HEPATITIS B VACCINE

Hepatitis B Vaccine

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On January 5, 2026, the US Department of Health and Human Services (HHS) announced the approval of a revised US childhood and adolescent immunization schedule ([Web]). Under the revised recommendations, CDC continues to organize the childhood immunization schedule in three distinct categories (Immunizations Recommended for All Children, Immunizations Recommended for Certain High-Risk Groups or Populations, and Immunizations Based on Shared Clinical Decision-Making) but changes individual vaccine placement within those categories. For additional information, see [Web] .

Introduction

Hepatitis B vaccine (recombinant; Engerix-B®, Recombivax HB®) and hepatitis B vaccine (recombinant) adjuvanted (Heplisav-B®) are inactivated recombinant vaccines containing hepatitis B surface antigen (HBsAg); they are used to stimulate active immunity to hepatitis B virus (HBV) infection.[132,133,292]

Uses

Prevention of Hepatitis B Infection

Hepatitis B vaccine is used to prevent infection caused by all known subtypes of hepatitis B virus (HBV).[132,133,293] Hepatitis B vaccine is commercially available in the US as three monovalent recombinant vaccines: hepatitis B vaccine (recombinant; Engerix-B® and Recombivax HB®) and hepatitis B vaccine (recombinant), adjuvanted (Heplisav-B®).[132,133,292] Engerix-B® and Recombivax HB® are used in patients of all ages; the dialysis formulation of Recombivax HB® is used specifically in predialysis and dialysis patients ≥18 years of age.[132,133] Heplisav-B® is only used in adults ≥18 years of age.[292] In general, the various brands of age-appropriate hepatitis B vaccines are interchangeable within an immunization series; however, adolescents who start their vaccination series with the adult formulation of Recombivax HB® cannot complete the series with the adult formulation of Engerix-B®, and adults who start their vaccination series with Heplisav-B® should complete it with the same product or receive a 3-dose series rather than the 2-dose series that is used with Heplisav-B®.[133,295,299]

Hepatitis B vaccine also is commercially available in a fixed-combination vaccine with hepatitis A virus vaccine (HepA-HepB; Twinrix®),[262] in a fixed-combination vaccine that contains diphtheria, tetanus, pertussis, hepatitis B, and poliovirus antigens (DTaP-HepB-IPV; Pediarix®),[104] and in a fixed-combination vaccine that contains diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and *Haemophilus influenza* type b (Hib) antigens (DTaP-IPV-Hib-HepB; Vaxelis®).[293] The HepA-HepB vaccine (Twinrix®) is used for active immunization against hepatitis A and hepatitis B in adults ≥18 years of age.[262] The DTaP-HepB-IPV vaccine (Pediarix®) is used for active immunization against diphtheria, tetanus, pertussis, hepatitis B, and poliomyelitis in patients 6 weeks to 6 years of age.[104] The DTaP-IPV-Hib-HepB vaccine (Vaxelis®) is used for active immunization against diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, and Hib in patients 6 weeks to 4 years of age.[293]

An additional hepatitis B vaccine (PreHevbrio®) was previously available; however, all remaining lots of this vaccine were recalled in November 2024 when the manufacturer

ceased operations.[298] A fixed-combination vaccine containing recombinant hepatitis B surface antigen (HBsAg) and Hib (Comvax®) was also previously available, but was discontinued by the manufacturer in 2015.[294]

Hepatitis B is a viral infection caused by HBV; it is one of several types of viral hepatitis infections that can cause systemic infection, with the liver as the primary site of pathology.[293] Infection with HBV can lead to serious outcomes including acute massive hepatic necrosis and chronic active hepatitis; individuals with chronic HBV infection are at increased risk for cirrhosis and hepatocellular carcinoma.[104,132,133,262,292] Although HBV infection occurs worldwide, it may be more common in some countries in Asia, Africa, South America, and the Caribbean.[301] Transmission of HBV occurs through percutaneous, mucosal, or nonintact skin exposure to infectious bodily fluids (e.g., blood, semen, saliva).[301,302] Transmission of the virus most often occurs during sexual contact, childbirth, or injection drug use; however, it can also be transmitted via bite wounds, accidental needlesticks, organ transplantation, dialysis, contact with open sores of an infected person, and sharing of personal items such as razors and toothbrushes.[301,302] Populations at highest risk for HBV infection include infants born to mothers with hepatitis B, people born in countries where hepatitis B is common, people with hepatitis C or human immunodeficiency virus (HIV), people with liver damage or inflammation, people on dialysis, men who have sex with men, people who live with an HBV-infected person or whose sexual partners have hepatitis B, people who have been incarcerated, injection drug users, and people who are exposed to blood as a result of their occupation.[302] People with diabetes may also be at increased risk for hepatitis B if they share glucose meters, fingerstick devices, or other equipment; HBV outbreaks have occurred among diabetic patients in institutional and medical settings as a result of improper infection control practices related to blood glucose monitoring.[301,302]

Infection with HBV can be asymptomatic, particularly in infants and young children.[301] All patients who test positive for HBsAg are considered infectious, unless they were recently vaccinated (i.e., within 18 days of vaccination for most patients, or within 52 days of vaccination for dialysis patients); patients who also test positive for hepatitis B e antigen (HBeAg) or high levels of HBV DNA are considered most infectious.[294,301] Approximately 50% of adults with acute HBV infection will present with signs and/or symptoms, which include abrupt onset of fever, malaise, anorexia, nausea, abdominal discomfort, dark urine, jaundice, light-colored stools, hepatic tenderness, and hepatomegaly.[301] Most acute infections in adults are followed by a complete recovery; however, fulminant hepatitis can occur in 1–2% of patients, and chronic HBV infection develops in approximately 5% of adults.[301] Rates of chronic HBV infection are higher among HBV-infected infants and young children, with an estimated 90% of HBV-infected infants and 30–50% of HBV-infected children 1–5 years of age developing chronic infection.[301] Although chronic HBV infection is generally asymptomatic, it is associated with significant morbidity and mortality.[301] Complications of chronic HBV infection can include chronic hepatitis, cirrhosis, liver failure, and hepatocellular carcinoma; approximately 25% of patients who become chronically infected during childhood and 15% of patients chronically infected as adults will die prematurely due to cirrhosis or liver cancer.[301]

Clinical Experience

Prevention of Perinatal Infection in Neonates

In a clinical study of infants born to HBsAg- and HBeAg-positive mothers who received a single dose of hepatitis B immune globulin (HBIG) at birth followed by the recommended 3-dose series of Recombivax HB®, 96% did not develop chronic HBV infection after 9 months of follow-up.[132] The estimated efficacy in prevention of chronic HBV infection was 95% as compared to the infection rate in untreated historical controls.[132] Receipt of both HBIG and Recombivax HB® was associated with decreased rates of HBV infection compared to receipt of HBIG alone.[132]

In a clinical study of 58 neonates born to HBsAg- and HBeAg-positive mothers, administration of Engerix-B® at 0, 1, and 2 months of age without concomitant HBIG was associated with a 95% protective efficacy rate against chronic HBV infection.[133] Only 2 infants became chronic HBV carriers during the 12-month follow-up period following vaccination.[133]

Primary Immunization of Infants, Children, and Adolescents

A 3-dose series of Recombivax HB® induced a protective level of anti-HBsAg antibodies in 100% of infants, 99% of children, and 99% of adolescents in clinical studies.[132] An open-label randomized study compared a 2-dose series of adult-dose Recombivax HB® to a 3-dose series of pediatric-dose Recombivax HB® in adolescents 11–15 years of age and found that the proportion of patients attaining a protective level of anti-HBsAg antibodies was similar between regimens.[132]

A 3-dose series of Engerix-B® (with doses given at 0, 1, and 6 months) induced a protective level of anti-HBsAg antibodies in 97% of infants and 98% of patients 6 months to 10 years of age.[133] In one trial of children and adolescents 5–16 years of age, protective levels of anti-HBsAg antibodies were observed in 99.5% of patients following a 3-dose series of Engerix-B® (with doses given at 0, 1, and 6 months).[133] In clinical trials of healthy adolescents 11–19 years of age, a 3-dose series of Engerix-B® (10 mcg, with doses given at 0, 1, and 6 months) induced a protective level of anti-HBsAg antibodies in 97% of patients.[133]

Primary Immunization of Adults

A 3-dose series of Recombivax HB® induced a protective level of anti-HBsAg antibodies in 96% of healthy adults in clinical studies; antibody responses were slightly reduced in older patients, with 89% of patients ≥40 years of age attaining protective levels of anti-HBsAg antibodies.[132] Seroprotection rates of 70% were observed among patients with chronic hepatitis C infection who were vaccinated with

Recombivax HB®.[132] Immune responses to Recombivax HB® may be reduced in patients who are predialysis or currently receiving dialysis, particularly if the vaccine is administered at an inappropriate site (i.e., the buttock); when 40 mcg of Recombivax HB® was administered in the deltoid muscle of 28 predialysis and dialysis patients, 86% developed protective antibody levels.[132]

In clinical trials enrolling healthy patients 16–65 years of age, a 3-dose series of Engerix-B® (20 mcg, with doses given at 0, 1, and 6 months) induced a protective level of anti-HBsAg antibodies in 96% of patients.[133] Among patients ≥40 years of age, protective levels of anti-HBsAg antibodies were achieved in 88% of patients 1 month after the third dose.[133] In a study of 244 homosexual men 16–59 years of age, no instances of HBV infection were observed within 18 months following completion of a 3-dose series of Engerix-B® (20 mcg, with doses given at 0, 1, and 6 months).[133] In a study of 67 adults 25–67 years of age with chronic hepatitis C, protective levels of anti-HBsAg antibodies were attained in all patients following a 3-dose series of Engerix-B® (20 mcg, with doses given at 0, 1, and 6 months).[133] Immune responses to Engerix-B® may be reduced in patients on hemodialysis; when 40 mcg of Engerix-B® was administered to 56 adults on hemodialysis at months 0, 1, 2, and 6, 67% had protective antibody levels 2 months after the last dose.[133] A study of 674 patients with or without type 2 diabetes found that protective levels of anti-HBsAg antibodies were achieved in 75% of patients with diabetes and 82% of patients without diabetes following a 3-dose series of Engerix-B® (20 mcg, with doses given at 0, 1, and 6 months).[133]

Three randomized controlled trials compared a 2-dose series of Heplisav-B® (with doses administered at 0 and 1 months followed by a saline placebo at 6 month) to a 3-dose series of Engerix-B® (with doses given at 0, 1, and 6 months) in adults.[292,313,314,315] In the first study (which enrolled adults 18–55 years of age), seroprotection rates at week 12 (for Heplisav-B®) or week 28 (for Engerix-B®) were 95.1 and 81.1%, respectively.[292,313] In the second study (enrolling adults 40–70 years of age), seroprotection rates at week 12 (for Heplisav-B®) or week 32 (for Engerix-B®) were 90 and 70.5%, respectively.[292,314] In the third study (enrolling adults 18–70 years of age), seroprotection rates at week 28 (for both vaccines) among patients with type 2 diabetes were 90 and 65.1% for Heplisav-B® and Engerix-B® respectively.[292,315] In the overall trial population, seroprotection rates at week 24 (for Heplisav-B®) or week 28 (for Engerix-B®) were 95.2 and 80.7%, respectively.[292,315] Heplisav-B® maintained similar serologic response rates across all age groups (91.6–100%), while the serologic response rates with Engerix-B® decreased as age increased (range: 72.6–93.9%).[292,315]

Clinical Perspective

Primary Immunization in Infants Born to HBsAg-negative Mothers

The American Academy of Pediatrics (AAP) and other experts recommend that all neonates and infants receive primary immunization against HBV with hepatitis B vaccine; the recommended vaccine schedule varies based on the mother's HBsAg status and the infant's birthweight.[299,300,308]

