**Hepatitis B (HepB) Vaccine (Recombinant)**

**Precautions and Contraindications**

Screen all patients for precautions and contraindications to immunization.

**Indications**

Hepatitis B vaccination is indicated for the following eligible groups for active immunization against infection caused by all known subtypes of hepatitis B virus (HBV):

* All infants, children, and adolescents as part of the routine infant, child, and adolescent immunization schedule
* Catch-up vaccination of unvaccinated children aged 4 months through 18 years
* Persons at risk for infection by sexual exposure
  + Sex partners of hepatitis B surface antigen (HBsAg)-positive persons
  + Sexually active persons who are not in a long-term mutually monogamous relationship (e.g., persons with more than one sex partner during the previous 6 months)
  + Persons seeking evaluation or treatment for a sexually transmitted infection
  + Men who have sex with men
* Persons at risk for infection by percutaneous or mucosal exposure to blood
  + Current or recent injection-drug users
  + 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 aged 19 through 59 years;
* Persons with diabetes aged 60 years and older at the discretion of the treating clinician or medical provider. Decisions to vaccinate these adults should incorporate consideration of the patient’s likelihood of acquiring HBV infection, including the risk posed by an increased need for assisted blood-glucose monitoring in long term care facilities, the likelihood of experiencing chronic sequelae if infected with HBV, and the declining immunologic responses to vaccines that are associated with frailty, a geriatric syndrome characterized by decreased physiologic reserve and increased vulnerability, leading to early mortality in older adults.
  + When a medical provider sends an order to a Local Health Department (LHD) or gives a prescription for HepB vaccine to the adult diabetic patient aged 60 years and older, the vaccine may be administered.
  + When a LHD nurse assesses that an adult diabetic patient aged 60 years and older meets criteria listed above, an order for HepB vaccine may be obtained from the LHD medical provider or private medical provider.
* Others
* International travelers to regions with high or intermediate levels of endemic HBV infection (i.e., HBsAg-positive prevalence of 2% or greater). See country specific travel recommendations for HepB vaccine on CDC’s Travelers’ Health Website, <https://wwwnc.cdc.gov/travel>.
* Persons with hepatitis C virus infection
* Persons with chronic liver disease (including, but not limited to, persons 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 HIV infection
* Incarcerated persons
* All other persons seeking protection from HBV infection

**Recommended Schedule\***

**Hepatitis B Vaccination Schedule for Infants and Children Younger than 11 Years of Age (see Table on page 5 for additional dosing schedules)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Dose** | **Vaccine** | **Recommended Age** | **Schedule if the Birth Dose  WAS NOT Given or  Catch-up Schedule** |
| 1 | HepB | Birth \* | Birth (or elected date) |
| 2 | HepB | 1 to 2 months, at least four weeks after dose 1 | **4 weeks after #1 dose** |
| 3 | HepB | 6 through 18 months, at least 8 weeks after dose 2 and at least 16 weeks  after dose 1 | **Dose #3 must be:**   * At least 8 weeks after dose 2, and * At least 16 weeks after dose 1 * At 24 weeks of age or older |

\*PEDIARIX® can be given at 2, 4 and 6 months to infants who received a birth dose of HepB   
 Vaccine (total of 4 doses). See CDC’s Pink Book 13th Edition, pg. 162.

\*HepB vaccine and hepatitis B immune globulin (HBIG) at birth:

