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Prescribing Information for a Registered Medical Practitioner

हेपेटाइटिस-बी वैक्सीन (आर डी एन ए)आई पी

# Hepatitis B Vaccine (rDNA) IP

## Revac-B*mcf*® रिवैक–बी एम सी एफ®

Thiomersal Free

### 1 NAME AND DESCRIPTION OF THE MEDICINAL PRODUCT

**Revac-B *mcf*®** is a sterile suspension containing purified, non-infectious major surface antigen of Hepatitis B virus and is manufactured by recombinant DNA technology. The antigen is adsorbed onto high affinity aluminum hydroxide gel molecules and hence the suspension appears almost white and translucent.

**Revac-B *mcf*®** fulfills WHO Requirements for Hepatitis-B Vaccine made by recombinant DNA technology

**RECOMBINANT TECHNOLOGY**

The Hepatitis-B surface Antigen (HBsAg) is produced in genetically engineered yeast cells of *Pichia pastoris* which carry the gene that codes for the major surface antigen protein of the Hepatitis-B virus. HBsAg expressed in yeast cells is purified by complex physical, chemical and biochemical processes. The resultant highly purified surface antigen assembles spontaneously into spherical particles of an average diameter of 20-24nm containing non-glycosylated polypeptides in a lipid matrix. An extensive and rigorous R&D processes characterized and confirmed that these 20-24nm spherical particles resemble the natural HBsAg protein in their antigenic properties. The efficacy and safety of the formulated **Revac-B *mcf*®** is ensured through stringent adherence to the highest standards of bio-process control and consistent Quality Assurance measures. No substance of human origin is used in the manufacture of HBsAg protein.

### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition : Each pediatric dose of 0.5 mL vial contains:

| | |
|---|---|
| Hepatitis B surface Antigen (HBsAG) | ≥10 µg |
| Aluminum hydroxide gel equivalent to Aluminum ($Al^{+++}$) | 0.25 mg |
| Phosphate buffered saline | q.s to 0.5 mL |

Composition: Each Adult dose of 1.0 mL vial contains:

| | |
|---|---|
| Hepatitis B surface Antigen (HBsAG) | ≥20 µg |
| Aluminum hydroxide gel equivalent to Aluminum ($Al^{+++}$) | 0.5 mg |
| Phosphate buffered saline | q.s to 1.0 mL |

### 3 PHARMACEUTICAL FORM

Suspension for Injection

### 4 CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATIONS

**Revac-B *mcf*®** is indicated for immunization of persons against infection by Hepatitis B virus. It can also be administered to Hepatitis Cand D virus infected patients to protect them against co-infection with Hepatitis B virus.

**Revac-B *mcf*®** is recommended primarily for neonates, infants and young adults not only for the prevention of the disease but also to protect them from probable Hepatitis B virus induced carrier state, cirrhosis and hepatic cellular carcinoma

In addition, for various groups of individuals as listed below **Revac-B *mcf*®** immunization is an essential requirement:

- Partners or people infected with Hepatitis B
- Patients prone to infection due to unscreened or improperly tested blood transfusions
- Men who have sex with men
- People with chronic liver or kidney disease
- Hemophiliacs and patients on hemodialysis.
- Travelers to specified high endemic areas.
- Residents in high endemic area.
- Drug addicts
- Personnel and residents of community homes or hostels
- Household contacts of persons with acute or chronic HBV infection
- Infants born to HBV carrier mothers and immune-compromised neonates

**Revac-B *mcf*®** is specifically advantageous for babies with neuro-developmental disorders and possible neuro-suppressant complications. It also allows normal immunization for low birth weight and preterm infants, which otherwise might be delayed.

### 4.2 POSOLOGY, SCHEDULE AND METHOD OF ADMINISTRATION

- 20µg/1 mL is the dose for adult and children above 10 years of age.
- 10µg/0.5mL is recommended for neonates, infants and children below 10 years of age.

