SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Hepatitis B Vaccine (rDNA) (Paediatric)
Hepatitis B Vaccine (rDNA) (Adult)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 0.5 ml 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)
Dose: 0.5 ml by intramuscular injection

3 PHARMACEUTICAL FORM

Suspension for injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Hepatitis B vaccine is indicated for active immunisation against hepatitis B 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 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 behaviour.
- Illicit users of addictive injectable drugs.
- Travellers to areas with a high endemicity of HBV.
- Infants born of mothers who are HBV carries.
- 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.

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.

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 not necessary, but when Hepatitis B immunoglobulin is given simultaneously with Hepatitis B vaccine 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 (eg needle stick with contaminated needle) the first dose of Hepatitis B vaccine 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.

METHOD OF ADMINISTRATION.
Hepatitis B vaccine (rDNA) should be injected intramuscularly in the deltoid region in children above 2 years of age 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. Once opened, multi-dose vials should be kept between +2ºC and +8ºC. Multi-dose vials of Hepatitis B from which one or more doses of vaccine have been removed during an immunisation session may be used in subsequent immunisation sessions for upto a maximum of 28 days, provided that all of the following conditions are met (as described in the WHO policy statement: Handling of multi dose vaccine vials after opening, WHO/IVB/14.07):

- The vaccine is currently prequalified by WHO;

- The vaccine is approved for use for up to 28 days after opening the vial, as determined by WHO;
- The expiry date of the vaccine has not passed;
- The vaccine vial has been, and will continue to be stored at WHO or manufacturer recommended temperatures; furthermore, the vaccine vial monitor, if one is attached, is visible on the vaccine label and is not past its discard point, and the vaccine has not been damaged by freezing.

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.

IMMUNE DEFICIENCY
Individuals infected with human immuno-deficiency virus (HIV), both asymptomatic and symptomatic, should be immunized with hepatitis B vaccine according to standard schedules.

4.3 Contraindications

Hepatitis B vaccine 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 unrecognised 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 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.
Hepatitis B vaccine should not be administered in the gluteal muscle or intradermally since this may result in a lower immune response.
Hepatitis B vaccine 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, Measles, Polio vaccine (OPV and IPV), yellow fever vaccine and vitamin A supplementation. It should not be mixed in the vial or syringe with any other vaccine unless it is manufactured as a combined product (e.g. DTP-HepB).

4.6 Fertility, 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, Phosphate Buffer Saline (10 mM) (Disodium Hydrogen Phosphate Anhydrous, Sodium dihydrogen phosphate dihydrate, Sodium chloride)

6.2 Incompatibilities

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

6.3 Shelf life

Thirty-six months from the date of manufacture.

6.4 Special precautions for storage

Hepatitis B vaccine (rDNA) should be stored at 2 - 8ºC. DO NOT FREEZE. Discard if vaccine has been frozen.

6.5 Nature and contents of container

0.5 ml - Single dose vial (Paediatric)
5 ml - 10 doses vial (Paediatric)

6.6 Special precautions for disposal and other handling

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 HOLDER

SERUM INSTITUTE OF INDIA PVT. LTD.
212/2, Hadapsar, Pune 411028, INDIA

8. MARKETING AUTHORISATION NUMBER(S)

15337
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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10. DATE OF REVISION OF THE TEXT