Hepatitis B Overview and Innovations in Immunization

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Why Hepatitis B Matters
Virology of the Hepatitis B Virus (HBV)

- The hepatitis B virus is a double-stranded DNA virus that enters the liver cell and is then transported into the nucleus of the cell\(^1\)
  - Inside the nucleus, the viral DNA is converted into a covalently closed circular DNA (cccDNA), which serves as a model for viral replication
- A hepatitis B infection can result in either an acute or chronic infection\(^2\)
  - An acute infection may last up to six months, and usually clears itself; some adults that are unable to get rid of the virus after six months are diagnosed as having a "chronic infection"
- Long-term outcomes of HBV infection can include a wide range of liver disease such as, acute (including fulminant hepatic failure) to chronic hepatitis, cirrhosis, and hepatocellular carcinoma\(^3\)
Chronic Hepatitis B Is a Major Public Health Challenge According to the CDC\(^1\)

Hepatitis B vaccines have been available for nearly 40 years, yet HBV infections are on the rise\(^2,3\)

Estimated new cases of HBV in the US have risen $\sim 11\%$ over a 5-year period\(^3\)

As many as 2.2 million people in the US are infected with hepatitis B\(^4\)

**HEPATITIS B INFECTIONS INCREASED BY 114% FROM 2006 TO 2013 IN SOME STATES AFFECTED BY THE OPIOID AND HEROIN EPIDEMICS**\(^5\)

Abbreviations: CDC, Centers for Disease Control and Prevention; HBV, hepatitis B virus.

**References:**
Hepatitis B Is an Important Public Health Concern

HBV is highly infectious, resilient, and environmentally stable

Chronic HBV infection can lead to serious complications and death

- HBV is up to 100x more infectious than HIV
- HBV remains infectious outside of the body for at least 7 days
- Most infected carriers remain asymptomatic and are unaware of their disease or risk for transmitting HBV
- Many of those recommended by the CDC for HBV immunization are not getting fully vaccinated—*including health care professionals (HCPs)*
Chronic HBV Infection Can Lead to Serious Complications and Death

- Patients with chronic liver disease and patients with diabetes, especially older adults, may be more likely to suffer serious consequences of HBV infection\textsuperscript{15,16}
- Over 5,000 HBV-related deaths occur each year in the United States\textsuperscript{17}

\textbf{THERE IS NO CURE FOR HEPATITIS B\textsuperscript{18}, BUT IT IS PREVENTABLE}
Hepatitis B Can Be Spread in Many Ways

- Unprotected sexual contact
- Sharing drugs, needles or "works" (cotton, cooker, spoon, etc.)
- A hepatitis B-infected mother to her baby during birth
- Contact with blood or open sores of a hepatitis B-infected person
- Sharing personal-care items such as razors or toothbrushes
- Sharing a household with a person with chronic (lifelong) hepatitis B infection
- Using unsterilized needles in ear- or body-piercing, tattooing, or acupuncture
- Poor infection control practices in medical settings, particularly with blood glucose monitoring
- Pre-chewing food for babies
- Needle sticks or sharps injuries on the job

The CDC Recommends HBV Vaccination for a Variety Risk Factors That Include Patients With Diabetes

### Medical Diagnoses
- Diabetes, aged 19 to 59 years
- Chronic liver disease
- HIV infection
- End-stage renal disease, including predialysis, hemodialysis, and home dialysis patients

### Sexual Exposure
- Sexually active patients who are not in a long-term, mutually monogamous relationship
- Patients seeking testing or treatment for a sexually transmitted disease
- Men who have sex with men
- Sexual partners of HBV-positive persons

### Occupational Risk
- Persons who have occupational risk of infection, including healthcare and public safety workers
- International travelers
- Employers must offer HBV immunization at no cost to healthcare and public safety workers

### Other Risk Factors
- Current or recent injection drug users
- Household contacts of HBV-positive persons
- All patients seeking protection from HBV infection