**PRIMARY IMMUNIZATION SCHEDULE:**

Indian Academy of Pediatrics recommends as follows for children:

- At Birth
- At 6 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 dose

**METHOD OF ADMINISTRATION**

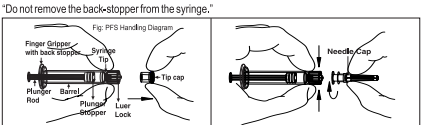
- **Revac-B *mcf*®** should be injected intramuscularly into the deltoid region in adults and in the Antero-lateral aspect of thigh in neonates Infants and young children.
- **Revac-B *mcf*®** should not be injected into the gluteal muscle. This route of administration may result in lower immune response. Under no circumstance **Revac-B *mcf*®** should be given intravenously.

**PFS HANDLING PROCEDURE:**

Prior to administration, ensure that the plunger rod is firmly attached to the rubber stopper by turning the plunger rod clockwise until slight resistance is felt. Do not over tighten. Remove rubber tip-cap from the syringe and fix the needle on syringe by turning in clock wise direction into luer lock until it is securely fixed to the syringe, remove the needle cap before injecting. Do not rotate luer lock. Finger grip with back stopper will prevent Plunger rod coming out from the syringe Barrel.

"Do not remove the back-stopper from the syringe."

Fig: PFS Handling Diagram




1) Hold the Syringe Barrel along with Luerlock in one hand, pull the Tip cap gently to dislodge cap from Syringe.

2) To insert the needle to the syringe, Turn the needle in the clockwise direction to Luerlock (See Illustration)

### 4.3 CONTRAINDICATIONS

- **Revac-B *mcf*®** is generally well tolerated. However, the vaccine should not be administered or repeated to persons known to be hypersensitive to any of the components of the vaccine.
- Avoid immunization during severe febrile illness, multiple Sclerosis and allergies to viral and tumor causing vaccines.

### 4.4 SPECIAL WARNINGS/ PRECAUTIONS

- Do not administer intravenously, intradermally, or subcutaneously.
- Like all other vaccines, supervision and appropriate medical treatment should always be available to treat any anaphylactic reactions following immunization.
- Epinephrine injection (1:1000) must be immediately available in case of an acute anaphylactic reaction or any allergic reaction occurs due to any component of the vaccine.
- The vaccinee should remain under medical supervision for at least 30 minutes after vaccination.

While using the multi-dose vial, care must be taken to use separate sterile syringe and needle for the administration of every dose. Used multi-dose vial that contains remaining vaccine must be stored at the recommended storage temperature and re-examined carefully prior to reuse.

A multi-dose vial of **Revac-B *mcf*®** from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to maximum of 4 weeks, provided that all the following conditions are met.

- The expiry date of the vaccine has not passed.
- The vaccine is used for up to 28 days after opening the vial
- The vaccines are stored under appropriate cold chain conditions.
- Aseptic technique has been used to withdraw all doses.

Before use, **Revac-B *mcf*®** should be shaken well to obtain a uniform, whitish translucent suspension. Vial should be visually checked for the presence of any particulate matter or other coloration, if any, prior to its administration, If in doubt, do not use the contents of the vial.

**Revac-B *mcf*®** should not be mixed with other vaccines.

**Revac-B *mcf*®** will not prevent Hepatitis caused by other viruses such as Hepatitis A, Hepatitis C and Hepatitis D and other agents known to infect liver.

NOTE: Because of the long incubation for Hepatitis B virus to manifest the symptoms, some subjects may receive the vaccine while infection stays unrecognized. In such cases, the vaccine may not prevent the onset of Hepatitis due to Hepatitis B virus

### 4.5 INTERACTIONS WITH OTHER MEDICINAL PRODUCTS

**Revac-B *mcf*®** can be administered concomitantly with BCG, DTP, OPV and measles vaccines that are extensively used in the Universal Immunization Program (UIP) and also with Hepatitis A, Haemophilus influenzae type b, Human papillomavirus (HPV) or it may use to complete a primary immunization course started either with plasma-derived or with other genetically-engineered Hepatitis B vaccines.

**Revac-B *mcf*®** should always administer at a different injection site in the event of its use along with other vaccines.

### 4.6 PREGNANCY AND LACTATION

Safety and effectiveness have not been established in pregnant women and in 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 **Revac-B *mcf*®** on the ability to drive and use machines have been performed

### 4.8 UNDESIRABLE EFFECTS

**Revac-B *mcf*®** is well tolerated. The common adverse reactions were pain at site of injection, persistent crying and fever, These resolved with symptomatic treatment with in 48 hrs.

