

**Protocol for Hepatitis B Containing Vaccines
(ENGERIX-B®, HEPLISAV-B®, PREHEVBRIO®, 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} (PREHEVBRIO®) 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 blood ⁷:
 - 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 with ⁷:
 - 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

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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) Prevacination Serological Testing⁷

- i) Pre-vaccination serological testing* is recommended for ⁷:
 - 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)

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- 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 Testing ⁷

- i) Pre-vaccination serological testing* is recommended for⁷:
 - Persons born in countries of high and intermediate hepatitis B virus endemicity (HBsAg prevalence $\geq 2\%$)
 - 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-responders ⁷

- 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.
- iv) Administration of more than two complete hepatitis B vaccine series is generally not recommended, except for hemodialysis, and potentially immunocompromised patients.

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10) Appendix

- A) N/A