**EFFECTIVE VACCINATION IS CRITICAL TO REDUCING THE SPREAD OF THE DISEASE**
Conventional 3-dose HBV Vaccines

~40% of HCPs did not receive all 3-doses³³

~75% of adults aged 19+ did not receive all 3-doses¹⁴†

In Clinical Studies, Many Failed to Achieve Protective Immunity Even After Completing All 3-doses of a Traditional Hepatitis B Vaccine‡

~20% to 30% of people failed to achieve protective immunity after initial series and remain unprotected²⁹

~35% of people with diabetes failed to achieve protective immunity and remain unprotected²⁹,³⁴

It Takes 6 Months to Complete a Traditional 3-dose Hepatitis B Vaccine Series²⁸

*From the 2008 National Health Interview Survey.
†Period covered Jan-Dec 2015. The total adult sample was 33,348 persons aged ≥19 years.
‡Data on file. Dynavax Clinical Trial.
# Hepatitis B Series Completion Rates Among Dose 1 Recipients

<table>
<thead>
<tr>
<th>Setting Type (facility)</th>
<th>Number or persons who received dose 1</th>
<th>Number (%) of dose 1 recipients who received dose 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>STD Clinics</td>
<td>11,245</td>
<td>1,928 (17.1)</td>
</tr>
<tr>
<td>Department of Corrections</td>
<td>5,150</td>
<td>908 (17.6)</td>
</tr>
<tr>
<td>Other</td>
<td>3,447</td>
<td>1,079 (31.3)</td>
</tr>
<tr>
<td>Federally Qualified Health Center</td>
<td>2,432</td>
<td>923 (38.0)</td>
</tr>
<tr>
<td>Drug Treatment</td>
<td>2,564</td>
<td>349 (13.6)</td>
</tr>
<tr>
<td>Healthcare Facility Targeting IDU</td>
<td>2,008</td>
<td>325 (16.2)</td>
</tr>
<tr>
<td>HIV Clinics</td>
<td>1,278</td>
<td>379 (29.7)</td>
</tr>
<tr>
<td>Local Health Department Clinic</td>
<td>876</td>
<td>531 (60.6)</td>
</tr>
<tr>
<td>Healthcare Setting Targeting MSM</td>
<td>457</td>
<td>135 (29.5)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>29,457</strong></td>
<td><strong>6,557 (22.3)</strong></td>
</tr>
</tbody>
</table>

A 2-dose Vaccine Helps Provide Earlier Protection in Fewer Doses Compared With a 3-dose Vaccine\textsuperscript{29}
First Non-Alum Adjuvanted Vaccine for the Prevention of HBV Infection in Adults-FDA Approved November 2017

Conventional 3-dose HBV Vaccines
Alum adjuvants activate multiple inflammatory pathways in a broad range of cell types by inducing membrane disruption and cell stress, with no specific cellular receptor for alum.

2-dose Vaccine
CpG 1018 is highly specific and exerts its actions through a single immune receptor, Toll-like receptor (TLR) 9, which is an important innate immune receptor for sensing the presence of bacterial and viral DNA.

The 2-dose vaccine utilizes proprietary adjuvant technology that is based on synthetic DNA sequences and is believed to activate the innate immune response by engaging TLR9. This may induce a highly specific, helper T-cell response to generate memory T and B cells.

