DYNAVAX
INNOVATING IMMUNOLOGY

2929 Seventh Street, Suite 100
Berkeley, California 94710

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Jude Alden, MBA, CPM
Heidi Gurov, BSN, RN
Immunization Unit
Wyoming Department of Health Public Health Division
6101 Yellowstone Road, Suite 420
Cheyenne, WY 82002

Dear Ms. Alden and Ms. Gurov,

The following information is being provided in response to your specific unsolicited request about HEPLISAV-B and "HEPLISAV-B in Previous nonresponders to Hepatitis B vaccine and data available on giving these patients a challenge dose of HEPLISAV-B."

HEPLISAV-B [Hepatitis B Vaccine (Recombinant), Adjuvanted] is indicated for prevention of infection caused by all known subtypes of hepatitis B virus. HEPLISAV-B is approved for use in adults 18 years of age and older.

Dynavax makes no recommendation on the use of HEPLISAV-B in any manner that is inconsistent with the approved labeling. Please refer to the enclosed HEPLISAV-B Package Insert for full prescribing and safety information.

HEPLISAV-B in Previous Nonresponders to Hepatitis B Vaccine

Your inquiry concerned the use of HEPLISAV-B [Hepatitis B Vaccine (Recombinant), Adjuvanted] and its use in patients who previously did not respond to a full series of a hepatitis B vaccine.

HEPLISAV-B [Hepatitis B Vaccine (Recombinant), Adjuvanted] is indicated for prevention of infection caused by all known subtypes of hepatitis B virus. HEPLISAV-B is approved for use in adults 18 years of age and older.

There are currently no adequate controlled studies of HEPLISAV-B in nonresponders or in utilizing HEPLISAV-B as a booster dose.

Halperin et al. (2013) conducted a study in 58 healthy adults 18 to 60 years of age in Canada who either did not develop seroprotection within 6 months after receiving the third injection of a standard 3-dose vaccine series of a licensed hepatitis B vaccine (primary study) or within 6 months after the last injection of 4 to 6 doses of a licensed hepatitis B vaccine (substudy). Seroprotection in the study was defined as anti-HBs concentration ≥ 10 mIU/mL.

Subjects in both the primary study and substudy were randomized in a 1:1 ratio to receive a single injection of HEPLISAV-B or Engerix-B. In the primary study, 19 subjects received HEPLISAV-B and 16 subjects received Engerix-B. In the substudy, 11 subjects received HEPLISAV-B and 12 received Engerix-B. Subjects who did not achieve a seroprotection were offered 2 additional injections with Engerix-B.

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Regarding immunogenicity, in the primary study there were no statistically significant differences in rates of seroprotection or geometric mean antibody concentrations. In the substudy, a similar proportion of subjects who received either HEPLISAV-B (63.6%) or Engerix-B (58.3%) achieved seroprotection levels ≥ 10 mIU/mL with similar rates of persistence at 26 weeks. There was a non-significant trend towards increased persistence at 52 weeks in the HEPLISAV-B group. The magnitude of immune response was significantly higher in the HEPLISAV-B group as measured by anti-HBs concentration ≥ 100 mIU/mL (54.5% vs.8.3%, p = 0.027). The geometric mean antibody concentrations was higher in the HEPLISAV-B recipients at 4 weeks (264 vs. 46.5 mIU/mL, p = 0.021) and 52 weeks (7.0 vs. 1.2 mIU/mL, p = 0.030). Three of 4 subjects compared to 2 of 7 subjects who did not respond to a single dose of HEPLISAV-B or Engerix-B, respectively responded with protective antibody levels following 2 subsequent injections with Engerix-B.

Regarding safety, both vaccines were generally well tolerated. HEPLISAV-B was associated with more injection-site tenderness (63.2% vs. 18.8%, p = 0.016 in the primary study and 81.8% vs. 15.4%, p = 0.003 in the substudy).

Thank you for your interest in HEPLISAV-B. If you have additional questions please contact Medical Information at 1-844-375-4728 or e-mail at Dynavaxmedinfo@lashgroup.com.

Kindest Regards,

Angela Henderson, RN
Dynavax Technologies Corporation
Case # DYN19-000005

ENCLOSURE

HEPLISAV-B [package insert]. Berkeley, CA: Dynavax Technologies Corporation; 2018.

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References:

HEPLISAV-B [package insert]. Berkeley, CA: Dynavax Technologies Corporation; 2018.

Halperin SA, Ward BJ, Dionne M, et al. Immunogenicity of an investigational hepatitis B vaccine (hepatitis B surface antigen co-administered with an immunostimulatory phosphorothioate oligodeoxyribonucleotide) in nonresponders to licensed hepatitis B vaccine. Human Vaccines & Immunotherapeutics. 9:7, 1438–1444; July 2013.