1. NAME OF THE MEDICINAL PRODUCT:

Hepatitis-B Vaccine (rDNA) I.P.

Brand Name: GeneVac-B®

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each dose of 0.5 ml (Pediatric) contains :-

10 mcg of purified Hepatitis B surface antigen*

Adsorbed on Aluminium hydroxide (Al^{+++}) 0.25 mg to 0.40 mg

Preservative: Thiomersal 0.005%

*Produced in *Hansenula polymorpha* (yeast)

Each dose of 1 ml (Adult) contains :-

20 mcg of purified Hepatitis B surface antigen*

Adsorbed on Aluminium hydroxide (Al^{+++}) 0.50 mg to 0.80 mg

Preservative : Thiomersal 0.005%

*Produced in *Hansenula polymorpha* (yeast)

3. PHARMACEUTICAL FORM

Suspension for Injection.

GeneVac-B (Hepatitis B Vaccine (rDNA) I.P.) is a non infectious recombinant DNA Hepatitis B Vaccine. It contains purified surface antigen of the virus obtained by culturing genetically-engineered *Hansenula polymorpha* yeast cells having the surface antigen gene of the Hepatitis B virus. The Hepatitis B surface antigen (HBsAg) expressed in the cells of Hansenula polymorpha is purified through several chemical steps and formulated as a suspension of the antigen adsorbed on aluminium hydroxide and thiomersal is added as preservative. The vaccine does not contain any material of human or animal origin.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

GeneVac-B is indicated for active immunisation against Hepatitis B virus (HBV) infection in subjects considered at risk of exposure to HBV-positive material.

Immunisation against hepatitis B is expected in the long term to reduce not only the incidence of this disease, but also its chronic complications such as chronic active hepatitis B and hepatitis B associated cirrhosis and primary hepatocellular carcinoma.

- In areas of low prevalence of hepatitis B, immunisation with Hepatitis-B vaccine (rDNA) is recommended for neonates/infants and adolescents as well as for subjects who are, or will be, at increased risk of infection such as:
- Health Care Personnel
- Patients receiving frequent blood products.
- Personnel and residents of institution.
- Persons at increased risk due to their sexual behavior.
- Illicit users of addictive injectable drugs.
- Travelers to areas with a high endemicity of HBV.
- Infants born of mothers who are HBV carriers.
- Persons originating from areas with a high endemicity of HBV.
- Others: Police personnel, fire brigade personnel, armed forces personnel and anybody who through their work or personal lifestyle may be exposed to HBV.
- Household contacts of any of the above groups and of patients with acute or chronic HBV infection.

In areas of intermediate or high prevalence of hepatitis B, with most of the population at risk of acquiring the disease, immunisation should be offered to all neonates and young children. Immunisation should also be considered for adolescents and young adults.

4.2 Posology and method of administration

Paediatric dose vaccine: 10 mcg dose (in 0.5 ml suspension) is recommended for neonates, infants, children and adolescents upto 19 years of age.

Adult dose vaccine: 20 mcg dose (in 1.0 ml suspension) is recommended for adults aged 20 years and above.

Immunisation Schedule:

Primary immunisation: A series of three intramuscular injections is required to achieve optimal protection.

The following immunisation schedules can be recommended.:

- 6,10,14 weeks for infants
- 0,1,6 months
- 0,1,2 months (rapid schedule)

The immunisation schedule should be adapted to meet local immunisation recommendations.

Booster dose

The need for the booster dose in healthy individuals who have received the full primary immunization, is not recommended. It would seem advisable to recommend a booster dose when Anti-HBs antibody titres fall below 10 IU/L for all people at risk and especially for patients who are immunocompromised (HIV infected patients) or those on haemodialysis. Hepatitis B vaccine (rDNA) can be administered with DTPw vaccine of SIIPL at separate site alone or as a combination vaccine i.e. DTPwHB (SIIPL).