Medically stable neonates weighing ≥2000 g born to HBsAg-negative mothers are recommended to receive a 3-dose series; administer 1 dose of single-antigen hepatitis B vaccine within 24 hours of birth.[299,300] The second dose of hepatitis B vaccine should be administered at 1–2 months of age, and the third dose should be given at 6–18 months of age.[299,300] The final dose in the series should not be administered before age 24 weeks.[300,303]

For neonates weighing <2000 g born to HBsAg-negative mothers, the AAP recommends a 3-dose series; delay the first dose of single-antigen hepatitis B vaccine until the time of hospital discharge or until the infant is 1 month of age (whichever is earlier).[299,300] The second dose of hepatitis B vaccine should be administered at 2 months of age, and the third dose should be given at 6–18 months of age.[299,300] The final dose in the series should not be administered before age 24 weeks.[299,300]

The fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, and poliovirus antigens (DTaP-HepB-IPV; Pediarix®) or the fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and Hib antigens (DTaP-IPV-Hib-HepB; Vaxelis®) may be used to complete the hepatitis B vaccination series after a first dose of hepatitis B vaccine is given at birth; however, DTaP-HepB-IPV and DTaP-IPV-Hib-HepB should not be used for the birth hepatitis B vaccine dose and should not be given to infants <6 weeks of age.[294,305] If DTaP-HepB-IPV or DTaP-IPV-Hib-HepB is used to complete the series, doses of the combination vaccine should be given at 2 months, 4 months, and 6 months (not before age 24 weeks).[294,299,305]

The Advisory Council on Immunization Practices (ACIP) recently recommended a shift from universal hepatitis B vaccination at birth to shared clinical decision making for infants of HBsAg-negative mothers, allowing parents to choose to delay the initial dose until at least 2

months of age.[317]

Prevention of Perinatal Infection and Primary Immunization in Infants Born to HBsAg-positive or HBsAg-unknown Mothers

The Centers for Disease Control (CDC), ACIP, AAP, and the American College of Obstetricians and Gynecologists (ACOG) recommend routine serologic screening of all pregnant women during an early prenatal visit (e.g., first trimester) to determine their HBsAg status, even if they were tested previously or have already been vaccinated against HBV.[294,299,310,312] All HBsAg-positive pregnant women should additionally be tested for HBV DNA to guide the use of maternal antiviral therapy during pregnancy to prevent perinatal transmission.[294,299,312] Pregnant women who were not tested prenatally, those with clinical hepatitis, and those whose behaviors place them at high risk for HBV infection should be tested for HBV infection at the time of admission to the hospital or birthing facility for delivery.[294,299]

To prevent perinatal HBV infection, the ACIP, AAP, and other experts recommend that all neonates born to HBsAg-positive mothers receive a dose of single-antigen hepatitis B vaccine and a dose of HBIG in separate limbs as soon as possible after birth (within 12 hours of birth), regardless of birth weight.[294,299,300,303,308,310,312] The hepatitis B vaccination series should then be completed according to the recommended schedule based on birthweight and the vaccine used.[294,299] If a single-antigen hepatitis B vaccine is used to complete the series, patients weighing ≥2000 g at birth should receive a second vaccine dose at 1–2 months and a third dose at 6 months.[294,299,308,310] Patients weighing <2000 g at birth should receive a second vaccine dose at 1 month, a third at 2–3 months, and a fourth at 6 months.[294,299,308,310] The final dose in the series should not be administered before age 24 weeks, regardless of birthweight.[294] Post-vaccination serologic testing is recommended at 9–12 months of age to assess HBsAg and anti-HBsAg antibody levels; revaccination is recommended for HBsAg-negative patients with anti-HBsAg antibody levels <10 mIU/mL (consult guidelines for more information).[294,299,300,308]

Infants born to mothers for whom HBsAg testing results are not available should be managed as if born to an HBsAg-positive mother if other evidence exists to suggest maternal HBV infection (e.g., positive HBeAg, presence of HBV DNA, known chronic HBV infection).[294,300,303] If maternal HBsAg status is unknown at birth, neonates weighing ≥2000 g should receive the first dose of single-antigen hepatitis B vaccine (within 12 hours of birth) and the mother's HBsAg status should be determined as quickly as possible; if positive, the infant should receive a dose of HBIG in a separate limb as soon as possible (no later than 7 days of age).[294,299,300,303,308] Because there is a risk of decreased immunogenicity of the vaccine in neonates weighing <2000 g, such infants should receive both the single-antigen hepatitis B vaccine and a single dose of HBIG in separate limbs within 12 hours of birth.[294,299,300,303,308] The hepatitis B vaccine series should then be completed according to the recommended schedule based on the mother's HBsAg status, the infant's birthweight, and the vaccine used.[294] If it is not possible to determine the mother's HBsAg status, the vaccine series should be completed and post-vaccination serologic testing should be performed according to the schedule recommended for infants born to HBsAg-positive mothers.[294,300]

The fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, and poliovirus antigens (DTaP-HepB-IPV; Pediarix®) or the fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and Hib antigens (DTaP-IPV-Hib-HepB; Vaxelis®) may be used to complete the hepatitis B vaccination series after the first dose of hepatitis B vaccine is given at birth in ***infants born to HBsAg-positive mothers or mothers of unknown HBsAg status [off-label]†****; however, DTaP-HepB-IPV and DTaP-IPV-Hib-HepB should not be used for the birth hepatitis B vaccine dose and should not be given to infants <6 weeks of age.[294,305] If DTaP-HepB-IPV or DTaP-IPV-Hib-HepB is used to complete the series, doses of the combination vaccine should be given at 2 months, 4 months, and 6 months (not before age 24 weeks).[294,299,305]*

Catch-up Vaccination in Children and Adolescents

The AAP recommends that all previously unvaccinated children ≥4 months of age through 18 years of age receive catch-up vaccination with hepatitis B vaccine.[300] Serologic testing prior to vaccination is not routinely recommended for children and adolescents.[299] However, the AAP recommends (but does not require) prevaccination serologic testing for children and adolescents at increased risk for HBV infection.[299] If serologic testing is performed prior to vaccination, providers do not need to wait for the test results to administer a vaccine dose.[299] CDC recommends routine hepatitis B vaccination only for children at higher risk (e.g., those with underlying comorbidities, those who may have unusual exposure to the disease, or those with risk of disease transmission to others) and immunization based on shared clinical decision making in children who are not at high risk.[318]

A 3-dose series of hepatitis B vaccine should be administered, with doses given at 0, 1–2, and 6 months.[300,303,308] For children with HIV, a double dose of the vaccine may be considered.[308] In children ≥4 months of age through 18 years, the minimum interval between dose 1 and dose 2 of the hepatitis B vaccine seriesis 4 weeks; the minimum interval between dose 2 and dose 3 is 8 weeks, with dose 3 being given at least 16 weeks after dose 1.[300,303] In lieu of a 3-dose series, adolescents 11–15 years of age may be vaccinated with 2 doses of the adult formulation of Recombivax HB® given at least 4 months apart.[300,303] Adolescents 18 years of age may alternatively receive a 2-dose series of Heplisav-B® (with doses given at least 4 weeks apart) or a 3- or 4-dose series of Twinrix® (if vaccination against both hepatitis A and hepatitis B is desired).[295,300,303]

All foreign-born persons and immigrants, refugees, and internationally adopted children born in Asia, the Pacific Islands, Africa, and other regions of high or intermediate hepatitis B endemicity should receive HBsAg testing, regardless of vaccination status.[299,306] Persons not known to be vaccinated against hepatitis B should receive an age-appropriate hepatitis B vaccination series; revaccination is not necessary if a complete hepatitis B vaccine series has been documented, unless the last hepatitis B vaccine dose was given at <24 weeks of age.[306]

Postvaccination serologic testing is not routinely required in children and adolescents.[294,299] However, certain groups should receive testing for anti-HBsAg antibodies 1–2 months after the hepatitis B vaccination series is complete.[294,299] These groups include hemodialysis patients (including predialysis, peritoneal dialysis, and home dialysis patients), HIV-infected patients, other immunocompromised patients (e.g., hematopoietic stem cell transplant recipients, people receiving chemotherapy), and sexual partners of HBsAg-positive people.[294,299,300,303,308] People with postvaccination anti-HBsAg antibody levels <10 mIU/mL should be revaccinated (consult guidelines for more information).[294,299,300,303,308] Patients receiving hemodialysis in outpatient centers should have their anti-HBsAg antibody levels assessed annually, with a booster dose of hepatitis B vaccine administered when anti-HBsAg antibody levels decline to <10 mIU/mL.[294,299]

The humoral response to hepatitis B vaccine may be reduced in children and adolescents who are immunocompromised (e.g., HIV-infected persons, hematopoietic stem cell transplant recipients, patients undergoing chemotherapy).[294,308] The ACIP and AAP state that annual anti-HBsAg antibody testing should be considered for immunocompromised patients with an ongoing risk for HBV exposure, and booster doses of hepatitis B vaccine should be administered if anti-HBsAg antibody levels decline to <10 mIU/mL.[294,299] The AAP additionally states that similar consideration may be given to children with cystic fibrosis, liver disease, or celiac disease if there is ongoing risk for HBV exposure.[299] The U.S. Department of Health and Human Services (HHS) states that assessment of anti-HBsAg antibodies in pediatric patients with HIV who respond to hepatitis B vaccination can be considered every 5 years, with booster doses of hepatitis B vaccine provided if anti-HBsAg antibody titers fall below 10 mIU/mL.[308]

Primary Immunization in Adults

The ACIP recommends that all adults 19–59 years of age receive primary immunization with hepatitis B vaccine.[296,304] Adults ≥60 years of age with risk factors for hepatitis B should also receive primary immunization against hepatitis B.[296,304] Risk factors for HBV infection may be related to sexual practices, risk of percutaneous or mucosal exposure to blood, or other factors.[296] Adults ≥60 years of age are at increased risk for hepatitis B if they have HBsAg-positive sexual partners, if they are seeking evaluation or treatment for a sexually transmitted infection, if they are men who have sex with men, or if they are sexually active and not in a long-term, mutually monogamous relationship.[296] The following populations are also at increased risk for hepatitis B based on the risk of exposure to infectious bodily fluids: current or recent injection drug users; people living with an HBsAg-positive person; residents and staff members of facilities for people with developmental disabilities; health care and public safety personnel with a reasonably anticipated risk for exposure to blood or blood-contaminated bodily fluids; and people who are predialysis or on maintenance dialysis, including peritoneal dialysis.[296] Other populations considered at-risk for hepatitis B include people who are incarcerated, people with HIV or hepatitis C, people with chronic liver disease, and international travelers to countries with high or intermediate hepatitis B endemicity.[296] Diabetes can be considered a risk factor for hepatitis B among adults ≥60 years of age, but administration of the hepatitis B vaccine based on this risk factor should be based on shared clinical decision making.[296,304] Unvaccinated adults ≥60 years of age without risk factors for hepatitis B may also receive hepatitis B vaccines if vaccination is desired.[296,304]

Although the CDC recommends HBV serologic testing for all adults ≥18 years of age at least once during their lifetime, testing is not a requirement for hepatitis B vaccination.[296,309] If serologic testing is performed prior to vaccination, providers do not need to wait for the test results to administer a vaccine dose.[309] In settings where serologic testing is not possible or refused by the patient, vaccination should

proceed according to ACIP recommendations.[296,309] The ACIP specifically recommends (but does not require) prevaccination serologic testing for the following groups: household, sexual, or needle-sharing contacts of HBsAg-positive people; HIV-positive people; hemodialysis patients; men who have sex with men; past or current injection drug users; people with elevated ALT/AST without a clear etiology; people born in countries of high or intermediate HBV endemicity; unvaccinated U.S.-born patients whose parents were born in countries with high HBV endemicity; people requiring immunosuppressive therapy; and donors of blood, plasma, organs, tissues, or semen.[294]

