing comprises testing for HbsAg, antibody to HbsAg (anti-HBs), and antibody to hepatitis B core antigen (anti-HBc).

G) Postvaccination Serological Testing⁷

- i) Pre-vaccination serological testing* is recommended for⁷:
 - Persons born in countries of high and intermediate hepatitis B virus endemicity (HbsAg prevalence $\geq 2\%$)
 - HIV positive persons
 - Household, sex, and needle-sharing contacts of HbsAg-positive persons
 - Men who have sex with men (MSM)
 - Past or current injection drug users
 - Adoptees born in Asia, the Pacific Islands, Africa, and other regions of high or intermediate hepatitis B endemicity should undergo serologic testing for HbsAg regardless of vaccination status. Adoptees born in countries other than those mentioned above whose records indicate receipt of ≥ 3 doses of vaccine can be considered protected if ≥ 1 dose was administered at age ≥ 6 months.
 - *Hepatitis B vaccine should be administered immediately after collection of blood for testing. Serologic testing comprises testing for HbsAg, antibody to HbsAg (anti-HBs), and antibody to hepatitis B core antigen (anti-HBc).

H) Revaccination for Non-responders⁷

- i) Persons with anti-HBs <10 milli-international units/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 to 2 months after the final dose.
- ii) Alternatively, revaccination may consist of administration of an additional single hepatitis B vaccine dose (challenge dose) followed by anti-HBs testing 1 to 2 months later.
- iii) If anti-HBs remains <10 milli-international units/mL, completion of a second hepatitis B vaccine series followed again by anti-HBs testing 1 to 2 months after the final dose.

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- iv) Administration of more than two complete hepatitis B vaccine series is generally not recommended, except for hemodialysis, and potentially immunocompromised patients.
- v) 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.
- vi) Healthcare personnel who do not respond to a challenge dose should complete revaccination and retesting for anti-HBs.

5) Pregnancy and Lactation

- A) 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®² or Prehevbrio^{®3}.
- B) Lactation: Breast feeding is not a contraindication to vaccination for mother or infant.

6) Warnings and Precautions ^{1,4}

- A) Engerix-B^{®1}, Recombivax HB^{®4} - dry natural rubber latex is used in the vial stopper, the syringe plunger stopper and tip cap.

7) Contraindications ⁵

- A) Severe allergic reaction (e.g., anaphylaxis) to a previous dose or to any vaccine component.
- B) See current prescribing information for more details about formulation and contents.
- C) Engerix-B®, Heplisav-B®, Recombivax HB®, Twinrix®: Hypersensitivity to yeast
- D) Heplisav-B®: Pregnancy
- E) Recombivax HB®: Hypersensitivity to soy peptones
- F) Twinrix®: Hypersensitivity to neomycin, polysorbate 80, polymyxin B

8) Storage and Handling

- A) Store medications according to [OAR 855-041-1036](#).
- B) See current prescribing information for more details about storage and handling.
- C) 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).

9) References

1. Engerix-B®. [Package insert]. June 2021. Available at: https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Engerix-B/pdf/ENGERIX-B.PDF. Accessed 25 July 2023.
2. Heplisav-B®. [Package insert]. May 2023. Available at: www.fda.gov/media/108745/download. Accessed 14 July 2023.

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5. Twinrix®. [Package insert]. April 2023. Available at: www.fda.gov/media/119351/download. Accessed 14 July 2023.
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9. Centers for Disease Control and Prevention. Adult Immunization Schedule Notes. Available at: <https://www.cdc.gov/vaccines/hcp/imz-schedules/adult-notes.html#note-hepb>

10) Appendix

A) N/A