27
HEPLISAV-B

CpG + HBs Antigen

CpG interacts with TLR9

Activated signal pathways

Antigen passes through to be expressed on the surface of the PDC

Plasmacytoid Dendritic Cell (PDC)

Cytokines and Interferons are released

Naïve T Cell

Th1 Cell

B Cell

Antibodies swarm the Hepatitis B virus

redirected for clarity
Patients With Diabetes & HBV
Essential Components of Diabetes Care Are Behind the Transmission of HBV

86.0% of patients with diabetes check blood glucose at least monthly.1

30.2% of blood glucose meters had blood contamination.2

From 1996 to 2010, 29 HBV outbreaks in long-term care facilities were reported to the CDC, with 25 involving adults with diabetes receiving assisted blood glucose monitoring.3

Sharing of multi-lancet fingerstick devices has been reported as a cause of HBV infections in nursing homes.4

Patients With Diabetes Are Already More Likely to Suffer Serious Consequences – Hepatitis Increases the Risk Further

- Diabetes is strongly linked to liver cancer\(^1\)
- HBV infection makes patients with diabetes even more likely to develop liver cancer and cirrhosis of the liver\(^2\)
- Protecting patients with diabetes earlier can help prevent serious complications

The ACIP Recommends Vaccination, but Little Progress Is Being Made

- The ACIP recommends hepatitis B vaccine for diabetes mellitus patients aged 19 through 59 as soon as feasible after diabetes diagnosis\(^1\)

- There has been little shift in HBV vaccination rates among adults who have diabetes\(^2\)
  - Among US adults with diabetes aged 19 to 59 years, 71% report that they never have received the HBV vaccine

- HBV rates are climbing and outbreaks continue\(^3,4\)
  - 24 outbreaks (2008-2017), 179 outbreak-associated cases, >10,900 persons notified for screening

Abbreviation: ACIP, Advisory Committee on Immunization Practices.

An Additional Opportunity To Protect Patients
Pharmacists Are Critical Point-Of-Care Practitioners for Elevating Diabetes Care

- Community pharmacists see their patients between 1.5 and 10 times more frequently than primary care physicians\(^1\)
- Prescription pickups may align with dosing regimen for a hepatitis B vaccine

You Have the Opportunity to Help Protect Patients With Diabetes From Hepatitis B

You protect your patients by checking comorbidities, compliance with medications, safe refills, and the flu shot. You can do the same with the CDC-recommended HBV vaccine.

Of the 261 pharmacists surveyed in a 2018 study:\(^1\):

- 34.7% assessed their customers for a hepatitis B vaccine (compared to 93.9% for the flu vaccine)\(^1\)
- 48% recommended a hepatitis B vaccine to their customers (compared to 86.7% for the flu vaccine)\(^1\)
- 51.4% stocked a hepatitis B vaccine (compared to 92.6% who stocked the flu vaccine)\(^1\)

You Can Be Proactive in Recommending Vaccination to Patients With Diabetes

What you can do to help in the effort to protect patients with diabetes from HBV

Be on the lookout for patients with diabetes. They might not know they are at risk.

Advocate for an internal alert system to help keep everyone accountable and involved.

Tell patients about the convenient 2-dose administration, which can be administered at the same time as other vaccines.

EMPHASIZE THAT PATIENTS NEED TO RETURN TO RECEIVE ALL DOSES IN ORDER TO BE PROTECTED
Clinical Data
Pivotal Studies (Trial 1, Trial 2, Trial 3)

- Three Phase III randomized, multicenter, noninferiority trials
- Two doses of the 2-dose vaccine at 0, 1 month with placebo at 6 months compared with Three doses of the 3-dose vaccine at 0, 1, and 6 months
- Exclusions¹,²,³
  - Current or previous hepatitis B infection or hepatitis B vaccine
  - HIV infection, immunosuppression, or history of autoimmune disease

Trial 1 (N=2415) 3:1
- 2-dose Vaccine (N=1809)
- 3-dose Vaccine (N=606)

Trial 2 (N=2452) 4:1
- 2-dose Vaccine (N=1969)
- 3-dose Vaccine (N=483)
  2. Heyward, 2013

Trial 3 (N=8374) 2:1
- 2-dose Vaccine (N=5592)
- 3-dose Vaccine (N=2782)
  3. Jackson, 2018

¹, ², ³: Source references
In Trial 1, Two Doses of the 2-dose Vaccine Provided Earlier and Higher Levels of Protective Immunity Than Three Doses of the 3-dose Vaccine in Patients Aged 18-55 Years