A 2-, 3-, or 4-dose series of hepatitis B vaccine may be appropriate for vaccination of adults, depending on patient comorbidities and the vaccine used (Engerix-B®, Recombivax HB®, Heplisav-B®, or Twinrix® [if vaccination against both hepatitis A and hepatitis B is desired]).[304] Pregnant women who require hepatitis B vaccination may receive any of the available single-antigen hepatitis B vaccines or Twinrix® (if vaccination against both hepatitis A and hepatitis B is desired).[297] Patients on dialysis should complete a 3-dose series (using the dialysis formulation of Recombivax HB®) or a 4-dose series (using a 2-mL dose of Engerix-B®).[304] Patients ≥20 years of age with immunocompromising conditions should complete a 2-dose series of Heplisav-B® or a 3- or 4-dose series with Recombivax HB® or Engerix-B® as described for dialysis patients.[304] Patients who began their hepatitis B vaccine series with PreHevbrio® (no longer available in the U.S.) should complete the 3-dose series using another licensed hepatitis B vaccine for the remaining doses.[298]

The ACIP states that postvaccination serologic testing is not routinely required to confirm immunity to HBV; however, certain groups should receive testing for anti-HBsAg antibodies 1–2 months after the hepatitis B vaccination series is complete.[294] These groups include health care providers and public safety workers at risk for blood or body fluid exposure, hemodialysis patients (including predialysis, peritoneal dialysis, and home dialysis patients), HIV-infected patients, other immunocompromised patients (e.g., hematopoietic stem cell transplant recipients, people receiving chemotherapy), and sexual partners of HBsAg-positive people.[294] People with postvaccination anti-HBsAg antibody levels <10 mIU/mL should be revaccinated (consult guidelines for more information).[294] Patients receiving hemodialysis in outpatient centers should have their anti-HBsAg antibody levels assessed annually, with a booster dose of hepatitis B vaccine administered when anti-HBsAg antibody levels decline to <10 mIU/mL.[294]

The humoral response to hepatitis B vaccine may be reduced in adults who are immunocompromised (e.g., HIV-infected persons, hematopoietic stem cell transplant recipients, patients undergoing chemotherapy).[294] The ACIP states that annual anti-HBsAg antibody testing should be considered for immunocompromised patients with an ongoing risk for HBV exposure, and booster doses of hepatitis B vaccine should be administered if anti-HBsAg antibody levels decline to <10 mIU/mL (consult guidelines for more information).[294]

Specific recommendations for hepatitis B vaccination in patients with HIV are available from the National Institutes of Health (NIH), the HIV Medicine Association, and the Infectious Diseases Society of America (IDSA).[307] These experts recommend hepatitis B vaccination for all people with HIV who do not have chronic HBV and are not immune to HBV infection (i.e., they are negative for anti-hepatitis B core antigen (HBcAg) antibodies and anti-HBsAg antibodies); patients who have failed a prior hepatitis B vaccination series should also be revaccinated.[307] A 2-dose series of Heplisav-B® is the preferred hepatitis B vaccination regimen for unvaccinated adults with HIV; if Heplisav-B® is not available, a 3-dose series of double-dose Engerix-B® or Recombivax HB® or a 3-dose series of Twinrix® may be used.[307] Although the response to Engerix-B® and Recombivax HB® is greater among patients with CD4 counts >350 cells/mm^3, vaccination should not be delayed in patients with CD4 count ≤350 cells/mm^3 who are at high risk of HBV infection.[307] Response to hepatitis B vaccination (i.e., anti-HBsAg antibody levels ≥10 mIU/mL) should be documented 4 weeks after the last dose of vaccine.[307] If adequate response is not achieved, revaccination is recommended (consult guidelines for more information).[307] Because immunity may wane, providers should consider monitoring anti-HBsAg antibody levels annually and giving booster doses of hepatitis B vaccine if levels fall below 10 mIU/mL, particularly in patients with ongoing risk factors for HBV.[307] Patients with HIV who present with isolated anti-HBcAg antibodies should be vaccinated with a standard dose of hepatitis B vaccine (Engerix-B®, Recombivax HB®, or Heplisav-B®); anti-HBsAg antibody titers should be checked 1–2 months afterward.[307] If the anti-HBsAg antibody titer is ≥100 mIU/mL, no additional doses of vaccine are needed, but if anti-HBsAg antibody titers are <100 mIU/mL, the rest of the hepatitis B vaccination series should be completed.[307]

Postexposure Prophylaxis

Hepatitis B vaccine is used for postexposure prophylaxis in certain individuals exposed to HBV through a distinct, identifiable percutaneous or mucosal exposure to blood or body fluids containing blood.[294,311] Depending on the exposure circumstances, the postexposure prophylaxis regimen may include combined active immunization with the vaccine and passive immunization with HBIG.[294,311]

Management of occupational exposures to HBV in healthcare providers depends primarily on the healthcare provider's immunization status.[294] If the healthcare provider has written documentation of a completed hepatitis B vaccine series and subsequent documentation of serologic response (i.e., anti-HBsAg antibody level ≥10 mIU/mL), no further action is required and no postexposure prophylaxis is necessary.[294] In all other circumstances, the source patient (if known) should be tested for HBsAg as soon as possible after the exposure.[294] Healthcare providers with written documentation of a completed hepatitis B vaccine series but no previous record of anti-HBsAg antibody testing should also be tested for anti-HBsAg antibodies as soon as possible after the exposure.[294] Postexposure anti-HBsAg antibody testing is not recommended for healthcare providers who are known vaccine non-responders (i.e., anti-HBsAg antibody level <10 mIU/mL after 2 complete vaccine series) or healthcare providers who are unvaccinated or incompletely vaccinated.[294] Subsequent exposure management will depend on the healthcare provider's vaccination status, the healthcare provider's anti-HBsAg antibody level (when tested), and the source patient's HBsAg status (see Table 1).[294] Healthcare providers who cannot provide documentation of 3 doses of hepatitis B vaccine should be considered unvaccinated and should complete the vaccine series.[294]

Table 1. Postexposure Prophylaxis of HBV following Occupational Percutaneous or Mucosal Exposure.[294]

VACCINATION AND ANTIBODY STATUS OF EXPOSED INDIVIDUAL	TREATMENT WHEN SOURCE IS: HBSAG-POSITIVE	TREATMENT WHEN SOURCE IS: HBSAG-NEGATIVE	TREATMENT WHEN SOURCE IS: UNKNOWN OR NOT AVAILABLE FOR TESTING
Unvaccinated or incompletely vaccinated	Single HBIG dose and initiate hepatitis B vaccine series with postvaccination serologic testing	Initiate hepatitis B vaccine series with postvaccination serologic testing	Single HBIG dose and initiate hepatitis B vaccine series with postvaccination serologic testing
Previously completed vaccination series: Known responder (anti-HBsAg antibodies ≥10 mIU/mL after complete vaccine series)	No treatment	No treatment	No treatment
Previously completed vaccination series: Known nonresponder (anti-HBsAg <10 mIU/mL after 2 complete vaccination series)	2 HBIG doses (first dose as soon as possible; second dose 1 month later)	No treatment	2 HBIG doses (first dose as soon as possible; second dose 1 month later)
Previously completed vaccination series: Antibody response unknown	Test exposed individual for anti-HBsAg antibodies If <10 mIU/mL, administer single dose of HBIG and initiate revaccination with postvaccination serologic testing If ≥10 mIU/mL, no treatment	Test exposed individuals for anti-HBsAg antibodies If <10 mIU/mL, initiate revaccination with postvaccination serologic testing If ≥10 mIU/mL, no treatment	Test exposed individual for anti-HBsAg antibodies If <10 mIU/mL, administer single dose of HBIG and initiate revaccination with postvaccination serologic testing If ≥10 mIU/mL, no treatment

For people with a distinct, identifiable percutaneous or mucosal exposure to HBV through blood or body fluids containing blood in a nonoccupational setting, recommendations for postexposure prophylaxis depend on the person's vaccination status and the HBsAg status of the exposure source.[294,311] If the exposed person was previously vaccinated against HBV, they should receive a single dose of hepatitis B vaccine following exposure if the source is determined to be HBsAg-positive; if the source is HBsAg-negative or the HBsAg status of the source is unknown, no postexposure prophylaxis is required.[294,311] If the exposed person has not been fully vaccinated against HBV, they should receive a complete hepatitis B vaccination series following exposure, regardless of the HBsAg status of the exposure source.[294,311] Persons who are in the process of completing a hepatitis B vaccination series do not need to restart the series following exposure.[294,311] In unvaccinated persons, the first dose of hepatitis B vaccine should be administered as soon as possible after the exposure (ideally within 24 hours).[294,311] If the exposure source is determined to be HBsAg-positive, the unvaccinated or partially vaccinated exposed person should additionally receive a dose of HBIG as soon as possible after exposure (ideally within 24 hours).[294,311] Postexposure prophylaxis is unlikely to be effective more than 7 days after a percutaneous exposure or more than 14 days after a sexual exposure.[294]

Dosage and Administration

General

Dispensing and Administration Precautions

- Appropriate medical treatment and supervision must be available in the event an acute anaphylactic reaction occurs following vaccination.[104,132,133,262,292,293]
- Ensure procedures are in place to avoid a falling injury from syncope following vaccination.[104,133,262]

Administration

Hepatitis B vaccines are administered by IM injection.[104,132,133,262,292,293]

Hepatitis B vaccine is commercially available as three monovalent vaccines: hepatitis B vaccine (recombinant; Engerix-B® and Recombivax HB®) and hepatitis B vaccine (recombinant), adjuvanted (Heplisav-B®).[132,133,292]

Hepatitis B vaccine also is commercially available in a fixed-combination vaccine with hepatitis A virus vaccine (HepA-HepB; Twinrix®),[262] in a fixed-combination vaccine that contains diphtheria, tetanus, pertussis, hepatitis B, and poliovirus antigens (DTaP-HepB-IPV; Pediarix®),[104] and in a fixed-combination vaccine that contains diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and *Haemophilus influenza* type b (Hib) antigens (DTaP-IPV-Hib-HepB; Vaxelis®).[293]

The manufacturers of the nonadjuvanted recombinant vaccines (Engerix-B®, Recombivax HB®) state that the vaccines may be administered by subcutaneous injection, but only when necessary in individuals at risk of hemorrhage following IM injections (e.g., patients with thrombocytopenia or a bleeding disorder such as hemophilia).[132,133] Subcutaneous administration is known to result in a lower antibody response.[132,133] Additionally, when other aluminum-adsorbed vaccines have been administered subcutaneously, an increased incidence of local reactions (e.g., subcutaneous nodules) has been observed.[132,133] The vaccines should not be administered IV or intradermally.[132,133]

To ensure delivery of hepatitis B vaccine into the muscle, IM injections should be made at a 90° angle to the skin using a needle size that is appropriate for the individual's age and body mass, the thickness of adipose tissue and muscle at the injection site, and the injection technique.[306] Depending on the age of the patient, the IM injection should be made preferably into the deltoid or anterolateral thigh.[306]

Since syncope may occur following vaccination, vaccinees should be observed for approximately 15 minutes after the vaccine dose is administered.[306] If syncope occurs, the patient should be observed until symptoms resolve.[306] Syncope after vaccination occurs most frequently in adolescents and young adults.[306]

Hepatitis B vaccine may be given simultaneously with other age-appropriate vaccines during the same health-care visit (using different injection sites).[298]

Monovalent hepatitis B vaccine (Engerix-B®, Recombivax HB®) may be given simultaneously with hepatitis B immune globulin (HBIG) (using different syringes and different injection sites) when passive immunization is considered necessary in addition to active immunization with the vaccine (e.g., in neonates born to hepatitis B surface antigen-positive [HBsAg-positive] women, in persons who experienced percutaneous or permucosal exposure to the virus).[132,133,306]

Recombivax HB®

The preferred site for IM administration of Recombivax HB® is the anterolateral aspect of the thigh for infants <1 year of age, and the deltoid muscle in older children (whose deltoid is large enough for an IM injection), adolescents, and adults.[132] Do not administer in the gluteal region since suboptimal response may occur.[132]

Prior to administration, the vaccine should be inspected visually for particulate matter and discoloration.[132] The vaccine should be shaken well immediately prior to administration and should not be used if it contains particulates or appears discolored.[132] After shaking, the vaccine occurs as a slightly opaque white suspension.[132]