* Administer monovalent (single-antigen) hepatitis B vaccine to all newborns within 24 hours of birth.
* For infants born to HBsAg-negative mothers, administer monovalent (single-antigen) HepB vaccine within 24 hours of birth.
* For infants born to HBsAg- positive mothers, administer HepB vaccine and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth. These infants should be tested for both HBsAg and quantitative anti-HBs (i.e., antibody to HBsAg) 1 to 2 months after completion of the HepB series, at age 9 through 18 months (generally at the next well-child visit).
* If mother’s HBsAg status is unknown, within 12 hours of birth administer HepB vaccine to all infants regardless of the birth weight. For infants weighing < 2,000 grams, administer HBIG in addition to HepB vaccine within 12 hours of birth. Determine mother’s HBsAg status as soon as possible and, if she is HBsAg-positive, also administer HBIG for infants weighing ≥ 2,000 grams (no later than age 1 week).
* Infants born to women for whom HBsAg testing results during pregnancy are not available but other evidence suggestive of maternal HBV infection exists (e.g., presence of HBV DNA, HBeAg-positive, or mother known to be chronically infected with HBV) should be managed as if born to an HBsAg-positive mother. The infant should receive both HepB vaccine and HBIG within 12 hours of birth
* If it is not possible to determine the mother's HBsAg status (e.g., when a parent or person with lawful custody safely surrenders an infant confidentially shortly after birth), the vaccine series should be completed according to a recommended schedule for infants born to HBsAg-positive mothers. The final dose in the series should not be administered before age 24 weeks (164 days). These infants should receive postvaccination serologic testing at age 9-12 months, and revaccination if necessary.

\*HepB vaccine doses following the birth dose:

* Administer monovalent (single-antigen) hepatitis B vaccine for doses administered before age 6 weeks.
* The second dose should be administered at age 1 or 2 months.
* Infants who did not receive a birth dose should receive three doses of a HepB containing vaccine on a schedule of 0, 1 to 2 months, and 6 months starting as soon as feasible.
* The minimum interval between dose 1 and dose 2 is 4 weeks and between dose 2 and dose 3 is 8 weeks. The final (third or fourth) dose in the HepB vaccine series should be administered no earlier than age 24 weeks and at least 16 weeks after the   
  first dose.
* Administration of a total of 4 doses of HepB vaccine is recommended when a combination vaccine containing HepB is administered after the birth dose.

**Hepatitis B Vaccination Schedule for Children and Adolescents**

|  |  |
| --- | --- |
| Age | Schedule1,6 |
| Children (1through10 years) | 0, 1, and 6 months2  0, 2, and 4 months2  0, 1, 2, and 12 months2,4 |
| Adolescents (11 through 18 years) | 0, 1, and 6 months2  0, 1, and 4 months2  0, 2, and 4 months2  0, 12, and 24 months2  0 and 4 through 6 months3  0, 1, 2, and 12 months2,4  0, 7 days, 21 through 30 days, 12 months5 |

**\*Table Notes:**

1. Children and adolescents may be vaccinated according to any of the schedules indicated, except as noted. Selection of a schedule should consider the need to optimize compliance with vaccination.
2. Pediatric/adolescent formulation.
3. A two-dose schedule of **RECOMBIVAX HB**® Adult Formulation is (10 micrograms) is licensed for adolescents aged 11 through 15 years. When scheduled to receive the second dose, adolescents aged more than 15 years should be switched to a three-dose series, with dose 2 and dose 3 consisting of the pediatric formulation administered on an appropriate schedule.
4. A four-dose schedule of **ENGERIX-B**® is licensed for all age groups.
5. TWINRIX® can be administered to persons 18 years of age or older before travel or any other potential exposure on an accelerated schedule at 0, 7, and 21 to 30 days, followed by a booster dose 12 months after the first dose.
6. Use of brand names is not meant to preclude the use of other comparable US licensed vaccines.

**Interrupted schedules and minimum dosing intervals**

* When the HepB vaccine schedule is interrupted, the vaccine series does not need to be restarted. If the series is interrupted after the first dose, the second dose should be administered as soon as possible, and the second and third doses should be separated by an interval of at least eight weeks. If only the third dose has been delayed, it should be administered as soon as possible.
* The final dose of vaccine must be administered at least eight weeks after the second dose and should follow the first dose by at least 16 weeks; the minimum interval between the first and second doses is four weeks. Inadequate doses of Hepatitis B vaccine or doses received after a shorter than recommended dosing interval should be re-administered, using the correct dosage or schedule.
* Vaccine doses administered 4 days or less before the minimum interval or age are considered valid. Because of the unique accelerated schedule for TWINRIX® the four-day guideline does not apply to the first three doses of this vaccine when administered on a 0 day, 7 day, 21 to 30 day, and 12 month schedule.
* In infants, administration of the final dose is not recommended before age 24 weeks (164 days).