95% of those who received the 2-dose vaccine achieved protection after 2 doses in 1 month*\(^{17,29}\)

- 13.7% difference (95% CI, 10.4-17.5) in protective immunity between patient groups at primary endpoint\(^{23}\)
- The primary analysis compared the rate of protective immunity\(^{†}\) at Week 12 for 2-dose vaccine with that at Week 28 for 3-dose vaccine\(^{29}\)
- Statistical significance was met; however, statistical significance was not prespecified in Trial 1\(^{17}\)

\(^*\)Compared to 81.3% who received three doses of the 3-dose vaccine

\(^{†}\)Protective immunity defined as antibody concentration ≥10 mIU/mL\(^{6}\)
In Trial 2, the 2-dose Vaccine Provided Statistically Significantly Higher Rates of Protective Immunity in Patients Aged 40–70 Years

Statistically significantly higher rates of protection vs 3-dose vaccine at every time point measured\(^{17,29}\)

- 19.6% (95% CI, 14.7–24.8) difference in protective immunity between patient groups at primary endpoint\(^{29}\)
- The primary analysis compared the rate of protective immunity* at Week 12 for 2-dose vaccine with that at Week 32 for 3-dose vaccine\(^{29}\)

*Protective immunity defined as antibody concentration \(\geq 10\) mIU/mL.\(^6\)
In Trial 3, the 2-dose Vaccine Delivered Protection for Patients With Factors That Typically Limit Immune Response

2-dose vaccine provided statistically significantly higher rates of protection in diabetics and other known hypo-responsive populations

<table>
<thead>
<tr>
<th>2-dose vaccine</th>
<th>3-dose vaccine</th>
<th>Peak SPR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>Total population</td>
<td>4,537</td>
<td>2,289</td>
</tr>
<tr>
<td>Non-diabetes</td>
<td>3,762</td>
<td>1,968</td>
</tr>
<tr>
<td>Diabetes</td>
<td>640</td>
<td>321</td>
</tr>
<tr>
<td>18 – 29 years</td>
<td>174</td>
<td>99</td>
</tr>
<tr>
<td>30 – 39 years</td>
<td>632</td>
<td>326</td>
</tr>
<tr>
<td>40 – 49 years</td>
<td>974</td>
<td>518</td>
</tr>
<tr>
<td>50 – 59 years</td>
<td>1,439</td>
<td>758</td>
</tr>
<tr>
<td>60 – 70 years</td>
<td>1,157</td>
<td>588</td>
</tr>
<tr>
<td>Men</td>
<td>2,203</td>
<td>1,150</td>
</tr>
<tr>
<td>Women</td>
<td>2,173</td>
<td>1,139</td>
</tr>
<tr>
<td>Obese</td>
<td>2,165</td>
<td>1,076</td>
</tr>
<tr>
<td>Non-obese</td>
<td>2,208</td>
<td>1,212</td>
</tr>
<tr>
<td>Smoker</td>
<td>1,371</td>
<td>711</td>
</tr>
<tr>
<td>Non-smoker</td>
<td>3,005</td>
<td>1,578</td>
</tr>
</tbody>
</table>

Trial 3 study design: A clinical trial in adults aged 18 to 70 years

*Protective immunity defined as antibody concentration ≥10 mIU/mL
In Trial 1, the most common (>10%) local reaction was injection site pain (39%), and the most common systemic reactions were fatigue (17%) and headache (17%)\textsuperscript{29}

