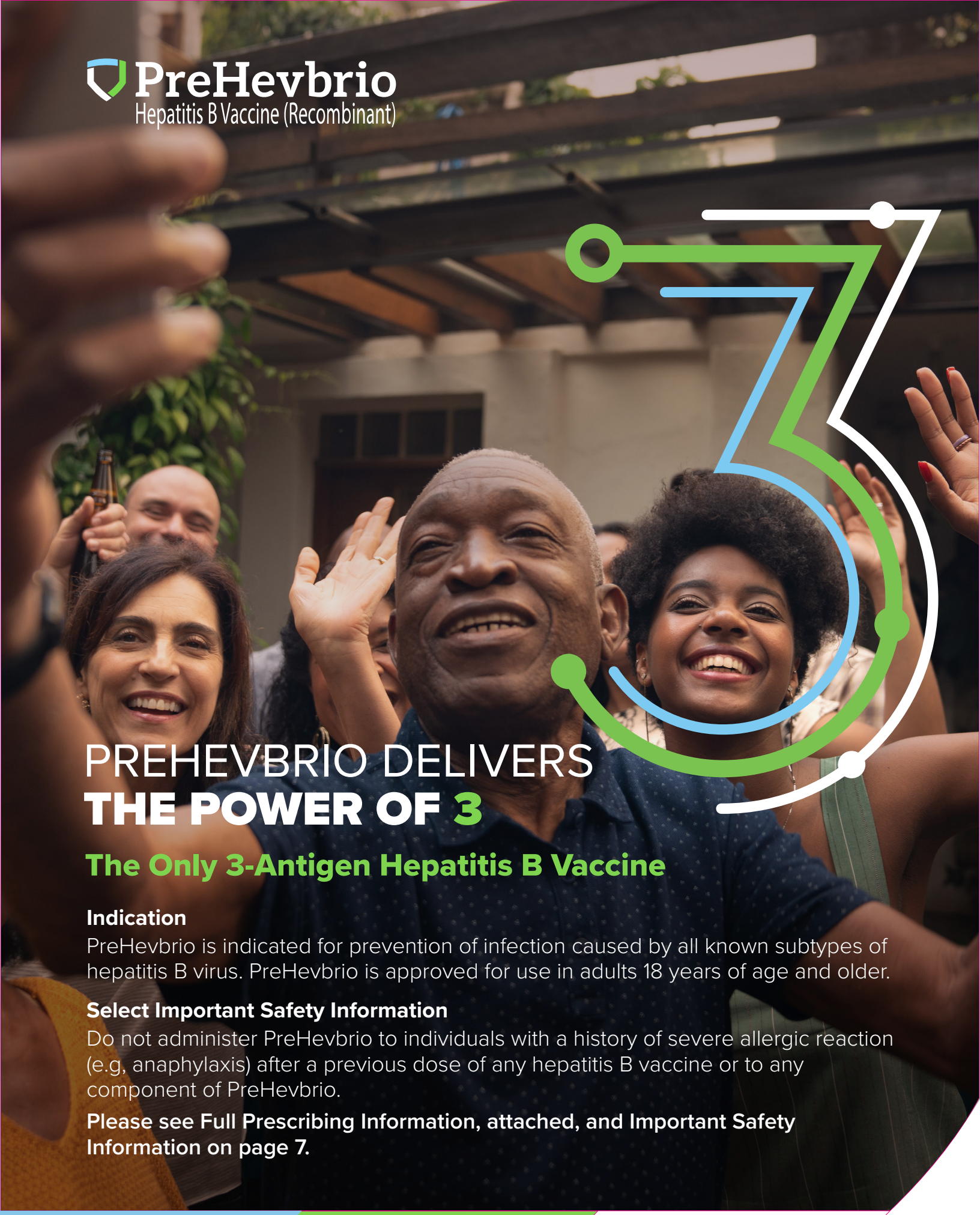
PreHevbrio
Hepatitis B Vaccine (Recombinant)



PREHEVBRIO DELIVERS **THE POWER OF 3**

The Only 3-Antigen Hepatitis B Vaccine

Indication

PreHevbrio is indicated for prevention of infection caused by all known subtypes of hepatitis B virus. PreHevbrio is approved for use in adults 18 years of age and older.