**Hepatitis B Vaccination Schedule for Healthcare Personnel (HCP)**

The Occupational Safety and Health Administration mandates that employers offer HepB vaccination to all employees who have occupational risk and that post exposure prophylaxis be available following an exposure**.**

* Healthcare Personnel who perform tasks that may involve exposure to blood or body fluids should receive a 3-dose series of hepatitis B vaccine at 0-, 1- and 6-month intervals. Test for antibody to hepatitis B surface antigen (i.e., quantitative anti-HBs) to document immunity 1 to 2 months after dose #3.
  + If anti-HBs is 10 mIU/mL or more (positive), the patient is immune. No further serologic testing or HepB vaccination is recommended.
  + If anti-HBs is less than 10 mIU/mL (negative), the patient is unprotected from hepatitis B virus (HBV) infection; revaccinate with a second complete 3-dose series. Retest (i.e., quantitative anti-HBs) 1 to 2 months after dose #3 of the second 3-dose series (i.e., after a total of 6 doses of HepB vaccine).
    - If anti-HBs is 10 mIU/mL or more (positive), the patient is immune. No further testing or HepB vaccination is recommended.
    - If anti-HBs is less than 10 mIU/mL (negative), after 6 doses of HepB vaccine, patient is a non-responder.
    - Wounds and skin sites that have been in contact with blood or body fluids should be washed with soap and water: mucous membranes should be flushed with water. Using antiseptics (e.g., 2%-4% chlorhexidine) for wound care or expressing fluid by squeezing the wound further have not been shown to reduce the risk for HBV transmission; however, the use of antiseptics is not contraindicated. The application of caustic agents (e.g., bleach) or the injection of antiseptics or disinfectants into the wound is not recommended.
  + **For non-responders:** HCP who are non-responders should be considered susceptible to HBV and should be counseled regarding precautions to prevent HBV infections and the need to obtain HBIG prophylaxis for any known or probably parenteral exposure to hepatitis B surface antigen (HBsAg)-positive blood. It is also possible that non-responders are people who are HBsAg positive. Testing should be considered. HCP found to be HBsAg positive should be counseled and medically evaluated.

**Note:** Anti-HBs testing is not recommended routinely for previously vaccinated HCP (who have written documentation of a complete HepB vaccine series) and were not tested 1 to 2 months after their original vaccine series. These HCP should be tested for anti-HBs and the source patient (if known) should be tested for HBsAg as soon as possible after exposure. Anti-HBs testing should be performed using a method that allows detection of the protective concentration of anti-HBs (≥ 10 mIU/mL). Testing the source patient and the HCP should occur simultaneously; testing the source patient should not be delayed while waiting for the HCP   
anti-HBs test results and likewise testing the HCP should not be delayed while waiting for the source patient’s HBsAg results. See figure 3.

For detailed guidance regarding post-exposure prophylaxis see CDC Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR, 2018, Vol. 67/No.1 <Https://www.cdc.gov/mmwr/volumes/67/rr/pdfs/rr670-H.pdf> (See Tables 5 and 6: “Postexposure Management of HCP and Nonoccupational Exposure” reproduced below:

:

