Size 95 x 245 mm (Front)

Hepatitis B Vaccine (rDNA) IP
(A Recombinant Vaccine)

EnivacHB

Proven Efficacy, Assured Protection

1. NAME AND DESCRIPTION OF THE MEDICINAL PRODUCT

EnivacHB, Hepatitis B Vaccine (rDNA) BP is a uniform suspension (after shaking) free from any extraneous particles. The vaccine contains Hepatitis B surface antigen adsorbed on aluminium hydroxide gel which is further suspended in Phosphate buffer saline to which thiomersal is added as a preservative. The Hepatitis B surface antigen (HBsAg) is produced from culture of genetically-engineered yeast cells (*Pichia pastoris*) which carries the gene coding for the major surface antigen of the Hepatitis B Virus (HBV). The production process of EnivacHB vaccine complies with WHO recommendations. The final vaccine is presented in USP type 1 glass vials closed with bromobutyl rubber stoppers and flip-off seal.

2. COMPOSITION

	Paediatric Dose Each 0.5 ml contains	Adult Dose Each 1.0 ml contains
Purified Surface Antigen (HBsAg)	10 mcg	20 mcg
Aluminium content (Al^{3+}) (As Aluminium Hydroxide gel)	0.25 mg	0.50 mg
Thiomersal	0.025 mg	0.05 mg
Phosphate Buffer Saline	q.s. to 0.5 ml	q.s. to 1.0 ml
Produced in *Pichia pastoris*		

3. PHARMACEUTICAL FORM

Suspension for injection.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

EnivacHB is indicated for immunization against infection caused by Hepatitis B virus.

EnivacHB is recommended for neonates, infants and young adults for routine vaccination and also recommended for following High-risk population groups:

- Health care personnel in direct contact with patients (Physicians, surgeons, dentists, nurses, first aid, ambulance and cleaning personnel etc.).
- Students in medical, dental and nursing school in contact with patients.
- People who work with blood or blood products.
- A Thalassaemic / Haemophilic / Other patient who receives blood transfusion.
- Haemodialysis and organ transplant recipients.
- Military personnel on active duty.
- Prisoners, prison guards and other prison employees.
- Persons living in institutions, community homes, and the staff of these institutions.
- Household contacts and sexual partners of infected persons.
- Newborn children of infected mothers.
- Persons at increased risk of disease due to their sexual practices such as promiscuous persons, male homosexuals, prostitutes and venereal disease patients.
- Injectable drug abusers.
- Travellers going to and coming from high-risk countries or regions.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

For neonates, infants and adolescent below the age of 19 years the recommended dosage of **EnivacHB** is 10 mcg of antigen protein in 0.5 mL suspension.

For adult over the age of 19 years, the recommended dosage of **EnivacHB** is 20 mcg of antigen protein in 1 mL suspension.

PRIMARY IMMUNIZATION SCHEDULE:

Indian Academy of Pediatrics recommends as follows for children:

- At Birth
- At 6 weeks of age
- At 10 weeks of age
- At 14 weeks of age

The final dose is administered not earlier than 24 weeks and at least 16 weeks after the first dose,

- As per Universal Immunization Program, Hepatitis B vaccine is provided as part of pentavalent vaccine at 6, 10 and 14 weeks apart from birth dose.
- **Adults:** An interval of 30 days given between the administration of the FIRST and SECOND doses, followed by the THIRD dose 180 days after the first dose.

SPECIAL RECOMMENDATIONS:

To neonates born to HBV infected mothers the recommended pediatric dose schedule:

- 1st dose on selected date
- 2nd dose 30 days after the first dose
- 3rd dose 60 days after the first dose
- One booster dose to be administered 1 year after the first dose

Immuno-compromised patients will require additional dose as per schedule given:

- 1st dose of 40µg(2mL) on the first day
- 2nd dose of 40µg(2mL), 30 days after the first dose
- 3rd dose of 40µg(2mL), 60 days after the first dose
- 4th dose of 40µg(2ml), 180 days after the first

EnivacHB should be shaken before use to homogenize the suspension. The vaccine should be injected intramuscularly.

EnivacHB should be injected intramuscularly into the deltoid region in adults and the anterolateral aspect of thigh in neonates, infants and young children.

EnivacHB should not be given in the gluteal region, as the immune response may be lower.

EnivacHB should be injected intramuscularly. IT SHOULD NOT BE GIVEN INTRAVENOUSLY.

4.3 CONTRAINDICATION

EnivacHB should not be administered to

- Persons who are hypersensitive to any component of the vaccine or to subjects who have shown signs of hypersensitivity after previous **EnivacHB** vaccination.
- Subjects with severe febrile infections.

4.4 SPECIAL WARNING AND PRECAUTION FOR USE

Special Warning

Immune response is generally weaker for the people over 40 years or age, obese individuals, subjects with immuno-deficiency or those receiving immunosuppressive therapy, Thus adequate anti-HBs antibody titres may not be obtained after primary immunisation course. In such subjects/ patient's additional doses of vaccine may be required.

The vaccine does not prevent infection by hepatitis A, Hepatitis C, Hepatitis D, Hepatitis E or other pathogens known to infect the liver. If the individual is already a carrier of Hepatitis B virus with or without disease he may not respond to vaccine. However the vaccine has not been shown to have any deleterious effects.

Precautions

As with any injectable vaccine, epinephrine should be available for use in case of anaphylaxis or anaphylactic reaction.

The vaccine should be well shaken before use.