Select Important Safety Information

Do not administer PreHevbrio to individuals with a history of severe allergic reaction (e.g, anaphylaxis) after a previous dose of any hepatitis B vaccine or to any component of PreHevbrio.

Please see Full Prescribing Information, attached, and Important Safety Information on page 7.

ACIP Adult Hepatitis B (HBV) Vaccine Recommendations[1]

In November 2021, the CDC's Advisory Committee on Immunization Practices (ACIP) unanimously voted to recommend the following groups be vaccinated against HBV:

19-59 years

All adults aged 19 to 59 years (universal recommendation)

60+ years

Those with risk factors among adults aged 60 years or older

Note: Recommendations are not official until published in MMWR.

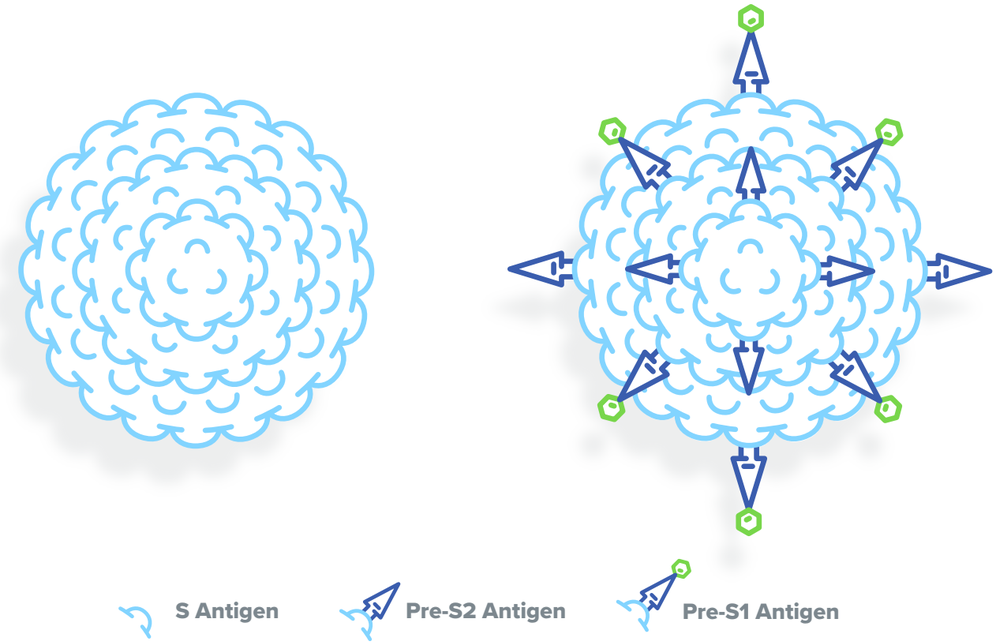
Only one HBV vaccine helps protect with **THE POWER OF 3**

PreHevbrio
Hepatitis B Vaccine (Recombinant)

PreHevbrio expresses the pre-S1, pre-S2, and S antigens of HBV, and is the only 3-antigen HBV vaccine for adults[2]

TRADITIONAL SINGLE-ANTIGEN VACCINE

THIRD-GENERATION 3-ANTIGEN VACCINE—PREHEVBRIO[3]



PREHEVBRIO CONTAINS ALL 3 SURFACE ANTIGENS OF HBV[4]

Select Important Safety Information

Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of PreHevbrio.

Please see Full Prescribing Information, attached, and Important Safety Information on page 7.

PROTECT—a Phase 3 clinical trial to evaluate immunogenicity and safety[5]