**TABLE 5. Postexposure management of health care personnel after occupational percutaneous or mucosal exposure to   
blood or body fluids, by health care personnel HepB vaccination and response status**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Postexposure testing** | | **Postexposure prophylaxis** | |  |
| **HCP status** | **Source patient (HBsAg)** | **HCP testing (anti-HBs)** | **HBIG** | **Vaccination** | **Postvaccination serologic testing** |
| Documented responder after complete series |  |  | No action needed |  |  |
| Documented nonresponder after two complete series | Positive/unknown | –\* | HBIG x2 separated by 1 month | – | N/A |
|  | Negative |  | No action needed | |  |
| Response unknown after complete series | Positive/unknown | <10 mIU/mL | HBIG x1 | Initiate revaccination | Yes |
|  | Negative | <10 mIU/mL | None | Initiate revaccination | Yes |
| Any result | ≥10 mIU/mL | No action needed | |  |
| Unvaccinated/incompletely vaccinated or vaccine refusers | Positive/unknown | – | HBIG x1 | Complete vaccination | Yes |
| Negative | – | None | Complete vaccination | Yes |

**Abbreviations**: anti HBs = antibody to hepatitis B surface antigen; HBIG = hepatitis B immune globulin; HBsAg = hepatitis B surface antigen;   
HCP = health care personnel; N/A = not applicable.

\* Not indicated.

**TABLE 6. Postexposure management after distinct nonoccupational percutaneous or mucosal exposure to blood or body fluids**

|  |  |  |
| --- | --- | --- |
|  | **Management** | |
| **Exposure\*** | **Unvaccinated person** | **Previously vaccinated person** |
| HBsAg-positive source | HepB vaccine series and HBIG | HepB vaccine dose |
| HBsAg status unknown for source | Hep B vaccine series | No management |

**Abbreviations:** HepB = hepatitis B; HBsAg = hepatitis B surface antigen; HBIG = hepatitis B immune globulin.

\* Exposures include percutaneous (e.g., bite or needlestick) or mucosal exposure to blood or body fluids, sex or needle-sharing contact, or victim   
 of sexual assault/abuse

See Figure 3 for “Preexposure evaluation for health care personnel previously vaccinated with complete, ≥3-dose HepB vaccine series who have not had postvaccination serologic testing” <https://www.cdc.gov/mmwr/volumes/67/rr/pdfs/rr6701-H.pdf>.

****

**Catch-Up Schedule**

* Unvaccinated persons should complete a 3-dose series.
* A 2-dose series (doses separated by at least 4 months) of adult formulation **RECOMBIVAX HB**® is licensed for use in adolescents aged 11 through 15 years.
* For other catch-up guidance from ACIP, see “Catch-up immunization schedule for persons aged 4 months through 18 years who start late or who are more than 1 month behind —United States, 2018,” <http://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf> .

**Booster Doses**

* Booster doses are not recommended for persons with normal immune status who were vaccinated as infants, children, adolescents, or adults. Serologic testing is not recommended to assess antibody concentrations in any age group, except in certain circumstances (see “Postvaccination Serologic Testing (PVST)” below).
* For hemodialysis patients, 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.
* 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. When anti-HBs levels decline to <10 mIU/mL, annual anti-HBs testing and booster doses should be considered for immunocompromised persons with an ongoing risk for exposure.

**Postvaccination Serologic Testing is NOT Routinely Recommended for Most Persons**

* Not routinely recommended following vaccination of infants, children, adolescents, or most adults.
* Routine postvaccination testing is not recommended for persons at low risk of exposure, such as public safety workers and healthcare personnel without direct patient contact.

**Postvaccination Serologic Testing is Routinely Recommended for Selected Individuals:**

* **When indicated, postvaccination serologic testing (i.e., quantitative anti-HBs) should be performed 1 to 2 months after completion of the HepB vaccine series)**
* Persons determined to have anti-HBs concentrations of ≥10 mIU/mL after receipt of the primary HepB vaccine series are considered immune, and the result should be documented.
* Postvaccination serologic testing is routinely recommended for:
  + Healthcare personnel who have contact with patients or blood
  + Infants born to HBsAg-positive women \*See Immunizations/Perinatal Hepatitis B Prevention Program and Case Management Protocol in the CCSG.
  + Sex partners of HBsAg-positive persons
  + Persons with HIV infection
  + Chronic hemodialysis patients
  + Other immunocompromised persons (e.g., hematopoietic stem-cell transplant recipients or persons receiving chemotherapy)