Recombivax HB® preparations do not contain any preservative.[132]

Store Recombivax HB® vials and syringes at 2–8°C.[132] Freezing of the vaccine results in a substantial decrease in potency and must be avoided.[132] Protect from light.[132] The vaccine is stable at temperatures from 0–25°C for 72 hours; these data are not recommendations for shipping or storage but may guide decisions for use if temporary temperature excursions occur.[132]

Engerix-B®

The preferred site for IM administration of Engerix-B® is the anterolateral aspect of the thigh for infants <1 year of age and the deltoid muscle in older children (whose deltoid is large enough for an IM injection) and adults.[133] Do not administer in the gluteal region since suboptimal response may occur.[133]

Prior to administration, the vaccine should be inspected visually for particulate matter and discoloration. [133] The vaccine should be shaken well immediately prior to

administration and should not be used if it contains particulates or appears discolored. [133]

Before shaking, the vaccine may occur as a fine white deposit with a clear colorless supernatant; after shaking, the vaccine occurs as a turbid white suspension.[133]

Store Engerix-B® in the refrigerator at 2–8°C.[133] Do not freeze; if freezing occurs, the vaccine should be discarded.[133] Do not dilute to administer.[133]

Engerix-B® Adult and Engerix-B® Pediatric/Adolescent preparations are formulated without preservatives.[133]

Heplisav-B®

Hepatitis B vaccine (recombinant), adjuvanted (Heplisav-B®) is administered by IM injection in the deltoid region.[292]

Prior to administration, the vaccine should be inspected visually for particulate matter and discoloration.[292] The vaccine should not be used if it contains particulates or appears discolored.[292]

Heplisav-B® does not contain any preservatives.[292]

Store in the refrigerator at 2–8°C.[292] Do not freeze; if freezing occurs, the vaccine should be discarded.[292]

Pediarix®

The preferred site for IM administration of the fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, and poliovirus antigens (DTaP-HepB-IPV; Pediarix®) is the anterolateral aspect of the thigh for infants <1 year of age, or the deltoid muscle in older children (whose deltoid is large enough for an IM injection).[104] Do not administer in the gluteal region since suboptimal response may occur.[104] Do not administer in areas where there may be a major nerve trunk.[104] The vaccine should not be given IV, intradermally, or subcutaneously.[104]

Prior to administration, the vaccine should be inspected visually for particulate matter and discoloration, and should not be used if it contains particulates or appears discolored.[104] The vaccine should be shaken well immediately prior to administration; do not use if resuspension does not occur with vigorous shaking.[104]

After vigorous shaking, Pediarix® appears as a homogeneous, turbid, white suspension.[104] Pediarix® does not contain any preservatives.[104]

Pediarix® should be refrigerated at 2–8°C and should not be frozen.[104] If freezing occurs, the vaccine should be discarded.[104]

Twinrix®

The fixed-combination vaccine containing hepatitis A and hepatitis B antigens (HepA-HepB; Twinrix®) is administered by IM injection into the deltoid region.[262] Do not administer in the gluteal region since suboptimal response may occur.[262] The vaccine should not be given IV, intradermally, or subcutaneously.[262]

Prior to administration, the vaccine should be inspected visually for particulate matter and discoloration, and should not be used if it contains particulates or appears discolored.[262] The vaccine should be resuspended prior to use; refer to the full prescribing information for specific steps for resuspending the vaccine.[262] Following thorough agitation, Twinrix® appears as a homogeneous, turbid, white suspension.[262]

Twinrix® does not contain any preservatives.[262]

Twinrix® should be refrigerated at 2–8°C and should not be frozen; if freezing occurs, the vaccine should be discarded.[262]

Vaxelis®

The fixed-combination vaccine that contains diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and Haemophilus influenza type b (Hib) antigens (DTaP-IPV-Hib-HepB; Vaxelis®) is administered by IM injection.[293] The vaccine is used only in infants and children 6 weeks of age through 4 years of age.[293]

The preferred site for administration in infants <1 year of age is the anterolateral aspect of the thigh.[293] Do not administer in the gluteal region since suboptimal response may occur.[293]

Prior to administration, the vaccine should be inspected visually for particulate matter and discoloration.[293] The vaccine should be shaken well immediately prior to administration and should not be used if it contains particulates or appears discolored.[293]

Do not combine the vaccine through reconstitution or mix with any other vaccine. Discard unused portion.[293]

Vaxelis® does not contain any preservatives.[293] Store at 2–8°C.[293] Do not freeze; if freezing occurs, the vaccine should be discarded.[293] Protect from light.[293]

Dosage

Dosage recommendations for hepatitis B vaccine vary depending on the specific preparation used, the recipient's age, the HBsAg status of the mother (for neonates), and the presence of underlying disease.[104,132,133,262,292,293]

Because the recommended doses for each vaccine are different, dosage recommendations for the specific preparation used should be followed.[104,132,133,262,292,293]

In general, the various brands of age-appropriate hepatitis B vaccines are interchangeable within an immunization series; however, adolescents who start their vaccination series with the adult formulation of Recombivax HB® cannot complete the series with the adult formulation of Engerix-B®, and patients who start their vaccination series with Heplisav-B® should complete it with the same product or receive a 3-dose series rather than the 2-dose series that is used with Heplisav-B®.[133,295,299]

The complete hepatitis B vaccine series must be administered to ensure optimal protection.[104,132,133,262,292,293] Refer to guidance for specific recommendations if there are interruptions or delays in dosing.[295,296,297,303,304]

Booster doses of hepatitis B vaccine are not recommended for immunocompetent individuals.[301] Consult expert guidelines for booster dose recommendations (when anti-HBsAg antibody levels decline to <10 mIU/mL) for patients receiving hemodialysis in outpatient centers, pediatric patients with HIV, and other immunocompromised patients with an ongoing risk for HBV exposure.[294,299,308]

Adults

Primary Immunization in Adults

The ACIP recommends that all unvaccinated adults 19–59 years of age receive primary immunization with hepatitis B vaccine.[296,304] *Unvaccinated adults ≥60 years of age with risk factors for hepatitis B should also receive primary immunization against hepatitis B.*[296,304] *Unvaccinated adults ≥60 years of age without risk factors for hepatitis B may also receive hepatitis B vaccines if vaccination is desired.*[296,304]

A 2-, 3-, or 4-dose series of hepatitis B vaccine may be appropriate for vaccination of adults, depending on patient comorbidities and the vaccine used (Engerix-B®, Recombivax HB®, Heplisav-B®, or Twinrix® [if vaccination against both hepatitis A and hepatitis B is desired]).[304] *Patients ≥20 years of age with immunocompromising conditions should complete a 2-dose series of Heplisav-B® or a 3- or 4-dose series with Recombivax HB® or Engerix-B® as described for dialysis patients.*[304] *Patients who began their hepatitis B vaccine series with PreHevbrio® (no longer available in the U.S.) should complete the 3-dose series using another licensed hepatitis B vaccine for the remaining doses.*[298]

When Recombivax HB® is used in adults 20 years of age or older, primary immunization consists of 3 doses of the adult formulation containing 10 mcg/mL.[132] *The initial dose of 10 mcg should be given on a selected date and the second and third 10-mcg doses should be given at 1 and 6 months, respectively, after the initial dose.*[132]

When Engerix-B® is used in adults 20 years of age or older, primary immunization consists of 3 doses of the adult formulation containing 20 mcg/mL.[133] *The initial dose of 20 mcg should be given on a selected date and the second and third 20-mcg doses should be given at 1 and 6 months, respectively, after the initial dose.*[133] *Alternatively, a 4-dose regimen can be used consisting of 20-mcg doses given on a selected date and at 1, 2, and 12 months after the initial dose.*[133]

When Heplisav-B® is used in adults 18 years of age and older, primary immunization consists of 2 doses (0.5 mL each) given on a selected date and 1 month after the initial dose.[292]

When Twinrix® is used in adults 18 years of age and older, primary immunization consists of 3 doses (1 mL each) of Twinrix® given at 0, 1, and 6 months.[262] *Alternatively, if an accelerated dosing schedule is needed, a series of 4 doses (1 mL each) may be given on days 0, 7, and 21–30 and a booster dose given at 12 months.*[262]

Consult expert guidelines for recommendations on revaccination (if anti-HBsAg antibody levels <10 mIU/mL) for certain populations, including hemodialysis patients, HIV-infected patients, and other immunocompromised patients.[294] *Consult expert guidelines for booster dose recommendations (when anti-HBsAg antibody levels decline to <10 mIU/mL) for patients receiving hemodialysis in outpatient centers, adults with HIV, and other immunocompromised patients with an ongoing risk for HBV exposure.*[294]

Postexposure Prophylaxis for Nonoccupational Exposure

For postexposure prophylaxis for nonoccupational exposure, the CDC and ACIP state that if the exposed person was previously vaccinated against HBV, a single dose of hepatitis B vaccine following exposure should be administered if the source is determined to be HBsAg-positive.[294,311] If the exposed person has not been fully vaccinated against HBV, a complete hepatitis B vaccination series should be administered following exposure, regardless of the HBsAg status of the exposure source.[294,311] Persons who are in the process of completing a hepatitis B vaccination series do not need to restart the series following exposure.[294,311] In unvaccinated persons, the first dose of hepatitis B vaccine should be administered as soon as possible after the exposure (ideally within 24 hours).[294,311] If the exposure source is determined to be HBsAg-positive, the unvaccinated or partially vaccinated exposed person should additionally receive a dose of HBIG as soon as possible after exposure (ideally within 24 hours).[294,311] Postexposure prophylaxis is unlikely to be effective more than 7 days after a percutaneous exposure or more than 14 days after a sexual exposure.[294] Complete the vaccine series according to the vaccination schedule.[294]

Postexposure Prophylaxis for Occupational Exposure

Management of occupational exposures to HBV in healthcare providers depends primarily on the healthcare provider's immunization status.[294] If the healthcare provider has written documentation of a completed hepatitis B vaccine series and subsequent documentation of serologic response (i.e., anti-HBsAg antibody level ≥10 mIU/mL), no postexposure prophylaxis is necessary.[294] In all other circumstances, exposure management will depend on the healthcare provider's vaccination status, the healthcare provider's anti-HBsAg antibody level (when tested), and the source patient's HBsAg status (see Table 1).[294] Healthcare providers who cannot provide documentation of 3 doses of hepatitis B vaccine should be considered unvaccinated and should complete the vaccine series.[294]

Pediatric Patients

Primary Immunization in Infants Born to HBsAg-negative Mothers

The American Academy of Pediatrics (AAP) and other experts recommend that all neonates and infants receive primary immunization against HBV with hepatitis B vaccine; the recommended vaccine schedule varies based on the mother's HBsAg status and the infant's birthweight.[299,308]

Monovalent Vaccines: Only Engerix-B® or Recombivax HB® should be used for the initial (birth) dose in neonates or infants younger than 6 weeks of age.[132,133]

Medically stable neonates weighing ≥2000 g born to HBsAg-negative mothers are recommended to receive a dose of single-antigen hepatitis B vaccine within 24 hours of birth.[299,300] The second dose of hepatitis B vaccine should be administered at 1–2 months of age, and the third dose should be given at 6–18 months of age.[299,300] The final dose in the series should not be administered before 24 weeks of age.[300]

For neonates weighing <2000 g born to HBsAg-negative mothers, the AAP recommends delaying the first dose of single-antigen hepatitis B vaccine until the time of hospital discharge or until the infant is 1 month of age (whichever is earlier).[299,300] The second dose of hepatitis B vaccine should be administered at 2 months of age, and the third dose should be given at 6–18 months of age.[300] The final dose in the series should not be administered before 24 weeks of age.[300]

When Recombivax HB® is used in neonates and infants, primary immunization consists of 3 doses of the pediatric/adolescent formulation containing 5 mcg/0.5 mL.[132] The manufacturer of Recombivax HB® recommends that 5-mcg doses be given at 0, 1, and 6 months of age.[132]