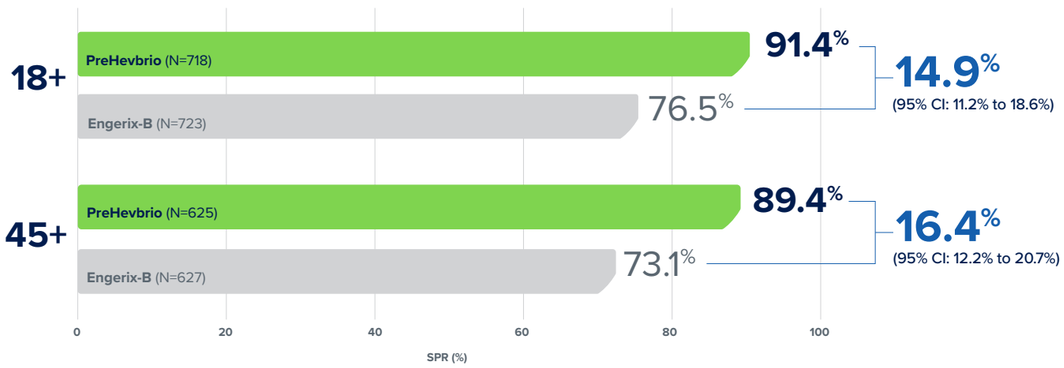
STUDY DESCRIPTION

PreHevbrio was evaluated in a two-arm, double-blind, randomized, safety and immunogenicity study of adults (n=1,607), including those with well-controlled chronic conditions across 28 sites in Europe, the U.S., and Canada. There were 2472 participants screened for the study, 1607 of which were randomized. In the Prehevbrio 10 µg arm of the study, 756 of the randomized 796 participants completed the study. In the Engerix-B arm of the study, 769 of the randomized 811 participants completed the study. Dosing schedule for both arms was at months 0, 1, 6. The two co-primary objectives of comparing SPR (% of subjects achieving anti-HBs titers ≥10 mIU/mL) at 4 weeks after receiving the third dose of PreHevbrio or Engerix-B were non-inferiority in adults ≥18 years of age and superiority in adults ≥45 years of age for PreHevbrio 10 µg compared to Engerix-B 20 µg. Key secondary endpoints included SPRs for PreHevbrio at days 56 and 168 and for Engerix-B at day 196; local and systemic solicited adverse events; and unsolicited adverse events. Key exploratory endpoints included SPRs for both study groups at days 0, 28, 56, 168, and 336; geometric mean concentration of anti-HBs antibody titers; and the proportion of participants having anti-HBs titers ≥100 mIU/mL at days 28, 56, 168, 196, and 336.

More adults achieved **higher seroprotection rates*** in the PROTECT study[2]

PreHevbrio elicited non-inferior seroprotection rates (SPR) in adults age 18+ with statistically significantly higher SPR in adults age 45+ than Engerix-B

SEROPROTECTION RATES AT DAY 196



*Seroprotection was defined as anti-HBs titers ≥10 mIU/mL; SPR was defined as the percentage of participants attaining seroprotection.

Seroprotection rates across age groups[2]

PreHevbrio
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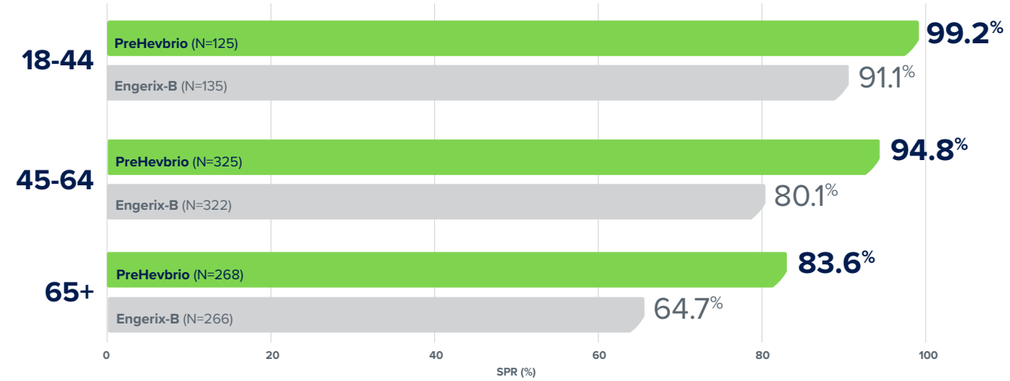
Exploratory endpoints in more detailed age groups:

