Hepatitis B Virus Vaccine IP Recombinant  
( Genetically Engineered) 
Enivac HB  
For intramuscular use only

DESCRIPTION

Enivac HB is a preparation of the surface antigen of the hepatitis B virus (HBV) obtained from cultures of a transformed yeast by insertion in its genome the gene coding for the surface antigen using recombinant DNA procedures. The production process of the recombinant Hepatitis B vaccine, conforms to WHO's Good Manufacturing Practices (GMP) & Good Laboratory Practices (GLP). The expression product of this gene is extracted and purified by a combination of physical, chemical and biochemical procedures. The purified surface antigen, obtained as an aggregate forming particles of approximately 22 nm is finally adsorbed on aluminium hydroxide gel (0.5 mg Al$_{3}^{3+}$/dose of 20 mcg) to which thiomersal is added as a preservative (0.05 mg/dose of 20 mcg). The final product has the appearance of a white or almost white suspension which may sediment at the bottom of the container on storage separating into two phases: a clear supernatant, essentially protein-free composed of phosphate-buffered saline (PBS) with the preservative substance dissolved in it, and aluminium-hydroxide gel with more than 98% of the antigen adsorbed. When shaken, a white or almost white suspension is formed, lasting for some minutes, which is the form in which the product should be administered.

COMPOSITION

Each dose of 20 mcg / 1.0 ml contains:

<table>
<thead>
<tr>
<th>Components</th>
<th>Composition</th>
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<tbody>
<tr>
<td>Purified Hepatitis B surface antigen protein (HBsAg) (&gt;97% purity)</td>
<td>1.0 ml/dose</td>
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<tr>
<td>Aluminium Content (Al$^{3+}$) (As Aluminium Hydroxide Gel)</td>
<td>20 mcg</td>
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<tr>
<td>Thiomersal I.P.</td>
<td>0.5 mg</td>
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<tr>
<td>Water for injection I.P.</td>
<td>0.05mg</td>
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INDICATIONS

Enivac HB is indicated for active immunization against infection by HBV and prevention of its potential consequences such as acute or chronic hepatitis, liver cirrhosis and primary carcinoma. Specially recommended for the following high risk population groups:

- Health workers in direct contact with patients. Morgue and forensic service staff.
- Students in medical and nursing schools and related technical schools in contact with patients.
- Persons who work with blood and blood products.
- Travellers going to or coming from high-risk countries or regions.
- Household contacts with positive cases.
- Handicapped persons receiving health services, persons living in institutions and community homes, and the staff of these institutions.
- Patients receiving regular blood transfusions or those affected with oncological disorders, nephropathies, cirrhosis or receiving hemodialysis or plasmapheresis among others.
- New born children of infected mothers or all new-born children in high or medium-risk countries or regions.
- Patients who will undergo elective surgery with sufficient time for seroconversion.
- Recipients of transplanted organs.
- Hemophiliacs.
- Soldiers and other military personnel on active duty.
- Prisoners, prison guards and other prison employees.
- Persons at risk of sexual contamination (e.g. promiscuous persons, male homosexuals, prostitutes and venereal-disease patients).
- Drug addicts.

CONTRAINDICATIONS

Enivac HB should not be administered to persons with pyrexia due to severe infections or those allergic to any of its components.

EFFECTIVENESS AND SAFETY

Within 15 to 30 days after the first dose of Enivac HB, a significant number of vaccinated persons may have detectable, specific antibodies. At 60 days (after second dose), more than 65 percent of all vaccinated persons have been shown to attain seroconversion, and 15 days after having received the third dose, almost 100 percent of these persons have been shown to remain completely protected for a long period of time\(^1,2,3\). 100 percent seroconversion has been reported even in severely healthcompromised thalassemic children\(^4\).

In cancer patients as well, 100 percent seroconversion was seen after 4 double doses of Enivac HB. The high level of purity of Enivac HB and the fact that it has been produced from a recombinant yeast source guarantees the absence of any risk of contamination from infective blood agents or other sources of infection.