When Engerix-B® is used in neonates and infants, primary immunization consists of 3 doses of the pediatric/adolescent formulation containing 10 mcg/0.5 mL.[133] The manufacturer of Engerix-B® recommends that 10-mcg doses be given at 0, 1, and 6 months of age.[133]

Fixed-combination Vaccines: The fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, and poliovirus antigens (DTaP-HepB-IPV; Pediarix®) or the fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and Hib antigens (DTaP-IPV-Hib-HepB; Vaxelis®) may be used to complete the hepatitis B vaccination series after the first dose of hepatitis B vaccine is given at birth; however, Pediarix® and Vaxelis® should not be used for the birth hepatitis B vaccine dose and should not be given to infants <6 weeks of age.[294,305]

The manufacturer of DTaP-HepB-IPV (Pediarix®) states that the vaccine may be used to complete the hepatitis B vaccination series following 1 or 2 doses of another hepatitis B (monovalent or combination) vaccine in children born of HBsAg-negative mothers who are also scheduled to receive the other vaccine components of Pediarix®.[104] A 3-dose series of Pediarix® may be administered to infants born of HBsAg-negative mothers and who received a dose of hepatitis B vaccine at or shortly after birth; however, there is limited information regarding the safety of the vaccine in such infants.[104] There are no data to support the use of a 3-dose series of Pediarix® in infants who have previously received more than 1 dose of hepatitis B vaccine.[104] Each 0.5-mL dose of Pediarix® is administered at 2, 4, and 6 months of age (at intervals of 6–8 weeks, preferably 8 weeks).[104] The initial dose usually is given at 2 months of age, but may be given as early as 6 weeks of age.[104] The final dose should not be administered before 24 weeks of age.[294,299,305]

For specific dosage recommendations for Pediarix® in children previously vaccinated with DTaP or IPV, refer to the full prescribing information.[104] Consult the prescribing information for recommendations on booster immunization (DTaP and IPV) following Pediarix®.[104]

The manufacturer of DTaP-IPV-Hib-HepB (Vaxelis®) states that the vaccine may be used to complete the hepatitis B vaccination series following 1 or 2 doses of another hepatitis B vaccine in children born of HBsAg-negative mothers who are also scheduled to receive the other vaccine components of Vaxelis®.[293] A 3-dose series of the vaccine may be administered to infants born of HBsAg-negative mothers and who have received a dose of any hepatitis B vaccine, prior to or at 1 month of age.[293] A 3-dose series of Vaxelis® may be administered to infants born of HBsAg-negative mothers and who received a dose of hepatitis B vaccine at or shortly after birth; however, there is limited information regarding the safety of the vaccine in such infants and children.[293] Each 0.5-mL dose of Vaxelis® is administered at 2, 4, and 6 months of age.[293] The final dose should not be administered before 24 weeks of age.[294,299,305]

For specific dosage recommendations for pertussis vaccination following Vaxelis® administration, as well as administration of Vaxelis® following previous doses of other DTap-containing vaccines, inactivated polio vaccine, or Haemophilus b conjugate vaccines, refer to the full prescribing information.[293]

Prevention of Perinatal Infection and Primary Immunization in Infants Born to HBsAg-positive or HBsAg-unknown Mothers

Monovalent Vaccines: Only Engerix-B® or Recombivax HB® should be used for the initial (birth) dose in neonates or infants <6 weeks of age.[132,133]

To prevent perinatal HBV infection, the ACIP, AAP, and other experts recommend that all neonates born to HBsAg-positive mothers receive a dose of single-antigen hepatitis B vaccine and a dose of hepatitis B immune globulin (HBIG) as soon as possible after birth (within 12 hours of birth).[294,299,300,303,308,310,312] The hepatitis B vaccination series should then be completed according to the recommended schedule based on birthweight and the vaccine used.[294,299]

If a single-antigen hepatitis B vaccine is used to complete the series, patients weighing ≥2000 g at birth should receive a second vaccine dose at 1–2 months and a third dose at 6 months.[294,299,308,310] Patients weighing <2000 g at birth should receive a second vaccine dose at 1 month, a third at 2–3 months, and a fourth at 6 months.[294,299,308,310] The final dose in the series should not be administered before 24 weeks of age, regardless of birthweight.[294] Post-vaccination serologic testing is recommended at 9–12 months of age to assess HBsAg and anti-HBsAg antibody levels; revaccination is recommended for HBsAg-negative patients with anti-HBsAg antibody levels <10 mIU/mL (consult guidelines for more information).[294,299,300,308]

Infants born to mothers for whom HBsAg testing results are not available should be managed as if born to an HBsAg-positive mother if other evidence exists to suggest maternal HBV infection (e.g., positive HBeAg, presence of HBV DNA, known chronic HBV).[294,300,303] If maternal HBsAg status is unknown at birth, neonates weighing ≥2000 g should receive the first dose of single-antigen hepatitis B vaccine (within 12 hours of birth) and the mother's HBsAg status should be determined as quickly as possible; if positive, the infant should receive a dose of HBIG as soon as possible (no later than 7 days of age).[294,299,300,303,308] Neonates weighing <2000 g should receive both the single-antigen hepatitis B vaccine and a single dose of HBIG within 12 hours of birth.[294,299,300,303,308] The hepatitis B vaccine series should then be completed according to the recommended schedule based on the mother's HBsAg status, the infant's birthweight, and the vaccine used.[294] If it is not possible to determine the mother's HBsAg status, the vaccine series should be completed and post-vaccination

serologic testing should be performed according to the schedule recommended for infants born to HBsAg-positive mothers.[294,300]

When Recombivax HB® is used in neonates and infants, primary immunization consists of 3 doses of the pediatric/adolescent formulation containing 5 mcg/0.5 mL.[132] The manufacturer of Recombivax HB® recommends that 5-mcg doses be given at 0, 1, and 6 months of age.[132]

When Engerix-B® is used in neonates and infants, primary immunization consists of 3 doses of the pediatric/adolescent formulation containing 10 mcg/0.5 mL.[133] The manufacturer of Engerix-B® recommends that 10-mcg doses be given at 0, 1, and 6 months of age.[133] Alternatively, the manufacturer states that a 4-dose regimen consisting of 10-mcg doses given at 0, 1, 2, and 12 months can be used in infants born of HBsAg-positive mothers.[133]

Fixed-combination Vaccines: The fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, and poliovirus antigens (DTaP-HepB-IPV; Pediarix®) or the fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and Hib antigens (DTaP-IPV-Hib-HepB; Vaxelis®) may be used to complete the hepatitis B vaccination series after the first dose of hepatitis B vaccine is given at birth in ***infants born to HBsAg-positive mothers or mothers of unknown HBsAg status [off-label]†****; however, Pediarix® and Vaxelis® should not be used for the birth hepatitis B vaccine dose and should not be given to infants <6 weeks of age.[294,305]*

If Pediarix® and Vaxelis® is used to complete the series, doses of the combination vaccine should be given at 2, 4, and 6 months (not before 24 weeks of age).[294,299,305] Each dose of Pediarix® or Vaxelis® is 0.5 mL.[104,293]

Catch-up Vaccination in Children and Adolescents

The AAP recommends that all previously unvaccinated children ≥4 months of age through 18 years of age receive catch-up vaccination with hepatitis B vaccine.[300] A 3-dose series of hepatitis B vaccine should be administered, with doses given at 0, 1–2, and 6 months.[300,308] For children with HIV, a double dose of the vaccine may be considered.[308] In children ≥4 months of age through 18 years of age, the minimum interval between dose 1 and dose 2 of the hepatitis B vaccine series is 4 weeks; the minimum interval between dose 2 and dose 3 is 8 weeks, with dose 3 being given at least 16 weeks after dose 1.[300] In lieu of a 3-dose series, adolescents 11–15 years of age may be vaccinated with 2 doses of the adult formulation of Recombivax HB® given at least 4 months apart.[300,303] Adolescents 18 years of age may alternatively receive a 2-dose series of Heplisav-B® (with doses given at least 4 weeks apart) or a 3- or 4-dose series of Twinrix® (if vaccination against both hepatitis A and hepatitis B is desired).[295,300,303]

Consult expert guidelines for recommendations on revaccination (if anti-HBsAg antibody levels <10 mIU/mL) for certain populations, including hemodialysis patients, HIV-infected patients, and other immunocompromised patients.[294,299,300,303,308]

Consult expert guidelines for booster dose recommendations (when anti-HBsAg antibody levels decline to <10 mIU/mL) for patients receiving hemodialysis in outpatient centers, pediatric patients with HIV, and other immunocompromised patients with an ongoing risk for HBV exposure.[294,299,308]

Children 10 Years of Age or Younger: When Recombivax HB® is used in children 10 years of age or younger, primary immunization (including catch-up vaccination) consists of 3 doses of the pediatric/adolescent formulation containing 5 mcg/0.5 mL.[132] The manufacturer recommends that the initial 5-mcg dose be given on a selected date and the second and third 5-mcg doses given at 1 and 6 months, respectively, after the initial dose.[132]

When Engerix-B® is used in children 10 years of age or younger, primary immunization (including catch-up vaccination) usually consists of 3 doses of the pediatric/adolescent formulation containing 10 mcg/0.5 mL.[133] The initial dose of 10 mcg should be given on a selected date and the second and third 10-mcg doses should be given at 1 and 6 months, respectively, after the initial dose.[133] Alternatively, the manufacturer states that children 5–10 years of age (for whom an extended administration schedule is acceptable based on risk of exposure) can receive a 3-dose regimen consisting of 10-mcg doses given on a selected date and at 12 and 24 months after the initial dose, or children 10 years of age or younger can receive a 4-dose regimen consisting of 10-mcg doses given on a selected dated and at 1, 2, and 12 months after the initial dose.[133]

Adolescents 11–19 Years of Age: When Recombivax HB® is used in adolescents 11–19 years of age, primary immunization (including catch-up

> *vaccination) usually consists of 3 doses of the pediatric/adolescent formulation containing 5 mcg/0.5 mL.[132] Alternatively, the manufacturer states that 2 doses of the adult formulation containing 10 mcg/mL can be used for primary immunization in adolescents 11–15 years of age.[132] If the pediatric/adolescent formulation is used, the manufacturer recommends that the initial 5-mcg dose be given on a selected date and the second and third 5-mcg doses be given at 1 and 6 months, respectively, after the initial dose.[132] If the adult formulation is used in adolescents 11–15 years of age, a 10-mcg dose should be given on a selected date and a second 10-mcg dose given 4–6 months later.[132]*
>
> *When Engerix-B® is used in adolescents 11–19 years of age, primary immunization (including catch-up vaccination) usually consists of 3 doses of either the pediatric/adolescent formulation containing 10 mcg/0.5 mL or the adult formulation containing 20 mcg/mL.[133] If the pediatric/adolescent formulation is used, the initial dose of 10 mcg should be given on a selected date and the second and third 10-mcg doses should be given at 1 and 6 months, respectively, after the initial dose.[133] Alternatively, in those 11–16 years of age, the manufacturer states that 10-mcg doses can be given on a selected date and at 12 and 24 months after the initial dose.[133] If the adult formulation is used, the initial dose of 20 mcg should be given on a selected date and the second and third 20-mcg doses should be given at 1 and 6 months, respectively, after the initial dose.[133] Alternatively, the manufacturer states that adolescents 11–19 years of age can receive a 4-dose regimen consisting of 20-mcg doses given on a selected date and at 1, 2, and 12 months after the initial dose.[133]*
>
> *When Heplisav-B® is used in adolescents 18 years of age, primary immunization consists of 2 doses (0.5 mL each) given on a selected date and 1 month after the initial dose.[292]*
>
> *When Twinrix® is used in adolescents 18 years of age, primary immunization consists of 3 doses (1 mL each) of Twinrix® given at 0, 1, and 6 months.[262] Alternatively, if an accelerated dosing schedule is needed, a series of 4 doses (1 mL each) may be given on days 0, 7, and 21–30 and a booster dose given at 12 months.[262]*