**Management of Nonresponse to Hepatitis B Vaccine**

* A seroprotective (adequate) level of anti-HBs after completion of a HepB vaccination series is defined as anti-HBs ≥10 mIU/mL; a response < 10 mIU/mL is inadequate and is not a reliable indicator of protection.
* Persons for whom postvaccination serologic testing is recommended but did not adequately respond to the first HepB vaccine series should complete a second three-dose HepB vaccine series. The second HepB vaccine series should be given on the usual schedule of 0, 1, and 6 months.
* Retest (i.e., quantitative anti-HBs) 1 to 2 months after completing the second HepB vaccine series
* An alternative, though less practical option, is to conduct serologic testing after each additional dose of HepB vaccine or after one or more doses of HepB vaccine.
* Persons who do not have a protective concentration of anti-HBs (≥10 mIU/mL) after revaccination (i.e., after receiving a total of 6 HepB doses) should be tested for HBsAg and anti-HBc to determine their hepatitis B virus infection status.

**Dosage and Route**

* **Pediatric Vaccination Schedule (infants and children younger than 11 years of age)**: The HepB vaccine series has three 0.5 mL doses – intramuscular (IM).
  + Administer 0.5 mL (5 mcg) of pediatric or adult formulation   
    **RECOMBIVAX HB**® (Merck) or
  + Administer 0.5 mL (10 mcg) of pediatric **ENGERIX-B** ® (GlaxoSmithKline)
* **Adolescent Schedule (11 through 19 years of age)**: The HepB vaccine series has three doses – intramuscular (IM).
  + For adolescents aged 11 through 19 years, administer 0.5 mL (5 mcg) of the pediatric or adult formulation of **RECOMBIVAX HB**® (Merck) or
  + Administer 0.5 mL (10 mcg) of the pediatric formulation of **ENGERIX-B**® (GlaxoSmithKline).
  + The adult formulation of **ENGERIX-**B® may be used in adolescents, but the approved dose is 1 mL (20 mcg).
* **Alternative Adolescent Vaccination Schedule (11 through 15 years of age only)**: The HepB vaccine series has two 1 mL (10 mcg) doses – intramuscular (IM). Administer 1 mL (10 mcg) only using the pediatric or adult formulation of **RECOMBIVAX HB**® when using this schedule.
* **Adult Schedule (20 years of age and older)**: The HepB vaccine series has three 1 mL doses – intramuscular (IM).
  + For adults aged 20 years and older, administer 1 mL (10 mcg) of pediatric or adult formulation **RECOMBIVAX HB**® (Merck) or
  + Administer 1 mL (20 mcg) of adult formulation **ENGERIX-B**® (GlaxoSmithKline). The pediatric formulation of **ENGERIX-B**® is not approved for use in adults.
  + Alternative adult schedules for single antigen HepB vaccine are   
    0, 1, and 6 months, 0, 1, and 4 months, and 0, 2, and 4 months for   
    both HepB vaccine brands. An adult schedule of 0, 1, 2, and 12 months is FDA approved for **ENGERIX-B**®. See the HepB vaccine package insert.
* **Adult patients receiving hemodialysis, predialysis patients, or with other immunocompromising conditions:** 
  + The HepB vaccine series has three 1 mL doses – intramuscular (IM) of the **RECOMBIVAX HB**® Dialysis Formulation (40 mcg/mL) administered on a   
    3-dose schedule at 0, 1, and 6 months, or
  + The HepB vaccine series has four 2 mL (40 mcg/2 mL) doses of adult formulation **ENGERIX-B**®– intramuscular (IM) administered on a 0, 1, 2, and 6 month schedule. Each dose in the series can be given as a single 2 mL dose or as   
    two 1-mL doses in one visit.
  + **RECOMBIVAX HB**® Dialysis Formulation (40 µg/mL) is not provided by the Kentucky Vaccine Program (KVP) but may be ordered with Local Health Department funds. **RECOMBIVAX HB**® Dialysis Formulation may be available at private provider offices and specialty clinics.
  + Serologic testing of hemodialysis patients and other immunocompromised persons is recommended 1--2 months after administration of the final dose of the primary HepB vaccine series to determine the need for revaccination (see Postvaccination Testing for Serologic Response). In addition, booster doses of vaccine might be needed. For hemodialysis patients, 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.

