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Take CME Exams

A Two-Dose Hepatitis B Vaccine for Adults (*Heplisav-B*)

The FDA has approved a two-dose hepatitis B virus (HBV) vaccine (*Heplisav-B* – Dynavax) for use in adults ≥18 years old. The three other HBV vaccines marketed in the US are usually administered in 3 doses. *Engerix-B* and *Recombivax HB* are licensed for use in persons of all ages. A combination hepatitis A/B vaccine *(Twinrix)* contains the same hepatitis B component as *Engerix-B* and is licensed for use only in adults.[1]

Pronunciation Key
***Heplisav-B*:** hep' li sav bee

HEPATITIS B VIRUS INFECTION — HBV infection is transmitted through percutaneous or mucosal contact with infectious blood or other bodily fluids. Risk factors for acquisition in adults include occupational exposure, IV drug abuse, unprotected sex, and hemodialysis. Chronic HBV infection can cause cirrhosis and hepatic cancer. Universal childhood vaccination against HBV, introduced in the US in 1991, has significantly reduced the incidence of HBV infection.[2]

THE VACCINES — All four HBV vaccines available in the US (see Table 1) contain recombinant yeast-derived hepatitis B surface antigen (HBsAg) with an immunostimulatory adjuvant. *Engerix-B*, *Recombivax HB*, and *Twinrix* use aluminum hydroxide as an adjuvant. *Heplisav-B* uses a synthetic cytosine phosphoguanine oligonucleotide (CpG 1018) derived from bacterial DNA; it is thought to stimulate the immune system through activation of the toll-like receptor 9 (TLR-9) pathway, which induces production of cytokines such as interleukin-12 and interferon-alpha.[3]

CLINICAL STUDIES — The immunogenicity of the new vaccine was evaluated in three randomized, observer-blinded studies that compared the rates of seroprotection (defined as an HBsAg antibody concentration ≥10 mIU/mL) after two doses of *Heplisav-B* given at 0 and 4 weeks to those after 3 doses of *Engerix-B* given at 0, 1, and 6 months. Seroprotection rates were significantly higher with *Heplisav-B* than with *Engerix-B* (see Table 2).[4-6]

One of the studies evaluated seroprotection rates by age group; the immune response to both vaccines decreased with age, but seroprotection rates in all prespecified age groups were significantly higher with *Heplisav-B* than with *Engerix-B* (see Table 3).[6]

ADVERSE EFFECTS — The most common adverse effects of *Heplisav-B* in clinical trials were injection-site pain (23-39%), fatigue (11-17%), and headache (8-17%). Injection-site pain, redness, and swelling occurred more often with *Heplisav-B* than with

Table 1. Hepatitis B Vaccines

Vaccine	Formulations	Dose	Schedule	Cost[1]
Hepatitis B				
Heplisav-B (Dynavax)	0.5 mL solution in single-dose vials	≥18 yrs[2]: 0.5 mL IM	2 doses (0 and 1 mo)	$230.00
Engerix-B (GSK)	0.5, 1 mL suspension in single-dose vials, prefilled syringes	Birth-19 yrs: 0.5 mL IM[3] ≥20 yrs: 1 mL IM[3]	3 doses (0, 1, and 6 mos)[4]	66.90 169.50
Recombivax HB (Merck)	0.5, 1 mL suspension in single-dose vials, prefilled syringes	Birth-19 yrs: 0.5 mL IM[3] ≥20 yrs: 1 mL IM[3]	3 doses (0, 1, and 6 mos)[4,5]	69.60 181.40
Hepatitis A/B				
Twinrix (GSK)	1 mL suspension in single-dose vials, prefilled syringes	≥18 yrs: 1 mL IM	3 doses (0, 1, and 6 mos)[6]	298.50

1. Approximate WAC for a complete vaccination series. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. January 5, 2018. Reprinted with permission by First Databank, Inc. All rights reserved. ©2018. www.fdbhealth.com/policies/drug-pricing-policy.
2. Not licensed for use in persons <18 years old.
3. May be administered subcutaneously to persons with hemophilia and others at risk for hemorrhage following intramuscular injection; the antibody response is lower with subcutaneous administration.
4. The recommended dosage of *Engerix-B* for patients receiving hemodialysis is 2 mL given at 0, 1, 2, and 6 months. *Recombivax HB* is available in a separate dialysis formulation (40 mcg/1 mL) that is given at 0, 1, and 6 months. These dosing schedules can also be considered for immunocompromised patients.
5. Adolescents 11-15 years old can alternatively receive two 1-mL doses of *Recombivax HB* given at 0 and 4-6 months.
6. *Twinrix* can also be administered on an accelerated schedule, with doses given on day 0, day 7, and day 21-30, and a booster dose given at month 12.