In presence of minor infection EnivacHB to be used only when clearly needed, and the possible advantage outweighs the possible risks.

4.5 INTERACTIONS WITH OTHER MEDICINAL PRODUCTS

Hepatitis B vaccine can be co-administered with DTP, DT and/ or OPV. Hepatitis B vaccine can be co-

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administered together with measles mumps-rubella vaccines, *Haemophilus influenzae* b vaccine, Hepatitis A vaccine, BCG and yellow fever vaccine.

EnivacHB should always administer at a different injection site in the event of its use along with other vaccines using separate needles and syringe.

EnivacHB can be used, for primary vaccination as well as for booster doses interchangeably with plasma derived or other rDNA based hepatitis B vaccines.

4.6 PREGNANCY AND LACTATION

Safety and effectiveness have not been established in pregnant women and nursing mothers. However the decision to immunize pregnant and lactating mothers may be taken by the physician in the context of case specific high-risk factors.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effect of **EnivacHB** on ability to drive and use machines have been performed.

4.8 UNDESIRABLE EFFECTS

EnivacHB is generally well tolerated.

In a randomized, multicentric, comparative clinical study of **EnivacHB** in healthy infants very common (≥ 1/10) adverse reactions were pain at injection site and fever. In common (≥ 1/100 to <1/10) adverse reactions were redness, lump & swelling at injection site, fussiness, restlessness, loss of appetite, vomiting, diarrhoea and sleepiness.

In a clinical trial of **EnivacHB** in adults, only pain at injections site was very common adverse reaction.

Following widespread use of the vaccine with the exception of local pain, reported events such as myalgia and transient fever have not been more frequent. Reports of severe anaphylactic reactions are very rare. Available data do not indicate a causal association between Hepatitis B vaccine and Guillain-Barre syndrome, or demyelinating disorders including multiple sclerosis, nor is there any epidemiological data to support a causal association between Hepatitis B vaccination and chronic fatigue syndrome, arthritis, autoimmune disorders, asthma, sudden infant death syndrome, or diabetes.

In case you experience any undesirable effect following intake of this medication please feel free to contact us at any of the following contact details: e-mail id: pvg@panaceabiotec.com; Fax no.: +91-11-41578085; M. No. +91-9650138282.

4.9 OVERDOSE

No case of overdose has been reported

5. PHARMACOLOGICAL PROPERTIES

5.1 PHAMACODYNAMIC PROPERTIES

EnivacHB generates specific protective immune response against HBsAg. For protection against HBV infection the anti-HBsAg titre (Anti HBs antibodies) should be ≥ 10 mIU/mL.

Immunogenicity Data

In a clinical study, conducted in 751 infants, immunogenicity of **EnivacHB** vaccine was evaluated in 6, 10, 14 weeks dose schedule. The seroprotection rate was 100% for **EnivacHB** and 94.9% for reference vaccine.

In a clinical study, conducted in 52 high risk adults, immunogenicity of **EnivacHB** vaccine was evaluated in 0, 1 & 2 months schedule. The seroconversion rate for **EnivacHB** was 100% while seroprotection was 97.87%.

5.2 PHARMACOKINETIC PROPERTIES

Not Applicable

5.3 PRE-CLINICAL SAFETY DATA

Acute toxicity of recombinant Hepatitis B vaccine was tested in Swiss mice, guinea pigs and rabbits in three parts study viz; Acute toxicity, single dose toxicity and pharmacodynamics and local tolerance. The study results indicated that Hepatitis B vaccine administered at the tested dosages was not toxic to mice, guinea pigs and rabbits.

6. PHARMACEUTICAL PARTICULARS

6.1 INCOMPATIBILITIES

No incompatibility studies were conducted with **EnivacHB.**

6.2 SHELF LIFE

36 months from the date of manufacturing when stored at 5°C ± 3ºC.

6.3 SPECIAL PRECAUTIONS FOR STORAGE

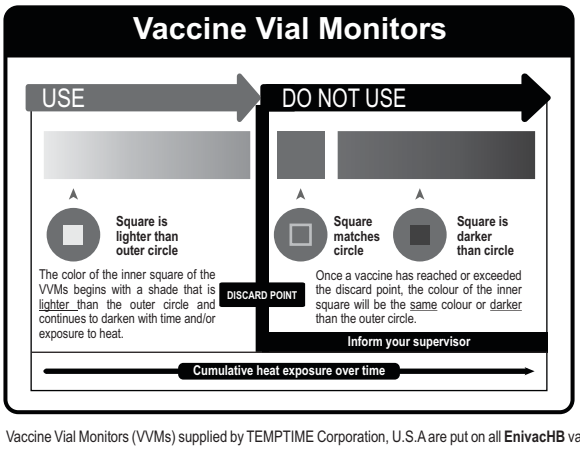
DO NOT FREEZE. Discard vial if contents are frozen. Stored and transported between 5°C ± 3ºC.

7. PRESENTATION

Single Pediatric dose vial containing 0.5 ml vaccine.

Single adult dose vial containing 1 ml vaccine.

Figure of the Vaccine Vial Monitor (VVM)



Vaccine Vial Monitors (VVMs) supplied by TEMPTIME Corporation, U.S.A are put on all **EnivacHB** vaccine vials. The colour dot which appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple. "Focus on the central square". If the colour of this square is lighter than the colour of the circle, the vaccine can be used. If the colour of the central square is same as that of the circle or of darker than the circle, the vaccine vial should be discarded.

PMPIS095

Manufactured by:
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Panacea Biotec
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