### PERCENTAGE WITH LOCAL OR SYSTEMIC REACTIONS WITHIN 7 DAYS OF VACCINATION\textsuperscript{29}

<table>
<thead>
<tr>
<th>Reaction</th>
<th>2-dose vaccine</th>
<th>3-dose vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Post Dose</td>
<td></td>
</tr>
<tr>
<td>Local</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection site pain</td>
<td>38.5%</td>
<td>34.8%</td>
</tr>
<tr>
<td>Injection site redness*</td>
<td>4.1%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Injection site swelling*</td>
<td>2.3%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Systemic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>17.4%</td>
<td>13.8%</td>
</tr>
<tr>
<td>Headache</td>
<td>16.9%</td>
<td>12.8%</td>
</tr>
<tr>
<td>Malaise</td>
<td>9.2%</td>
<td>7.6%</td>
</tr>
<tr>
<td>Fever\textsuperscript{†}</td>
<td>1.1%</td>
<td>1.5%</td>
</tr>
</tbody>
</table>

*Redness and swelling ≥2.5 cm.
\textsuperscript{†}Oral temperature ≥100°F (38.0°C).

Please see additional Important Safety Information throughout this presentation and accompanying full Prescribing Information.
In Trial 2, the most common (>10%) local reaction was injection site pain (23%), and the most common systemic reactions were fatigue (11%) and headache (8%)\(^{29}\)

<table>
<thead>
<tr>
<th>Reaction</th>
<th>2-dose vaccine</th>
<th>3-dose vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Post Dose 1</td>
<td>Post Dose 1</td>
</tr>
<tr>
<td>Local</td>
<td>N=1952</td>
<td>N=1905</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>23.7%</td>
<td>22.8%</td>
</tr>
<tr>
<td>Injection site redness*</td>
<td>0.9%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Injection site swelling*</td>
<td>0.9%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Systemic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>12.6%</td>
<td>12.8%</td>
</tr>
<tr>
<td>Headache</td>
<td>11.8%</td>
<td>8.1%</td>
</tr>
<tr>
<td>Malaise</td>
<td>7.7%</td>
<td>7.0%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>8.5%</td>
<td>6.4%</td>
</tr>
<tr>
<td>Fever†</td>
<td>N=1923</td>
<td>N=472</td>
</tr>
<tr>
<td></td>
<td>0.6%</td>
<td>0.6%</td>
</tr>
</tbody>
</table>

\*Redness and swelling ≥2.5 cm.
†Oral temperature ≥100°F (38.0°C).

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In Trial 3, the most common (≥1%) treatment-emergent, medically attended adverse events were upper respiratory tract infections, bronchitis, sinusitis, hypertension, urinary tract infection, and back pain.

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>2-dose vaccine (N=5587)</th>
<th>3-dose vaccine (N=2781)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with ≥1 qualify MAE</td>
<td>46.0 (2569)</td>
<td>46.2 (1286)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>3.4 (192)</td>
<td>3.3 (92)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>3.2 (176)</td>
<td>3.7 (102)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>2.7 (149)</td>
<td>3.0 (84)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.4 (133)</td>
<td>2.1 (59)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>2.4 (132)</td>
<td>2.3 (64)</td>
</tr>
<tr>
<td>Back pain</td>
<td>2.1 (116)</td>
<td>1.9 (54)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>1.8 (98)</td>
<td>1.9 (54)</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>1.4 (77)</td>
<td>1.2 (32)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>1.3 (72)</td>
<td>1.0 (28)</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td>1.2 (67)</td>
<td>1.3 (37)</td>
</tr>
<tr>
<td>Cough</td>
<td>1.1 (62)</td>
<td>1.3 (37)</td>
</tr>
<tr>
<td>Acute sinusitis</td>
<td>1.1 (59)</td>
<td>1.3 (37)</td>
</tr>
<tr>
<td>Laceration</td>
<td>1.0 (54)</td>
<td>0.7 (19)</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>0.8 (45)</td>
<td>1.1 (30)</td>
</tr>
</tbody>
</table>

MAE=medically attended event.