SEROPROTECTION RATES AT DAY 196

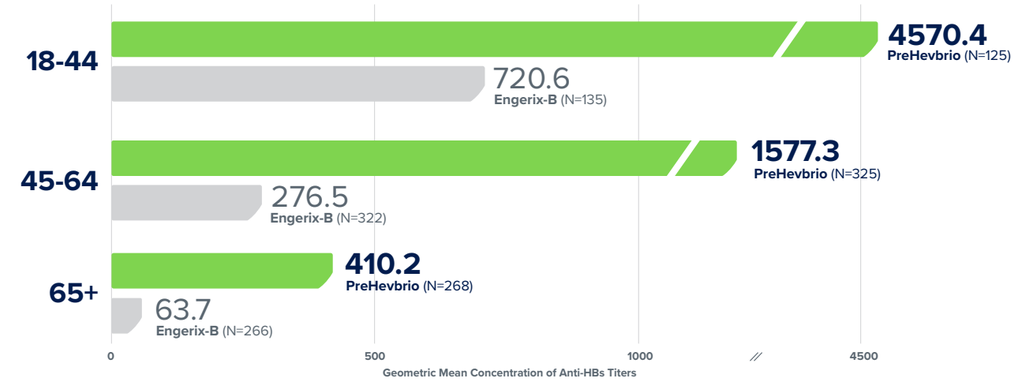


Exploratory analysis.

Concentration of Anti-HBs antibody titers across age groups[6]

Exploratory endpoints in more detailed age groups:

ANTIBODY TITERS AT DAY 196



Results include all enrolled subjects regardless of age.

Select Important Safety Information

The most common side effects (>10%) in adults age 18-44, adults age 45-64, and adults age 65+ were pain and tenderness at the injection site, myalgia, fatigue, and headache.

Please see Full Prescribing Information, attached, and Important Safety Information on page 7.

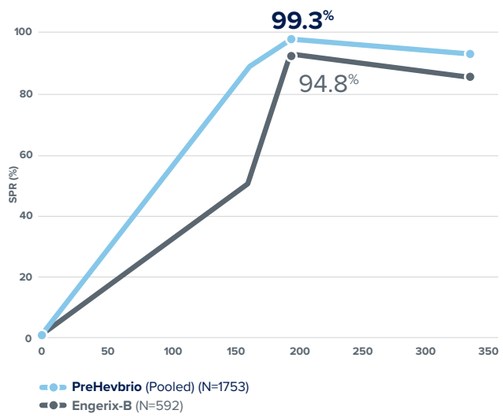
CONSTANT—Phase 3 clinical trial to evaluate lot-to-lot consistency[7]

STUDY DESCRIPTION

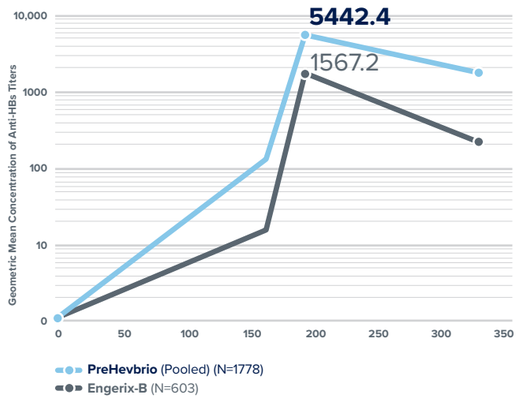
PreHevbrio was evaluated in a four-arm, double-blind, randomized, lot-to-lot consistency study of adults age 18 to 45 (n=2,838) across 35 sites in Europe, the U.S., and Canada. There were 4452 participants screened for the study, 2838 of which were randomized. In the PreHevbrio 10 µg Lot A arm of the study, 650 of the 711 participants completed vaccination. In the PreHevbrio 10 µg Lot B arm of the study, 661 of the 709 participants completed vaccination. In the PreHevbrio 10 µg Lot C arm of the study, 656 of the 706 participants completed vaccination. In the Engerix-B 20 µg arm of the study, 671 of the 712 participants completed vaccination. Dosing schedule for all arms was 3 doses at month 0, 1, 6. The primary objective was to demonstrate consistency of immune response as measured by geometric mean concentration of antibodies across three consecutively manufactured lots of PreHevbrio 10 µg. The secondary objective was to demonstrate non-inferiority of SPR (% of subjects achieving anti-HBs titers ≥10 mIU/mL) of PreHevbrio (pooled) compared to Engerix-B at Day 196.

Kinetics of seroprotection rates in adults age 18-45[2,7]

4 weeks after 3rd dose, PreHevbrio achieved SPRs non-inferior to Engerix-B



Kinetics of Anti-HBs antibody titers in adults age 18-45[7]



Seroprotection was defined as anti-HBs titers ≥10 mIU/mL; SPR was defined as the percentage of participants attaining seroprotection.