Enivac HB does not prevent hepatitis caused by other agents different from HBV (as virus A,C and E) but it is considered effective in preventing hepatitis caused by the delta agent.

BOOSTER DOSE

The most appropriate moment for a booster or reactivation dose after having received the full vaccination protocol has not yet been established with complete accuracy, yet this booster shot should always be administered when serum concentration of the specific antibody level drops below 10 IU/ Litre (WHO/EPI/GEN/95.3). Taking into account the incubation period of the disease as well as the rapid and efficient immune response to the
administration of the vaccine Enivac HB, there is no evidence to support the need of a booster shot earlier than 10 years in immunocompetent individuals who have been adequately vaccinated.

PRECAUTIONS
On the basis of limited experiences, there is no apparent risk of adverse effects to developing fetuses when hepatitis B vaccine is administered to pregnant women. The vaccine contains noninfectious HBsAg particles and should cause no risk to the fetus. HBV infection affecting a pregnant woman may result in severe disease for the mother and chronic infection for the new born. Therefore, neither pregnancy nor lactation should be considered a contraindication to vaccination of women. [Recommendations of the Immunization Practices Advisory Committee (ACIP)]\(^6\).WHO does not recommend mixing different vaccines in one syringe before injection. As with any type of vaccine, a 1:1000 adrenaline solution must be immediately available ready for use in an unexpected and rare case of anaphylactic reaction.

WARNING
Due to the long incubation period of Hepatitis B (up to 6 months or more), cases where prior exposure to Hepatitis B Virus has taken place, vaccination may not be effective.

DO NOT ADMINISTER INTRAVENOUSLY

ADVERSE REACTIONS
Enivac HB has very low reactogenicity (1.14% only)\(^5\). Only slight local reactions such as a limited induration, erythema and pain at the site of the injection may appear in some cases; less frequent than other vaccines using the same adjuvant (aluminium hydroxide). Systemic reactions such as fever, headache, nausea and weakness may appear in a few subjects, but whether these are related to the vaccination, is doubtful and difficult to demonstrate or reject. So far, no serious side effect has been reported with Enivac HB.

INTERACTIONS WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTIONS
Have not been described.

DOSAGE AND ADMINISTRATION

- Adults : 20 mcg
- Neonates, children and adolescents upto 19 years : 10 mcg

There are two different schedules

(i) - 2 doses at 1 month interval followed by a third dose, 6 months after the first (0-1-6).

(ii) - 3 doses at 1 month interval, followed by a reactivation dose a year later (0-1-2 + 12).

This schedule is recommended in cases where there is a high risk of infection.

The preparation should be administered by deep intramuscular injection in the deltoid region in adults and the anterolateral region of the thigh in neonates. (WHO/EPI/GEN/95.3). The buttock should not be used routinely as an immunization site for infants, children or adults because of the risk of injury to the sciatic nerve. Other forms of administration are not recommended by the EPI (WHO).

In immunosuppressed patients, protective levels of antibodies may not be attained, so
higher doses (usually twice the normal dose) may be necessary.

**Dosage recommendation for haemodialysis patients:** Immunization schedule for hemodialysis patients is 4 doses of 40 mcg (2 X 20 mcg/vaccine dose) to be administered at intervals of 0, 1, 2 and 6 months.\(^7\)

**Dosage recommendation for subjects above age of 40 years:** An open labelled study conducted in subjects above the age of 40 years showed that seroprotective response was up to 85% which became 100% after a 4\(^{th}\) dose taken 6 months after the third dose of the 0-1-6 schedule.\(^3\)

**STABILITY AND STORAGE**

Enivac HB preparation remains stable for three years if stored at 5°C ± 3°C.

- Short exposures to room temperature (25-30°C) do not affect the shelf life of Enivac-HB but storage and transportation should be carried out at 5°C ± 3°C.

**DO NOT FREEZE, discard the vaccine if frozen.**

**SHAKE WELL BEFORE USE.**

**PRESENTATION**

- Uniject Safsy: Prefilled ready to use device of 20 mcg /1.0 ml

**REFERENCES**