Special Dosage Recommendations:
Dosage recommendation for neonates born of mothers who are HBV carriers

The 0, 1, 2 month immunisation schedule is recommended, and should start at birth. Concomitant administration of Hepatitis B immunoglobulin is not necessary, but when Hepatitis B immunoglobulin is given simultaneously with Hepatitis B vaccine (rDNA) a separate injection site must be chosen.

Dosage recommendation for known or presumed exposure of HBV

In circumstances where exposure to HBV has recently occurred (e.g. needles stick with contaminated needle) the first dose of Hepatitis B vaccine (rDNA) can be administered simultaneously with Hepatitis B immunoglobulin which however must be given at a separate injection site. The rapid immunisation schedule should be advised.

Dosage recommendation for immunocompromised persons

The primary immunisation schedule for chronic haemodialysis patients or persons who have an impaired immune system is four doses of 40 mcg at 0, 1, 2 and 6 months from the date of first dose. The immunisation schedule should be adapted in order to ensure that the anti-HBs antibody titre remains above the accepted protective level of 10 IU/L.

Method of Administration

Hepatitis-B Vaccine (rDNA) should be injected intramuscularly in the deltoid region in adults and children or in the anterolateral thigh in neonates, infants and young children. The vaccine

may be administered subcutaneously in patients with thrombocytopenia or bleeding disorders. The vaccine should be well shaken before use. Only sterile needle and syringes should be used for each injection.

The vaccine should be visually inspected for any foreign particulate matter and /or variation of physical aspect prior to administration. In event of either being observed discard the vaccine.

4.3 Contraindications

GeneVac-B should not be administered to subjects with known hypersensitivity to any component of the vaccine, or to subjects having shown signs of hypersensitivity after previous Hepatitis B Vaccine administration.

4.4 Special warnings and precautions for use

Because of the period of latency of hepatitis B infection it is possible for unrecognized infection to be present at the time of immunisation. The vaccine may not prevent hepatitis B infection in such cases.

The vaccine will not prevent infection caused by other agents such as hepatitis A, hepatitis C and hepatitis E and other pathogens known to infect the liver.

The immune response to Hepatitis B vaccines is related to age. In general, people over 40 years of age respond less well.

In haemodialysis patients and persons with an impaired immune system, adequate anti-HBs antibody titres may not be obtained after the primary immunisation course and such patients may therefore require administration of additional doses of vaccine (see Dosage recommendation for Immunocompromised persons).

As with all injectable vaccines, appropriate medication (e.g. adrenaline) should always be readily available for treatment in case of rare anaphylactic reactions following the administration of the vaccine.

Special care should be taken to ensure that the injection does not enter a blood vessel.
Hepatitis B vaccine (rDNA) should not be administered in the gluteal muscle or intradermally since this may result in a lower immune response.

Hepatitis B vaccine (rDNA) may be used to complete a primary immunisation course started either with plasma- derived or with other genetically-engineered hepatitis B vaccines, or as a booster dose in subjects who have previously received a primary immunisation course with plasma-derived or with other genetically-engineered hepatitis B vaccines.

4.5 Interaction with other medicinal products and other forms of Interaction

The vaccine can be safely and effectively given simultaneously but at different injection site with DTP, DT, TT, BCG, Polio vaccine (OPV and IPV) and yellow fever vaccine, *Haemophilus influenzae* type b and vitamin A supplementation. It should not be mixed in the vial or syringe with any other vaccine.

4.6 Pregnancy and lactation

Adequate human and animal data on use during pregnancy and lactation is not available

4.7 Effects on ability to drive and use machines

Effect of Hepatitis B vaccine on the ability to drive and use of machines is not known.

4.8 Undesirable effects

The undesirable events are temporally related to the administration of Hepatitis B Vaccine. They are usually mild and confined to the first few days of the vaccination. The most common reactions are mild soreness, erythema, induration, fatigue, fever, malaise, influenza-like symptoms. Less common systemic reactions include nausea, vomiting, diarrhoea, abdominal pain, abnormal liver function tests, arthralgia, myalgia, rash, pruritus, urticaria.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Viral Vaccines

Hepatitis B, purified antigen, ATC code: J07BC01.

