### 1.6.1 Prescribing Information (Summary of Product Characteristics)

## 1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

**Hepatitis-B Vaccine (rDNA) (Adult) - Single Dose**

## 2. QUALITATIVE AND QUANTATIVE COMPOSITION

| | |
|---|---|
| Each dose of 1 ml contains | |
| Purified Hepatitis B Surface Antigen. | 20 mcg |
| Adsorbed on Aluminum Hydroxide ($Al^{+++}$) | 0.50 mg to 0.80mg |
| Preservative: Thiomersal | 0.005 % |
| Produced in *Hansenula polymorpha* (yeast) | |

## 3. PHARMACEUTICAL FORM

Suspension for injection

## 4. CLINICAL PARTICULARS

## 4.1 Therapeutic indication

Hepatitis-B vaccine is indicated for active immunization against Hepatitis B infection in subjects considered at risk of exposure to HBV-positive material

## 4.2 Posology and method of administration

**Dose –** 20 mcg dose (in 1ml suspension) is recommended for adults aged 20 years and above.

**IMMUNIZATION SCHEDULE**

Primary immunization. - A series of three intramuscular injections is required to achieve optimal protection.
The following immunization schedules can be recommended:
- 0, 1, 6 months
- 0, 1, 2 months (rapid schedule)

The immunization schedule should be adapted to meet local immunization 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 advisiable to recommend a booster dose when Anti-HBs antibody titres fall below 10IU/L for all people at the risk and especially for patients who are immunocompromised (HIV infected patients) or those on haemodialysis.

SPECIAL DOSAGE RECOMMENDATIONS :

*DOSAGE RECOMMENDATIONS FOR NEONATES BORN OF MOTHERS WHO ARE HBV CARRIERS.*
The 0, 1, 2 month immunization 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, 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. needlestick 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 immunization schedule should be advised.

*DOSAGE RECOMMENDATION FOR IMMUNOCOMPROMISED PERSONS:*
The primary immunization 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 immunization schedule should be adapted in order to ensure that the anti-HBs antibody titre remains above the accepted protective level of 10 IU/L

## 4.3 Method of Administration

Hepatitis-B vaccine should be injected intramuscularly in the deltoid region in adults. 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.

## 4.4 Contraindication

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.

## 4.5 Special Warning and Precaution

Because of the period of latency of hepatitis B infection it is possible for unrecognized infection to be present at the time of immunization. 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 vaccine 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 immunization 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 immunization 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 immunization course

with plasma derived or with other genetically engineered hepatitis B vaccines.

## 4.6 Interaction With other Medicinal Products, Other Interactions

**Hepatitis B Immune Globulin**

Passively acquired antibody to hepatitis B surface antigen (anti-HBs), which is present in hepatitis B immune globulin (HBIG), does not appear to interfere with the active immune response stimulated by hepatitis B vaccine (recombinant). Clinical studies in neonates indicate that the immune response to the recombinant vaccine is not altered by the concomitant use of HBIG.

**Haemophilus. b Conjugate Vaccines**

Hepatitis B vaccine may be administered concomitantly with haemophilus b conjugate vaccine; however the vaccines should be administered separately at a different site. Hepatitis B vaccine should not be mixed extemporaneously with any haemophilus b conjugate vaccine.

**Other Vaccines**

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.

**Immunosuppressive Agents**

Individuals receiving immunosuppressive therapy may require larger than usual doses of hepatitis B vaccine (recombinant) in order to develop adequate circulating antibody levels.

## 4.7 Pregnancy and Lactation

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

## 4.8 Effects On Ability To Drive And Use Machines

Adult has no or negligible influence on the ability to drive and use machines.

## 4.9 Adverse Reactions

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 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, liver function.

## 4.10 Overdose

No case of overdose has been reported

# 5. PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Viral Vaccine 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.

## 5.2 Pharmacokinetics Properties

Pharmacokinetic studies are not required for vaccines.

## 5.3 Preclinical Safety Data

Preclinical data reveals no special hazard for humans based on general safety studies.
It reveals:

1) Hepatitis B vaccine at the dose of 80 µg/kg in mice during the acute toxicity study doesn't show any sign and symptoms of toxicity. None of the animals died during the observation period. Hence Hepatitis B vaccine is safe in Swiss Albino mice.
2) Subacute toxicity study revealed that Hepatitis B vaccine has not affected Albino Wistar rats as evident from body weight, feed and water intake. The result in control group are comparable with treated groups. The differences observed are statistically significant.
3) No significant change in the blood chemistry and haematological parameters observed in treated groups.
4) No abnormality was observed with urine analysis in control and treated groups.
5) Histopathological study revealed no gross pathological lesions in treated groups.
6) The Hepatitis B vaccine is safe, an evident from the safety test in mice and guinea pigs according to USP 1995.
7) Based on the above facts, the Hepatitis B vaccine is safe for the doses specified in the species studied.

## 6.0 PHARMACEUTICAL PROPERTIES

### 6.1 List of Excipients

Aluminium Hydroxide gel; Thiomersal; Phosphate Buffer Saline (10mM) (Disodium Hydrogen Phosphate Anhydrous, Sodium dihydrogen Phosphate dihydrate, Sodium chloride)

### 6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

### 6.3 Shelf Life

36 months from date of manufacture

### 6.4 Special Precautions for storage

Hepatitis -B vaccine should be stored at +2°C to +8°C. Do not Freeze. Discard if vaccine has been frozen.

### 6.5 Nature and Contents of Packaging

**Single dose** 1ml of suspension in a 1ml Type I clear, Tubular colourless ampoule

**Ampoule** : with white colour OPC dot.65 mm height. 10 ampoules in blister pack.10x 5 = **50 ampoules per box.**

**Single dose Vial:** 1 ml of suspension in a 4 ml tubular flint vial (type I glass) with a gray plain bromobutyl rubber stopper and aluminium flip off cap. Box of 50 vials.

## 6.6 Instructions regarding the preparation of medicinal products for its use and handling

- The vaccine should be well shaken before use. Only sterile needle and syringes should be used for each injection.

## 1.7 MARKETING AUTHORIZATION HOLDER

**SERUM INSTITUTE OF INDIA PVT LTD**
**212/2, HADAPSAR, PUNE-411028. INDIA.**
**TELEPHONE: ++ 91-20-26993900/04/26602363**
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## 1.8 NUMBER IN THE REGISTER OF MEDICINAL PRODUCTS

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## 1.9 DATE OF AUTHORIZATION OR LAST RENEWAL OF AUTHORIZATION

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## 1.10 DATE OF REVISION OF TEXT

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## 1.11 DOSIOMETRY

Not Applicable.

## 1.12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not Applicable.