■ Special Populations

Hepatic Impairment

The manufacturers make no specific dosage recommendations for patients with hepatic impairment.[104,132,133,262,292,293]

Renal Impairment

Adults on dialysis should complete a 3-dose vaccination series (using the dialysis formulation of Recombivax HB®) or a 4-dose vaccination series (using a 2-mL dose of Engerix-B®).[304]

When Recombivax HB® is used in adult predialysis/dialysis patients, primary immunization consists of 3 doses of the dialysis formulation containing 40 mcg/mL.[132] The initial 40-mcg should be given on a selected date and the second and third 40-mcg doses should be given at 1 and 6 months, respectively, after the initial dose.[132] A booster dose or revaccination with the Recombivax HB® Dialysis Formulation should be considered in predialysis/dialysis patients if the anti-HBs level is <10 mIU/mL at 1–2 months after the third dose.[132] Assess the need for a booster dose annually by antibody testing, and administer a booster dose when the anti-HBs level declines to less than 10 mIU/mL.[132] Consult the ACIP for specific recommendations on booster dose administration.[294]

When Engerix-B® is used in adult hemodialysis patients, primary immunization consists of four 40-mcg doses using the adult formulation containing 20 mcg/mL.[133] Each 40-mcg dose may be given using 1 or 2 injections.[133] An initial 40-mcg dose should be given on a selected date followed by additional 40-mcg doses at 1, 2, and 6 months after the initial dose.[133] In hemodialysis patients, antibody response is lower in patients undergoing hemodialysis than in healthy persons and protection may persist only as long as antibody levels remain above 10 mIU/mL.[133] Assess the need for booster doses by annual antibody testing, and administer a 2-mL booster dose (as a single 2-mL dose or two 1-mL doses) when antibody levels decline <10 mIU/mL.[133] Consult the ACIP for specific recommendations on booster dose administration.[294]

Geriatric Patients

The manufacturers of Engerix-B®, Recombivax HB®, Twinrix®, and Heplisav-B® make no specific dosage recommendations for geriatric patients.[132,133,262,292] The hepatitis B vaccine may be less immunogenic in geriatric individuals than in younger adults.[132,133]

Vaxelis® and Pediarix® are not indicated for use in adults, including geriatric adults.[104,293]

Patients with HIV

Experts recommend hepatitis B vaccination for all people with HIV who do not have chronic HBV and are not immune to HBV infection (i.e., they are negative for anti-hepatitis B core antigen (HBcAg) antibodies and anti-HBsAg antibodies); patients who have failed a prior hepatitis B vaccination series should also be revaccinated.[307] A 2-dose series of Heplisav-B® is the preferred hepatitis B vaccination regimen for unvaccinated adults with HIV; if Heplisav-B® is not available, a 3-dose series of double-dose Engerix-B® or

Recombivax HB® or a 3-dose series of Twinrix® may be used.[307] Although the response to Engerix-B® and Recombivax HB® is greater among patients with CD4 counts >350 cells/mm^3, vaccination should not be delayed in patients with CD4 count ≤350 cells/mm^3 who are at high risk of HBV infection.[307] Response to hepatitis B vaccination (i.e., anti-HBsAg antibody levels ≥10 mIU/mL) should be documented 4 weeks after the last dose of vaccine.[307] If adequate response is not achieved, revaccination is recommended (consult expert guidelines for more information).[307]

Because immunity may wane, providers should consider monitoring anti-HBsAg antibody levels annually and giving booster doses of hepatitis B vaccine if levels fall below 10 mIU/mL, particularly in patients with ongoing risk factors for HBV.[307] Patients with HIV who present with isolated anti-HBcAg antibodies should be vaccinated with a standard dose of hepatitis B vaccine (Engerix-B®, Recombivax HB®, or Heplisav-B®); anti-HBsAg antibody titers should be checked 1–2 months afterward.[307] If the anti-HBsAg antibody titer is ≥100 mIU/mL, no additional doses of vaccine are needed, but if anti-HBsAg antibody titers are <100 mIU/mL, the rest of the hepatitis B vaccination series should be completed.[307]

Cautions

■ Contraindications

- Hypersensitivity to any ingredient in the vaccine, including yeast (Engerix-B®, Recombivax HB®, Heplisav-B®).[132,133,292]
- History of previous hypersensitivity to any hepatitis B vaccine (Engerix-B®, Recombivax HB®, Heplisav-B®).[132,133,292]
- History of hypersensitivity to any ingredient in the vaccine (e.g., yeast, neomycin, polymyxin B) (Pediarix®).[104]
- History of hypersensitivity to a previous dose of the vaccine or any vaccine component (Vaxelis®).[293]
- History of serious allergic reaction (e.g., anaphylaxis) after a previous dose of any diphtheria toxoid-, tetanus toxoid-, pertussis antigen-, hepatitis B-, or poliovirus-containing vaccine (Pediarix®).[132]
- History of serious allergic reaction (e.g., anaphylaxis) after a previous dose of any diphtheria toxoid, tetanus toxoid, pertussis antigen, hepatitis B, inactivated poliovirus, or *H. influenzae* type b-containing vaccine (Vaxelis®).[293]
- Encephalopathy (e.g., coma, decreased consciousness, prolonged seizures) within 7 days of a previous dose of vaccine containing pertussis antigens that could not be attributed to another identifiable cause (Pediarix®, Vaxelis®).[104,293]
- Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, or progressive encephalopathy; vaccine should not be administered to patients with these conditions until the neurological status has stabilized (Pediarix®, Vaxelis®).[104,293]
- Hypersensitivity to any ingredient in the vaccine, including yeast and neomycin (Twinrix®).[262]
- Previous hypersensitivity reactions to any hepatitis A- or hepatitis B- containing vaccines (Twinrix®).[262]

■ Warnings/Precautions

Use of Combination Vaccines

When the fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, and poliovirus antigens (DTaP-HepB-IPV; Pediarix®), the fixed-combination vaccine containing hepatitis A and hepatitis B antigens (HepA-HepB; Twinrix®), or the fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and *Haemophilus influenza* type b (Hib) antigens (DTaP-IPV-Hib-HepB; Vaxelis®) is used, the adverse effects, precautions, and contraindications associated with each antigen should be considered.[104,262,293]

Allergic Vaccine Reactions

Appropriate medical treatment (e.g., epinephrine) and supervision must be available in the event an acute anaphylactic reaction occurs following vaccination.[104,132,133,262,292,293] Prior to vaccination, the healthcare provider should review the patient's immunization history for possible vaccine sensitivity and previous vaccination-related adverse reactions in order to assess benefits and risks.[104,133,262]

Hypersensitivity to Latex

Some packaging components (vial stopper and the syringe plunger stopper and tip cap) of Recombivax HB® contain dry natural latex rubber, which may cause hypersensitivity reactions in latex-sensitive individuals.[132]

Syncope

Syncope (which may be accompanied by transient neurological signs such as visual disturbance, paresthesia, and tonic-clonic limb movements) can occur in association with administration of injectable vaccines.[104,133,262] Ensure procedures are in place to avoid a falling injury and to restore cerebral perfusion following syncope.[104,133,262]

Apnea in Premature Infants

Apnea following IM vaccination has been observed in some infants born prematurely.[104,132,133,293] Decisions about when to administer an IM vaccine to infants born prematurely should be determined based on an individualized assessment of the infant's clinical condition, weighing the potential benefits of immunization against possible risks.[104,132,133,293]

For Engerix-B® or Recombivax HB®, the manufacturer states that evaluation should include consideration of the mother's hepatitis B antigen status and the high risk of maternal transmission of hepatitis B virus to infants born to mothers who are hepatitis B surface antigen (HBsAg) positive if vaccination is delayed.[132,133]

Infants Weighing Less than 2000 g

Hepatitis B vaccination should be deferred until 1 month of age or until hospital discharge for infants with a birth weight of less than 2000 g whose mothers are confirmed to be HBsAg negative at the time of delivery.[132,133] Infants weighing less than 2000 g who are born to mothers who are HBsAg positive or whose HBsAg status is unknown should receive both hepatitis B vaccine and hepatitis B immune globulin (HBIG) in accordance with the US Public Health Service Advisory Committee on Immunization Practices (ACIP) recommendations.[132,133]

Limitations of Vaccine Effectiveness

Hepatitis B vaccine (Engerix-B®, Recombivax HB®, Heplisav-B®) may not prevent hepatitis B infection in individuals with an unrecognized hepatitis B infection at the time of vaccination.[132,133,292] Additionally, vaccination with hepatitis B vaccine may not protect all individuals.[132,293] The vaccine may not prevent infection in individuals who do not achieve protective antibody titers.[133]

Twinrix® may not prevent hepatitis A or hepatitis B infection in individuals with an unrecognized hepatitis A or hepatitis B infection at the time of vaccination.[262] Additionally, the vaccine may not protect all individuals.[262]

Individuals with Altered Immunocompetence

The possibility that the immune response to the vaccine may be reduced in immunocompromised individuals, including those on immunosuppressant therapy, should be considered.[133,262,292,293]

Consult the ACIP for specific information on hepatitis B vaccination in individuals with altered immunocompetence.[294,306]

Moderate or Severe Acute Illness

To avoid diagnostic confusion between possible vaccine adverse effects and manifestations of an acute illness, the manufacturers of Engerix-B® and Twinrix® state that vaccination should be postponed in individuals with moderate or severe acute febrile illness unless they are at immediate risk of hepatitis B infection (or hepatitis A infection with Twinrix®).[133,262]

Multiple Sclerosis

The manufacturers of Engerix-B® and Twinrix® state that findings from 2 clinical studies indicate no association between hepatitis B vaccination and the development of multiple sclerosis; vaccination with hepatitis B vaccine does not appear to increase the short-term risk of relapse in individuals with multiple sclerosis.[133,262]

Fever

In clinical trials, administration of Pediarix® in infants was associated with higher rates of fever compared to separately administered vaccines.[104]

Guillain-Barré Syndrome

If Guillain-Barré syndrome occurs within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the decision to administer Pediarix®, Vaxelis® or any tetanus toxoid-containing vaccine should be based on careful consideration of the potential benefits and risks; the risk for Guillain-Barré syndrome may be increased following vaccination.[104,293]

Children at Risk for Seizures

For children with a higher risk of seizures than the general population, administration of an appropriate antipyretic at the time of vaccination with a pertussis-containing vaccine, including Pediarix®, and continued for the following 24 hours may be considered to reduce the likelihood of post-vaccination fever.[104]

Adverse Reactions following Prior Pertussis Vaccination

If any of the following adverse events occur in temporal association with administration of a pertussis-containing vaccine, the decision to administer additional doses of any pertussis-containing vaccine, including Pediarix® or Vaxelis®, should be made after careful evaluation of the potential benefits and possible risks: a temperature ≥40.5°C within 48 hours not attributable to another identifiable cause; collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours; persistent, inconsolable crying lasting ≥3 hours within 48 hours; or seizures, with or without fever, occurring within 3 days of vaccination.[104,293]

Interference with Laboratory Tests

Hepatitis B surface antigen (HBsAg) derived from hepatitis B vaccines has been transiently detected in blood samples following vaccination.[132,133,262,292] Therefore, detection of serum HBsAg may lack diagnostic significance within 28 days after administration of a hepatitis B vaccine, including Recombivax HB®, Engerix-B®, Twinrix®, or Heplisav-B®.[132,133,262,292]

Urine antigen detection may not have definitive diagnostic value in suspected *H. influenzae* type b disease following administration of Vaxelis®.[293]

Specific Populations

Pregnancy

Engerix-B® or Recombivax HB®: Animal reproduction studies have not been performed with the vaccine.[132,133] There are no adequate and well-controlled studies of the vaccine in pregnant women in the U.S.[132,133] Available data do not suggest an increased risk of major birth defects or miscarriage in women who received the vaccine during pregnancy.[132,133]