**Anatomical Site** (ACIP and the AAFP recommendations for intramuscular injections)

* In children and adolescents (persons 12 months through 19 years of age), the deltoid muscle can be used if the muscle mass is adequate. The needle size can range from 22 to 25 gauge and from 7/8 to 1¼ inches, based on the size of the muscle. For infants and toddlers, the anterolateral thigh can be used, but the needle should be longer, usually 1 inch.
* For adults (persons 20 years of age and older) the deltoid muscle is recommended for routine intramuscular vaccinations. The anterolateral thigh can be used. The suggested needle size is 1-1½ inches and 22-25 gauge.

**Precautions**

* See precautions in package insert.
* Latex allergy – See WARNINGS and/or PRECAUTIONS in the package insert for information about any latex components in the vial stopper and or prefilled syringes for the particular brand of hepatitis B vaccine being used.
* As with other intramuscular injections, use with caution in patients on anticoagulant therapy.

**Contraindications**

* Allergy to vaccine components
* Anaphylactic reaction to the vaccine or a constituent of the vaccine
* Acute, moderate or severe illness with or without fever

**Adverse Events**

* See the product’s package insert
* See Adverse Events Following Vaccinations page of this section

**Storage and Handling**

* Store in refrigerator at 36oF – 46oF (2oC – 8oC)
* DO NOT FREEZE; discard if product has been frozen.

**Other Important Notes**

* If HepB vaccine is administered concomitantly with hepatitis B immune globulin (HBIG), use a separate syringe and a different site, preferably a different limb.
* Exposed unvaccinated persons should receive the HepB vaccine series with the first dose administered as soon as possible after exposure, preferably within 24 hours. The vaccine series should be completed according to the vaccination schedule.

**References:**

CDC Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR, 2018, Vol. 67/No.1

<https://www.cdc.gov/mmwr/volumes/67/rr/pdfs/rr6701-H.pdf>.

Immunization Action Coalition (IAC): Needle Tips; ACIP Votes to Update Recommendations for HPV, Tdap, MenB and HepB Vaccines; Volume 26-Number 4; December 2016 <http://www.immunize.org/nt/>

ACIP VFC Resolution 2/17-1, “Vaccines to Prevent Hepatitis B”

<http://www.cdc.gov/vaccines/programs/vfc/downloads/resolutions/2017-02-01-hepb.pdf>

Healthcare Personnel Vaccination Recommendations: [www.immunize.org/catg.d/p2017.pdf](http://www.immunize.org/catg.d/p2017.pdf)

CDC. Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger, United States, 2018, <http://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html>

CDC. Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States, 2018, <http://www.cdc.gov/vaccines/schedules/hcp/adult.html>

Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine-Preventable Diseases. Hamborsky J, Kroger A, Wolfe S, eds. 13th ed. Washington D.C. Public Health Foundation, 2015. (Pink Book): <https://www.cdc.gov/vaccines/pubs/pinkbook/hepb.html>

Hepatitis B. Centers for Disease Control and Prevention. CDC Yellow Book 2018: Health Information for International Travel. New York: Oxford University Press; 2017.  
<https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/hepatitis-b>

Updated July 1, 2014, July 1 2017, and July 1, 2018