In rare cases of post-vaccinal hypersensitivity, the common symptoms that are quickly recognized by the physician are dizziness, headache, nausea, abdominal pain, rash, pruritis, urticaria, arthralgia, myalgias and similar associated symptoms and side effects.

**4.9 OVERDOSE -** No case of overdose has been reported

### 4.10 PRE-CLINICAL & CLINICAL TRIAL EXPERIENCE

- A 60-day repeat dose non-clinical toxicity study was conducted in mice and guinea pigsto obtain information on the chronic toxicity of Hepatitis B vaccine. Mice and guinea pigs were administered with vaccine by intramuscular route on 0, 7th and 14th day. Food consumption, body weight, biochemical, hematology parameters were estimated and all the parameters were normal. No detectable signs of edema or inflammation were observed at site of injection, **Revac-B™** was safe at the doses used in chronic toxicity study in mice and guinea pigs.

- In Phase IV study, 50 healthy subjects were enrolled to evaluate safety and Immunogenicity of **Revac-B *mcf*®** in children aged between 3 days (new born) to 14 years. Two doses of **Revac-B *mcf*®** was administered with four weeks interval. The mean titer value increased from 3mIU/mL to 123.2mIU/mL with 95.5% seroprotection and 88.9% seroconversion

- The common adverse reactions were pain (2.3%) at site of injection, persistent crying (1.1%) and fever (5.2%). These resolved with symptomatic treatment with in 48 hrs.

### 5 PHARMACOLOGICAL PROPERTIES

### 5.1 PHARMACODYNAMIC PROPERTIES

**Revac-B *mcf*®** generates specific protective immune response against HBsAg. For protection against HBV infection, the anti-HBsAg titer (Anti HBs Anti bodies) should be ≥10 mIU/mL.

Hepatitis B vaccines are made from noninfectious parts of HBV using recombinant DNA technology. The vaccines are sterile preparations for intramuscular injection and contain purified inactive proteins from the surface of HBV. The proteins can activate the immune system but cannot give rise to a replicating virus, Viral proteins used in HBV vaccines are manufactured in yeast cells (*Pichia pastoris*) using recombinant technology. Hepatitis B vaccines work by stimulating the immune system to attack the viral proteins. When a hepatitis B vaccine is administered, the body's immune system recognizes the viral proteins in the vaccine as foreign, and develops antibodies against them, thus providing immunity from future infections. In the event of HBV exposure following vaccination, the body will already be primed to fight the infection

### 5.2 PHARMACOKINETIC PROPERTIES

Not Applicable

### 6 PHARMACEUTICAL PARTICULARS

### 6.1 LIST OF EXCIPIENTS

Aluminium Hydroxide gel equivalent to Aluminium ($Al^{+++}$)

### 6.2 INCOMPATIBILITIES

No incompatibility studies were conducted with **Revac-B *mcf*®**.

### 6.3 SHELF LIFE

The expiry date of **Revac-B *mcf*®** is indicated on the label and carton of the product. Do not use the product after the expiration date shown on the label and carton of the product. Experimental data both at the production and R&D laboratories have shown the formulation to be stable and potent for 36 months at +2°C to +8°C. Exposure of vaccine to higher temperature at 37°C for 1 month & 45°C for 1 week did not result in the loss of its immunogenicity.

### 6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at +2°C to +8°C. Shake well before use. Do not freeze. Discard if frozen. Keep out of reach of children.

### 7 PRESENTATION

**Revac-B *mcf*®** is presented in USP type 1 glass vial and Pre-filled syringe.The content upon storage may present a fine white with a clear colorless supernatant. Once shaken the vaccine is slightly opaque.

**Revac-B *mcf*®** is available in single dose vials and Pre-filled syringes
Single dose PFS (Pediatric dose): 0.5mL
Single dose vial (Pediatric Dose): 0.5 mL
Single dose vial (Adult dose): 1.0mL

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*Manufactured & Marketed by :*

BHARAT BIOTECH
Lead Innovation

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