Hepatitis-B vaccine (recombinant) stimulates active immunity to hepatitis-B virus (HBV) infection. Hepatitis B surface antigen (HBsAg), which is present in hepatitis-B vaccine (recombinant), promotes the production of antibody to HBsAg (anti-HBs); anti-HBs neutralizes the HBV so that its infective or pathogenic properties are inhibited.

Administration of hepatitis B vaccine (recombinant) during the incubation period of infection (i.e. after exposure to hepatitis B virus but prior to onset of clinical symptoms) may only modify or ameliorate, rather than prevent infection.

The active immune response produced by hepatitis B vaccine (recombinant) does not appear to be suppressed by hepatitis B immune globulin (HBIG) when HBIG is administered concomitantly at separate sites.

Immunological Data:

Various clinical trials performed to assess Immunogenicity and reactogenicity of the vaccine proved that the vaccine is immunogenic. In various populations, following Hepatitis B vaccination, the seroprotection ranges from 95.6 - 100% in adults, 81.81 – 90.74% in adults with chronic renal failure, 100% in children and adolescents, and 94.36 - 100% in infants.

5.2 Pharmacokinetic properties

Pharmacokinetic studies are not required for vaccines.

5.3 Preclinical safety data

Single- and repeated-dose toxicity studies of Hepatitis B vaccine have been done in Swiss albino mice and Wistar rats by intramuscular administration. The vaccine in single- and repeated-dose toxicity studies in both the species had no effects on their general health. There were no changes in body temperature, cumulative net body weight gains and hematological, clinical chemistry and urinalysis parameters in animals of either sex. No gross or microscopic histopathological changes were detected. Preclinical data reveals no special hazard for humans based on general safety studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium hydroxide (Al^{+++}), Thiomersal

6.2 Incompatibilities

The vaccine should not be mixed in the vials or syringe with any other vaccine unless it is manufactured as combined product (e.g. DTP-HB).

6.3 Shelf life

36 months.

6.4 Special precautions for storage

The vaccine should be stored at 2^0C to 8^0C. Protect from light. Do not freeze.

Discard if vaccine has been frozen.

6.5 Nature and contents of container

Vials (adult or Paediatric):

Material	Suppliers	Size
Type 1, clear tubular glass	Kaisha Manfacturers Pvt., Ltd., Daman Tube Glass Containers Pvt., Ltd., Badalapur.	5 mL (fill vol. 5.0 mL) 13 mm neck 40 mm ht. 16.5 mm dia.
Rubber stopper Grey (Bromobutyl)	Helvoet Pharma, Belgium West Pharmaceutical Services, Singapore	13 mm
Aluminium flip-off seal For pediatric (Pentone process blue colour)	Autofits Ltd., Nashik.	13 mm
Aluminium flip-off seal for Adult (Pentone process green colour)	Autofits Ltd., Nashik.	13 mm

Amopules (adult or pediatric):

Material	Suppliers	Size
Type 1, clear tubular glass ampoule, white colour break for 0.5 to 1.0 mL product)	Kaisha Manufacturers Pvt., Ltd., Daman	-1.0 mL (1.8 mL shoulder capacity) -65 mm ht. -10.25 mm dia.

6.6 Special precautions for disposal

Once vaccine has been administered, the injection equipment and vaccine containers should be disposed of according to the standard procedures for medical waste.

7. MARKETING AUTHORISATION / PREQUALIFICATION HOLDER

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Telephone: ++ 91-20- 26993900
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Website: www.seruminstitute.com

8. MARKETING AUTHORISATION NUMBER(S)

Drug Mfg. License. No. 10 (in Form 28-D)

Hepatitis B Vaccine (rDNA) (Adult) Permission No: MF/BIO/19/000009 in Form 46

Hepatitis B Vaccine (rDNA) (Paediatric) Permission No: MF/BIO/19/000008 in Form 46

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorization: 21.07.2000

Date of last renewal Hepatitis B Vaccine (rDNA) (Adult): 19th February 2019

Date of last renewal Hepatitis B Vaccine (rDNA) (Paediatric): 19th February 2019

Date: 31 December 2022