Twinrix®: An animal development study in female rats found no adverse effects on fetal or pre-weaning development when the vaccine was administered prior to mating and during gestation.[262] There are no adequate and well-controlled studies of the vaccine in pregnant women in the U.S.[262] Available data do not suggest an increased risk of major birth defects or miscarriage in women who received the vaccine within 28 days prior to conception or during pregnancy.[262]

Heplisav-B®: An animal development toxicity study in female rats found no evidence of fetal harm due to a vaccine formulation containing 2.5 mcg HBsAg and 3000 mcg cytidine phospho-guanosine (CpG) 1018 adjuvant administered prior to mating and during gestation; a full human dose of Heplisav-B® contains 20 mcg HBsAg and 3000 mcg CpG 1018 adjuvant.[292] There are no adequate and well-controlled studies of the vaccine in pregnant women.[292] Available data, primarily in individuals who received one dose of the vaccine in the 28 days prior to or during pregnancy, do not suggest an increased risk of major birth defects and miscarriage.[292]

Vaxelis® and Pediarix® are not indicated for use in women of childbearing age.[104,293]

ACIP states that pregnant women who require hepatitis B vaccination may receive any of the available single-antigen hepatitis B vaccines or Twinrix® (if vaccination against both hepatitis A and hepatitis B is desired).[297]

Lactation

Engerix-B®, Recombivax HB®, Twinrix®, and Heplisav-B®: It is not known whether the vaccine is distributed into human milk, or affects the breast-fed child or milk production.[132,133,262,292] The manufacturers state that the benefits of breast-feeding and the importance of the vaccine to the mother should be considered along with the potential adverse effects on the breast-fed child from the vaccine or from the underlying maternal condition (i.e., susceptibility to meningococcal infection).[132,133,262,292]

Although specific data are not available, ACIP states that breast-feeding is not a contraindication to administration of hepatitis B vaccine and lactating women should receive the vaccine as recommended for other adults.[316]

Pediatric Use

Recombivax HB® is approved for use in pediatric patients of any age.[132] In neonates, passively acquired maternal anti-HBs antibodies do not appear to interfere with the active immune response to hepatitis B vaccine.[132] Safety and efficacy of Recombivax® HB Dialysis Formulation have not been established in children.[132]

Engerix-B® is approved for use in pediatric patients of any age.[133] In neonates, passively acquired maternal anti-HBs antibodies do not appear to interfere with the active immune response to hepatitis B vaccine.[133] The timing of the first dose in infants weighing <2000 g at birth depends on the HBsAg status of the mother.[133]

> *Safety and efficacy of Heplisav-B® have not been established in pediatric patients younger than 18 years of age.[292]*
>
> *Safety and efficacy of Pediarix® have not been established in infants younger than 6 weeks of age or in children 7 years of age or older.[104]*
>
> *Safety and efficacy of Twinrix® have not been established in pediatric patients younger than 18 years of age.[262]*
>
> *Safety and efficacy of Vaxelis® have not been established in infants younger than 6 weeks of age or in children 5 years of age or older.[293]*

> ### Geriatric Use
>
> *Clinical studies of Engerix-B® and Recombivax HB® did not include sufficient numbers of individuals 65 years of age or older to determine whether these individuals respond differently than younger individuals.[132,133] However, later studies have found that a diminished antibody response may occur in geriatric individuals >60 years of age.[132,133]*
>
> *In clinical studies of Heplisav-B®, 90% of adults 65–70 years of age achieved seroprotective antibody levels to HBsAg, compared with 96% of adults 18–64 years of age.[292] The safety and efficacy of Heplisav-B® in adults over 70 years of age were extrapolated from data obtained in participants younger than 70 years of age.[292]*
>
> *Clinical studies of Twinrix® did not include sufficient numbers of individuals 65 years of age or older to determine whether geriatric individuals respond differently than younger adults.[262]*
>
> *Vaxelis® and Pediarix® are not indicated for use in adults, including geriatric adults.[104,293]*

■ Common Adverse Effects

In healthy infants and children (≤10 years of age), the most frequently reported systemic adverse reactions (>1% of the injections) with Recombivax HB® were irritability, fever, diarrhea, fatigue/weakness, diminished appetite, and rhinitis.[132] In healthy adults, injection site reactions were reported following 17% of the injections and systemic adverse reactions were reported following 15% of the injections.[132]

The most common solicited adverse reactions with Engerix-B® were injection-site soreness (22%) and fatigue (14%).[133]

The most common solicited adverse reactions following any dose (≥25%) of Pediarix® included local injection site reactions (pain, redness, and swelling), fever (≥38.0°C), drowsiness, irritability/fussiness, and loss of appetite.[104]

The most common (≥10%) solicited injection site reactions following any dose of Twinrix® included soreness (35–41%) and erythema (8–11%), and the most common solicited systemic adverse reactions were headache (13–22%) and fatigue (11–14%).[262]

The most common local reaction with Heplisav-B® was injection site pain (9–39%), and the most common systemic reactions were fatigue (10–17%) and headache (5–17%).[292]

The most common solicited adverse reactions following any dose of Vaxelis® were irritability (≥55%), crying (≥45%), injection site pain (≥44%), somnolence (≥40%), injection site erythema (≥25%), decreased appetite (≥23%), fever ≥38.0°C (≥19%), injection site swelling (≥18%), and vomiting (≥9%).[293]

Drug Interactions

■ Immune Globulins

There is no evidence that immune globulin (immune globulin IM [IGIM], immune globulin IV [IGIV]) or specific immune globulin (e.g., hepatitis B immune globulin [HBIG]) interferes with the immune response to inactivated vaccines.[306] The US Public Health Service Advisory Committee on Immunization Practices (ACIP) states that inactivated vaccines such as hepatitis B vaccine may be given simultaneously with (using different syringes and injection sites) or at any interval before or after immune globulin preparations.[306]

The manufacturer states that Engerix-B® may be administered concomitantly with immune globulin.[133] When concomitant use of Engerix-B® and immune globulin is required, administer the products with different syringes at different injection sites.[133]

Antibody to hepatitis B surface antigen (anti-HBs) acquired passively from HBIG does not appear to interfere with the active immune response to hepatitis B vaccine.[132,133] Hepatitis B vaccine (Engerix-B® or Recombivax HB®) may be administered concomitantly with HBIG.[132,133] When combined active immunization with hepatitis B vaccine and passive immunization with HBIG is indicated, the first dose of vaccine may be administered simultaneously with HBIG (using different syringes and different injection sites).[132]

When concomitant use of Twinrix® and immune globulin is required, administer the products with different syringes at different injection sites.[262]

The manufacturer states there are no data to assess the concomitant use of Heplisav-B® with immune globulin.[292] When concomitant use of the vaccine and immune globulin is required, administer the products with different syringes at different injection sites.[292]

Immunosuppressive Agents

Individuals receiving immunosuppressive therapy (e.g., irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids [used in greater than physiologic dosages]), may have a reduced response to hepatitis B vaccine.[104,262]

Consult the ACIP for specific guidance on hepatitis B vaccination in individuals receiving immunosuppressive therapy.[306]

Vaccines

The hepatitis B vaccine can be administered concomitantly with other age-appropriate vaccines; there is no evidence that concomitant administration reduces vaccine response or effectiveness.[298] Each parenteral vaccine should be administered at a different injection site.[298]

When concomitant use of Recombivax HB® or Engerix-B® and other vaccines is required, the manufacturer states that the products should be administered with different syringes at different injection sites.[132,133] Do not mix Recombivax HB® or Engerix-B® with any other vaccine in the same syringe or vial.[132,133]

When concomitant use of Pediarix® and other vaccines is required, administer the products with different syringes at different injection sites.[104] Do not mix Pediarix® with any other vaccine in the same syringe.[104]

The manufacturer states there are no data to assess the concomitant use of Twinrix® with other vaccines.[262] Do not mix Twinrix® with any other vaccine in the same syringe.[262]

Diphtheria and Tetanus Toxoids and Pertussis Vaccines

In clinical trials in children, Recombivax HB® has been administered concomitantly with diphtheria, tetanus, and whole-cell pertussis vaccine (DTwP), along with other vaccines in some cases.[132] Safety and immunogenicity were comparable to those observed when the vaccines were administered separately.[132]

In clinical trials in children, Recombivax HB® has been administered concomitantly with a booster dose of diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed (DTaP), along with other vaccines in some cases.[132] Safety and immunogenicity were comparable to those observed when the vaccines were administered separately.[132]

The fixed-combination vaccine that contains Hib conjugate and hepatitis B recombinant (no longer licensed) has been administered concomitantly with the primary series of DTaP to a limited number of infants.[132] No serious vaccine-related adverse events were reported.[132]

Haemophilus b Vaccines

In clinical trials in children, Recombivax HB® has been administered concomitantly with the *Haemophilus influenzae* type b (Hib) conjugate vaccine, along with other vaccines in some cases.[132] Safety and immunogenicity were comparable to those observed when the vaccines were administered separately.[132]

The fixed-combination vaccine that contains Hib conjugate and hepatitis B recombinant has been administered concomitantly with the primary series of DTaP to a limited number of infants.[132] No serious vaccine-related adverse events were reported.[132]

Pediarix® was administered concomitantly with Hib conjugate vaccine and 7-valent pneumococcal conjugate vaccine in infants at 2, 4, and 6 months of age; there was no evidence of interference with the immune responses to the vaccines.[104]

Measles, Mumps, and Rubella Vaccines

In clinical trials in children, Recombivax HB® has been administered concomitantly with the live measles, mumps, and rubella (MMR) virus vaccine, along with other vaccines in some cases.[132] Safety and immunogenicity were comparable to those observed when the vaccines were administered separately.[132]

Pneumococcal Vaccines

Pediarix® was administered concomitantly with Hib conjugate vaccine and 7-valent pneumococcal conjugate vaccine in infants at 2, 4, and 6 months of age; there was no evidence of interference with the immune responses to the vaccines.[104]

Poliovirus Vaccines

In clinical trials in children, Recombivax HB® has been administered concomitantly with the oral poliomyelitis vaccine, along with other vaccines in some cases.[132] Safety and immunogenicity were comparable to those observed when the vaccines were administered separately.[132]

The fixed-combination vaccine that contains Hib conjugate and hepatitis B recombinant was administered concomitantly with enhanced inactivated poliovirus vaccine (eIPV) at separate injection sites using separate syringes.[132] No serious vaccine-related adverse events were reported, and no evidence of impaired immune response to the poliovirus antigens was observed.[132]

Varicella Vaccines

The fixed-combination vaccine that contains Hib conjugate and hepatitis B recombinant was administered concomitantly with Varivax® (varicella live virus vaccine) at separate injection sites using separate syringes.[132] No serious vaccine-related adverse events were reported, and no evidence of impaired immune response to the varicella virus antigens was observed.[132]

Description

Hepatitis B vaccine (recombinant) stimulates active immunity to HBV infection.[282] Hepatitis B virus (HBV) is a DNA virus with a long incubation period.[132,301] Hepatitis B virus (HBV) is a DNA virus with a long incubation period.[132,301] Hepatitis B surface antigen (HBsAg), which is present in hepatitis B vaccine, promotes the production of antibody to HBsAg (anti-HBs); anti-HBs neutralizes HBV so that its infective or pathogenic properties are inhibited.[282] Antibody concentrations ≥10 mIU/mL against HBsAg are recognized as conferring protection against HBV infection.[104,132,133,262,292,293]

Hepatitis B vaccine is commercially available in the U.S. as three monovalent vaccines: hepatitis B vaccine (recombinant; Engerix-B® and Recombivax HB®) and hepatitis B vaccine (recombinant), adjuvanted (Heplisav-B®).[132,133,292] Hepatitis B vaccine also is commercially available in a fixed-combination vaccine with hepatitis A virus vaccine (HepA-HepB; Twinrix®),[262] in a fixed-combination vaccine that contains diphtheria, tetanus, pertussis, hepatitis B, and poliovirus antigens (DTaP-HepB-IPV; Pediarix®),[104] and in a fixed-combination vaccine that contains diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and *Haemophilus influenza* type b (Hib) antigens (DTaP-IPV-Hib-HepB; Vaxelis®).[293]