Well-established safety profile

PreHevbrio
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Rates of Solicited Local and Systemic Adverse Reactions[2]

- In Phase 3 studies, the most common local reactions were pain and tenderness, and the most common systemic reactions were headache, fatigue, and myalgia
- No increase in reactogenicity symptoms over the 3-dose vaccination schedule

LOCAL REACTION	Individuals **18-44** Years of Age	Individuals **45-64** Years of Age	Individuals **≥65** Years of Age
Injection site pain	52.0 – 58.3%	42.2 – 48.8%	26.7 – 34.8%
Injection site tenderness	52.6 – 59.6%	43.2 – 50.5%	30.2 – 32.8%
SYSTEMIC REACTION			
Headache	17.2 – 25.8%	13.8 – 21.3%	7.3 – 12.2%
Fatigue	20.1 – 28.3%	14.3 – 19.7%	11.5 – 14.5%
Myalgia	22.2 – 29.9%	16.7 – 24.1%	11.5 – 16.6%

Range represents rates following each of the doses of PreHevbrio.

Unsolicited adverse events[2]

In both phase 3 studies, unsolicited adverse events were reported by 48.3% and 48.4% within 28 days of any vaccination with PreHevbrio and Engerix-B, respectively.

Rates of severe adverse events[2]

In pivotal phase 3 studies, severe adverse events were reported by 0.9% and 0.6% within 28 days of vaccination with PreHevbrio or Engerix-B, respectively. Severe adverse events were reported by 2.5% and 1.6% from the first vaccination through 6 months after the third vaccination with PreHevbrio or Engerix-B, respectively.

Unsolicited adverse events in subjects who received PreHevbrio, for which available information suggests a causal relationship to vaccination[2]

Injection site bruising	1.4%
Dizziness/vertigo	1.1%
General pruritus/itchiness	0.2%
Arthralgia	0.2%
Urticaria/hives	0.2%
Lymphadenopathy/lymph node pain	0.1%

Important Safety Information

Do not administer PreHevbrio to individuals with a history of severe allergic reaction (e.g, anaphylaxis) after a previous dose of any hepatitis B vaccine or to any component of PreHevbrio.

Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of PreHevbrio.

Immunocompromised persons, including those on immunosuppressant therapy, may have a diminished immune response to PreHevbrio.

PreHevbrio may not prevent hepatitis B infection, which has a long incubation period, in individuals who have an unrecognized hepatitis B infection at the time of vaccine administration.

The most common side effects (>10%) in adults age 18-44, adults age 45-64, and adults age 65+ were pain and tenderness at the injection site, myalgia, fatigue, and headache.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women who received PreHevbrio during pregnancy. Women who receive PreHevbrio during pregnancy are encouraged to contact 1-888-421-8808 (toll-free).

To report SUSPECTED ADVERSE REACTIONS, contact VBI Vaccines at 1-888-421-8808 (toll-free) or VAERS at 1-800-822-7967 or www.vaers.hhs.gov

Please see attached Full Prescribing Information.

PREHEVBRIO DELIVERS
THE POWER OF 3

Differentiated as the **ONLY 3-ANTIGEN** hepatitis B vaccine[5]

Elicits a **MORE ROBUST IMMUNE RESPONSE** than the most widely used single-antigen hepatitis B vaccine[2,5,7]

PROTECTS A BROAD RANGE OF YOUR PATIENTS[2,5]

Select Important Safety Information

Immunocompromised persons, including those on immunosuppressant therapy, may have a diminished immune response to PreHevbrio.

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For more information, visit www.prehevbrio.com.

References

1. Centers for Disease Control. Advisory Committee on Immunization Practices. https://www.cdc.gov/vaccines/acip/index.html. Accessed January 21, 2022. **2.** PREHEVBRIO Prescribing Information. Cambridge, MA. VBI Inc. **3.** Gerlich WH. *Med Microbiol Immunol.* 2015;204:39-55. **4.** Liang TK. Hepatitis B: the virus and disease. *Hepatology*. 2009 May;49(5 Suppl): S13-21. **5.** Vesikari T, et al. *Lancet Infect Dis.* 2021; https://doi.org/10.1016/ S1473-3099(20)30780-5. **6.** Langley J, et al. Poster Presented at AASLD, The Liver Meeting 2020. November 13-16, 2020. A0742. **7.** Vesikari T, et al. *JAMA Network Open*. 2021;4(10):e2128652. doi:10.1001/jamanetworkopen.2021.28652.

VBI VACCINES

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