Please see additional Important Safety Information throughout this presentation and accompanying full Prescribing Information.
Real-World Considerations For Hepatitis B Protection
Successfully vaccinating adults at risk for HBV is an ongoing challenge\textsuperscript{17}

• The purpose of HBV vaccination is to maximize seroprotection in a susceptible population\textsuperscript{17}

• Achieving this goal is influenced by 3 factors\textsuperscript{17}:

  - Conventional 3-dose HBV vaccines may be limited by poor adherence to the 6-month vaccination schedule\textsuperscript{38}

ONLY ABOUT 25% OF ADULTS AGED 19 AND OLDER ARE FULLY VACCINATED AGAINST HEPATITIS B\textsuperscript{39}
Unanimously recommended by the CDC’s ACIP, with a vote of 14 to 0.¹

“The benefits of protection with 2 doses administered over 1 month make the 2-dose vaccine an important option for prevention of hepatitis B.”¹

Abbreviation: ACIP, Advisory Committee on Immunization Practices.

Dosing and Administration

• 2-dose vaccine is administered in 2 doses at 1 month apart (1 dose each, given at 0 and 1 month)
• Each prefilled syringe (0.5 mL dose) should be administered by intramuscular injection in the deltoid region
• Do not inject intravenously, subcutaneously, or intradermally

How Supplied/Storage and Handling

• 2-dose vaccine is a single-dose prefilled syringe at 0.5 mL dose
• Stored in a refrigerator at 2°C to 8°C (35°F to 46°F). Do not freeze
• Do not use the vaccine after the expiration date shown on the label
• NDC is for 1 box that contains 5 prefilled syringes (NDC 43528-003-05)
• One case contains 20 boxes, for a total of 100 prefilled syringes; weight is approximately 3 lb

Please see additional Important Safety Information throughout this presentation and accompanying full Prescribing Information.
2-dose Vaccine: Faster and Higher Rates of Protection From Hepatitis B\textsuperscript{29}

- As many as 2.2 million people in the US are infected with hepatitis B and rates are on the rise\textsuperscript{4, 6, 7}

- Traditional 3-dose hepatitis B vaccines may leave many adults unprotected and at risk\textsuperscript{17}

- The novel 2-dose vaccine is the only 2-dose hepatitis B vaccine available for adult patients and is unanimously recommended by the ACIP\textsuperscript{35}

The most common patient-reported adverse reactions within 7 days of vaccination were injection site pain (23\%-39\%), fatigue (11\%-17\%), and headache (8\%-17\%).

Please see additional Important Safety Information throughout this presentation and accompanying full Prescribing Information.
Thank You!
Questions?
Questions for the speaker:
kmckoy@dynavax.com

To be put in contact with your local representative:
spaul@dynavax.com
References

17. FDA Advisory Committee Briefing Document: HEPLISAV-B™ [Hepatitis B Vaccine (Recombinant), Adjuvanted]. Presented at: Meeting of the Vaccines and Related Biological Products Advisory Committee; Silver Spring, MD; July 28, 2017.
References (cont’d)

The 2-dose HEPLISAV-B vaccine series only applies when both doses in the series consist of HEPLISAV-B†.

Series consisting of a combination of 1 dose of HEPLISAV-B and a vaccine from a different manufacturer should consist of 3 total vaccine doses and should adhere to the 3-dose schedule minimum intervals of 4 weeks between dose 1 and 2, 8 weeks between dose 2 and 3, and 16 weeks between dose 1 and 3. Doses administered at less than the minimum interval should be repeated†.

However, a series containing 2 doses of HEPLISAV-B administered at least 4 weeks apart is valid, even if the patient received a single earlier dose from another manufacturer†.
Indication and Important Safety Information

INDICATION

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

IMPORTANT SAFETY INFORMATION

Do not administer HEPLISAV-B 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 HEPLISAV-B, including yeast.

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

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to HEPLISAV-B.

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

The most common patient-reported adverse reactions reported within 7 days of vaccination were injection site pain (23%-39%), fatigue (11%-17%), and headache (8%-17%).