Table 2. Results of *Heplisav-B* Seroprotection Studies

	Heplisav-B	*Engerix-B*	SPR Difference (95% CI)
Study 1[1]: Patients 18-55 years old (n=2032)			
Timepoint	12 weeks	28 weeks	
SPR	95.0%	81.3%	13.7% (10.4, 17.5)
Study 2[2]: Patients 40-70 years old (n=1474)			
Timepoint	12 weeks	32 weeks	
SPR	90.1%	70.5%	19.6% (14.7, 24.8)
Study 3[3]: Patients 18-70 years old (n=6665)			
Timepoint	24 weeks	28 weeks	
SPR	95.4%	81.3%	14.2% (12.5, 15.9)
Study 3[3]: Patients 18-70 years old with type 2 diabetes (n=961)			
Timepoint	28 weeks	28 weeks	
SPR	90.0%	65.1%	24.9% (19.3, 30.7)

SPR = seroprotection rate
1. SA Halperin. Vaccine 2012; 30:2556.
2. WL Heyward et al. Vaccine 2013; 31:5300.
3. S Jackson et al. Vaccine 2017 Dec 27 (epub).

Engerix-B, but the reported rates of death and serious adverse events with the two vaccines were similar.

RECOMMENDATIONS FOR ADULT IMMUNIZATION — Any person who wants protection against HBV infection should be immunized; no risk factor needs to be identified for vaccination to be indicated.

Hepatitis B immunization is specifically recommended for adults with a medical, occupational, or behavioral risk factor for HBV acquisition. Medical indications include chronic liver disease, end-stage renal disease and hemodialysis (*Heplisav-B* has not been studied in hemodialysis patients), diabetes (particularly in persons 19-59 years old), and HIV infection. Occupational indications include healthcare or public safety work with potential exposure to blood or bodily fluids. Adults with behavioral risks include injection drug users and those who have had multiple sex partners in the previous 6 months or recently acquired another sexually transmitted infection.

Other adult populations that should be vaccinated against HBV infection include men who have sex with men, residents of facilities for the aged and chronically ill, staff and clients of facilities that test for and treat sexually transmitted infections or drug abuse, residents and staff of institutions for the developmentally disabled, inmates and staff of correctional facilities, household contacts and sex partners of persons with chronic HBV infection, and travelers to countries with intermediate or high rates of chronic HBV infection.[7,8]

Table 3. Seroprotection Rate by Age Group (Study 3)[1]

Age Group (yrs)	*Heplisav-B*	*Engerix-B*
18-29	100%	93.9%
30-39	98.9%	92.0%
40-49	97.2%	84.2%
50-59	95.2%	79.7%
60-70	91.6%	72.6%

1. S Jackson et al. Vaccine 2017 Dec 27 (epub).

CONCLUSION — *Heplisav-B*, a new hepatitis B virus vaccine with a synthetic oligonucleotide immunostimulatory adjuvant, is licensed for use in adults ≥18 years old. In clinical trials, two doses of *Heplisav-B* were more immunogenic than three doses of an older hepatitis B virus vaccine *(Engerix-B)*, but *Heplisav-B* caused more injection-site reactions. The rates of serious adverse effects with the two vaccines were similar, but the long-term safety of *Heplisav-B* remains to be established. ■

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4. SA Halperin et al. Comparison of safety and immunogenicity of two doses of investigational hepatitis B virus surface antigen co-administered with an immunostimulatory phosphorothioate oligodeoxyribonucleotide and three doses of a licensed hepatitis B vaccine in healthy adults 18-55 years of age. Vaccine 2012; 30:2556.
5. WL Heyward et al. Immunogenicity and safety of an investigational hepatitis B vaccine with a Toll-like receptor 9 agonist adjuvant (HBsAg-1018) compared to a licensed hepatitis B vaccine in healthy adults 40–70 years of age. Vaccine 2013; 31:5300.
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7. S Schillie et al. Prevention of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2018; 67:1.
8. Vaccines for travelers. Med Lett Drugs Ther 2014; 56:115.

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