Both Recombivax HB® and Engerix-B® contain HBsAg prepared using yeast cells (*Saccharomyces cerevisiae*) and recombinant DNA technology.[132,133] These vaccines are available in several formulations containing different concentrations of HBsAg.[132,133] Recombivax HB® is supplied in 3 formulations.[132] Each 1-mL dose of Recombivax HB® Adult Formulation contains 10 mcg of HBsAg; each 0.5-mL dose of Recombivax HB® Pediatric/Adolescent Formulation contains 5 mcg of HBsAg; and each 1-mL dose of Recombivax HB® Dialysis Formulation contains 40 mcg of HBsAg.[132] In each formulation, the antigen is adsorbed onto approximately 0.5 mg of aluminum (as amorphous aluminum hydroxyphosphate sulfate) per mL of vaccine.[132] Engerix-B® is supplied as syringes or vials for adults, and syringes for children and adolescents.[133] Each 1-mL dose of Engerix-B® Adult contains 20 mcg of HBsAg adsorbed onto 0.5 mg of aluminum (as aluminum hydroxide) and each 0.5-mL dose of Engerix-B® Pediatric/Adolescent contains 10 mcg of HBsAg adsorbed onto 0.25 mg of aluminum (as aluminum hydroxide).[133]

Heplisav-B® contains HBsAg expressed in a recombinant strain of Hansenula polymorpha yeast.[292] Heplisav-B® is prepared by combining the purified HBsAg together with the CpG 1018 adjuvant.[292] Heplisav-B® is supplied as prefilled syringes; each 0.5-mL dose is formulated to contain 20 mcg of HBsAg and 3000 mcg of CpG 1018 adjuvant.[292] Each dose may contain residual amounts of yeast protein (≤5% of total protein), yeast DNA (<20 picogram), and deoxycholate (<0.9 ppm) from the HBsAg manufacturing process.[292]

DTaP-HepB-IPV (Pediarix®) is a fixed-combination vaccine containing diphtheria, tetanus, pertussis, hepatitis B, and poliovirus antigens.[104] The hepatitis B antigen contained in Pediarix® is identical to that contained in Engerix-B® monovalent hepatitis B vaccine.[104] The diphtheria, tetanus, and pertussis antigens are identical to those contained in Infanrix® (DTaP) vaccine.[104] The poliovirus antigens contained in Pediarix® are similar to those contained in the commercially available monovalent inactivated poliovirus vaccine (IPV) vaccine.[104] Each 0.5-mL dose of Pediarix® is formulated to contain 25 Lf of diphtheria toxoid, 10 Lf of tetanus toxoid, 58 mcg of pertussis antigens, 10 mcg of HBsAg, 40 D-antigen units (DU) of Type 1 poliovirus, 8 DU of Type 2 poliovirus, and 32 DU of Type 3 poliovirus.[104] Each 0.5 mL of Pediarix® contains 4.5 mg of sodium chloride, not more than 0.85 mg of aluminum adjuvant, not more than 100 mcg of polysorbate 80, and not more than 100 mcg of residual formaldehyde.[104] Although neomycin sulfate and polymyxin B are used in the manufacturing process of the poliovirus antigen component, Pediarix® contains no more than 0.05 and 0.01 ng, respectively, of these anti-infectives per dose.[104] No more than 5% yeast protein may be present in Pediarix® as part of the hepatitis B antigen component.[104]

HepA-HepB (Twinrix®) is a fixed-combination vaccine that contains both hepatitis A and hepatitis B antigens.[262] Twinrix® is a sterile suspension containing the antigenic components used to produce Havrix® monovalent hepatitis A virus vaccine inactivated and Engerix-B® monovalent hepatitis B vaccine.[262] Each antigenic component is adsorbed separately onto aluminum phosphate or aluminum hydroxide and then pooled to form the fixed-combination vaccine.[262] Each 1-mL dose of Twinrix® contains 720 units of hepatitis A viral antigen and 20 mcg of HBsAg and also contains 0.45 mg of aluminum (as aluminum hydroxide and aluminum phosphate).[262] Each 1-mL dose of the vaccine also contains residual MRC-5 cellular (not exceeding 2.5 mcg), yeast proteins (not exceeding 5%), trace amounts of formaldehyde (not exceeding 0.1 mg), trace amounts of neomycin sulfate (not exceeding 0.02 mcg), and amino acids in a phosphate-buffered saline solution with polysorbate (Tween®) 20.[262]

DTaP-IPV-Hib-HepB (Vaxelis®) is a fixed-combination vaccine that contains diphtheria, tetanus, pertussis, hepatitis B, poliovirus, and Hib antigens.[293] Vaxelis® contains HBsAg prepared using yeast cells (*Saccharomyces cerevisiae* containing the gene for the adw subtype of HBsAg) and recombinant DNA technology.[262] Each 0.5 mL dose of Vaxelis® contains 15 Lf diphtheria toxoid, 5 Lf tetanus toxoid, acellular pertussis antigens (20 mcg detoxified pertussis toxin, 20 mcg filamentous hemagglutinin, 3 mcg pertactin, 5 mcg fimbriae types 2 and 3), inactivated polioviruses (29 DU Type 1, 7 DU Type 2, 26 DU Type 3), 3 mcg polyribosylribitol phosphate of *H. influenzae* type b covalently bound to 50 mcg of the outer membrane protein complex of *Neisseria meningitidis* serogroup B, and 10 mcg HBsAg.[262] Each 0.5 mL dose contains 319 mcg aluminum from aluminum salts used as adjuvants.[262]

The hepatitis B vaccine is highly immunogenic in immunocompetent neonates, children, adolescents, and adults.[132,133,282,301] More than 90% of infants, children,

adolescents, and healthy adults under 40 years of age develop protective antibody levels following completion of the hepatitis B vaccine series.[301] However, immunogenicity decreases with advancing age, with only 75% of individuals 60 years of age achieving seroprotection after completion of the vaccine series.[301] Among adults receiving Heplisav-B®, 90–100% develop adequate antibody titers after the 2-dose regimen.[301]

The hepatitis B vaccine is 80–100% effective in preventing infection or clinical hepatitis when the full series is administered.[301] Higher vaccine doses or additional doses are often required to achieve seroprotection in dialysis patients and other immunocompromised populations.[301] Although antibody concentrations wane over time, immune memory persists for more than 30 years, providing continued protection against clinically significant HBV infection; therefore, booster doses are not recommended for immunocompetent individuals.[301]

Advice to Patients

The following information contains important points for the clinician to discuss with patients during counseling. For more comprehensive monographs suitable for distribution to the patient, please refer to the *AHFS Patient Medication Information* monographs available from MedlinePlus (in English and Spanish; written at a 6th- to 8th-grade reading level).

- Prior to administration of each vaccine dose, provide a copy of the appropriate CDC Vaccine Information Statement (VIS) to the patient or patient's legal representative as required by the National Childhood Vaccine Injury Act (VISs are available at [Web]).[104,132,133,262,292,293]
- Advise the patient and/or patient's parent or guardian of the risks and benefits of vaccination with hepatitis B vaccine.[104,132,133,262,292,293]
- Advise the patient and/or patient's parent or guardian of the importance of receiving the complete primary immunization series to ensure the highest level of protection against HBV.[104,132,133,262,292,293]
- Advise the patient and/or patient's parent or guardian of the importance of informing clinicians if any severe or unusual adverse reactions occur.[104,132,133,262,292,293] Clinicians or individuals can report any adverse reactions that occur following vaccination to the Vaccine Adverse Event Reporting System (VAERS) at 800-822-7967 or [Web] .[104,132,133,262,292,293]
- Advise the patient and/or patient's parent or guardian of the importance of informing clinicians of existing or contemplated concomitant therapy, including prescription and OTC drugs, as well as any concomitant illnesses.[104,132,133,262,292,293]
- Advise patients to inform their clinicians if they are or plan to become pregnant or plan to breast-feed.[104,132,133,262,292,293]
- Advise patients of other important precautionary information.[104,132,133,262,292,293]

Additional Information

The American Society of Health-System Pharmacists, Inc. represents that the information provided in the accompanying monograph was formulated with a reasonable standard of care, and in conformity with professional standards in the field. Readers are advised that decisions regarding use of drugs are complex medical decisions requiring the independent, informed decision of an appropriate health care professional, and that the information contained in the monograph is provided for informational purposes only. The manufacturer's labeling should be consulted for more detailed information. The American Society of Health-System Pharmacists, Inc. does not endorse or recommend the use of any drug. The information contained in the monograph is not a substitute for medical care.

Preparations

Excipients in commercially available drug preparations may have clinically important effects in some individuals; consult specific product labeling for details.

Hepatitis B Vaccine (Recombinant)

ROUTES	*FORMS*	*STRENGTHS*	*BRAND NAMES*	*MANUFACTURER*
Parenteral	*Injectable suspension, for IM use*	*5 mcg (of hepatitis B surface antigen) per 0.5 mL*	*Recombivax HB Pediatric/Adolescent Formulation®*	*Merck*
		10 mcg (of hepatitis B surface antigen) per mL	*Recombivax HB Adult Formulation®*	*Merck*
		10 mcg (of hepatitis B surface	*Engerix-B Pediatric/Adolescent Formulation®*	*GlaxoSmithKline*

		antigen) per 0.5 mL		
		20 mcg (of hepatitis B surface antigen) per mL	*Engerix-B Adult Formulation®*	*GlaxoSmithKline*
		40 mcg (of hepatitis B surface antigen) per mL	*Recombivax HB Dialysis Formulation®*	*Merck*

Hepatitis B Vaccine (Recombinant), Adjuvanted

ROUTES	FORMS	STRENGTHS	BRAND NAMES	MANUFACTURER
Parenteral	*Injectable solution, for IM use*	*20 mcg (of hepatitis B surface antigen) and 3000 mcg of CpG 1018 adjuvant per 0.5 mL*	*Heplisav-B®*	*Dynavax*

Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Hepatitis B (Recombinant) and Inactivated Poliovirus Vaccine Combined (DTaP-HepB-IPV)

ROUTES	FORMS	STRENGTHS	BRAND NAMES	MANUFACTURER
Parenteral	*Injectable suspension, for IM use*	*Diphtheria Toxoid 25 Lf units, Tetanus Toxoid 10 Lf units, Acellular Pertussis Vaccine 58 mcg (of pertussis antigen), Hepatitis B Surface Antigen 10 mcg, Poliovirus Type 1 40 DU, Poliovirus Type 2 8 DU, and Poliovirus Type 3 32 DU per 0.5 mL*	*Pediarix®*	*GlaxoSmithKline*

Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine Combined (DTaP-IPV-Hib-HepB)

ROUTES	FORMS	STRENGTHS	BRAND NAMES	MANUFACTURER
Parenteral	*Injectable suspension, for IM use*	*Diphtheria Toxoid 15 Lf units, Tetanus Toxoid 5 Lf units, Acellular Pertussis Antigen Detoxified 20 mcg (of pertussis antigen), Hepatitis B Surface Antigen 10 mcg, Poliovirus Type 1 29 DU, Poliovirus Type 2 7 DU, and Poliovirus Type 3 26 DU, 3 mcg PRP of H. influenzae type b covalently bound to 50 mcg of the OMPC of Neisseria meningitidis serogroup B per 0.5 mL*	*Vaxelis®*	*MSP*

Hepatitis A and Hepatitis B (Recombinant) Vaccine (HepA-HepB)

ROUTES	FORMS	STRENGTHS	BRAND NAMES	MANUFACTURER
Parenteral	*Injectable suspension, for IM use*	*Hepatitis A Virus Vaccine Inactivated 720 ELISA units (of viral antigen) and Hepatitis B Vaccine (Recombinant) 20 mcg (of hepatitis B surface antigen) per mL*	*Twinrix®*	*GlaxoSmithKline*

† Use is not currently included in the labeling approved by the US Food and Drug Administration.

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