

Registration No.: 1C 27/54(B)

Importer/Manufacturer: BioNet-Asia Co.,Ltd / Bharat Biotech International Limited.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICAL PRODUCT

Revac-*Bmcf* [Hepatitis B Vaccine (rDNA. *Pichia pastoris*) (Thiomersal Free)]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Revac-*Bmcf* is a sterile suspension containing purified, non-infectious major surface antigen of the hepatitis B virus and is manufactured using recombinant DNA technology. The antigen is adsorbed onto high affinity Aluminium hydroxide gel molecules, and hence the suspension appears almost white and translucent. The Vaccine fulfils WHO Requirements for Hepatitis-B Vaccine made by recombinant DNA techniques

RECOMBINANT TECHNOLOGY:

The Hepatitis-B surface Antigen (HBsAg) is produced in genetically engineered yeast cells at *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 characterised 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-*Bmcf* 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.

Each 0.5 mL contains (Paediatric Single dose):

Purified HBsAg (>98% purity).....	10.0 mcg
Aluminum Hydroxide Gel as Al ⁺⁺⁺	0.25 mg
Phosphate Buffered Saline Solution* q.s. to.....	0.5 mL

Each 1.0 mL contains (Adult Single dose):

Purified HBsAg (>98% purity).....	20.0 mcg
Aluminum Hydroxide Gel as Al ⁺⁺⁺	0.50 mg
Phosphate Buffered Saline Solution* q.s. to.....	1.0 mL

3. PHARMACEUTICAL FORM

Sterile suspension for Injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Revac-*Bmcf* is indicated for immunization of persons against infection by hepatitis-B virus and its common sub-types. It can also be given to hepatitis C virus infected patients to protect them against co-infection with hepatitis-B virus. Revac- *Bmcf* is recommended primarily for neonates, infants and young adults for the prevention of the disease or to protect them from probable hepatitis-B virus-induced carrier state, cirrhosis and hepatocellular carcinoma. In addition, for various groups of individuals as listed below, Revac- *Bmcf* immunization is an essential requirement:

4.2 Posology and method of administration

Revac-*Bmcf* should be injected deep intramuscularly into the deltoid region in adults and in the antero-lateral aspect of the thigh in neonates, infants and young children.

Revac-*Bmcf* should NOT be injected into the gluteal muscle. This route of administration may result in lower immune response. Under no circumstances Revac-*Bmcf* should be given intravenously.

As indicated in the composition, an adult dose (20µg/mL) is formulated for adults and children above 10 years of age. Paediatric dose is (10µg/0.5mL) recommended for neonates, infants and children at and below 10 years of age.

A. Primary immunization schedule:

An interval of 30 days is given between the administration of the FIRST and SECOND doses, followed by the THIRD dose 180 days after the first dose.

1 st dose	On selected date
2 nd dose	30 days after the first dose
3 rd dose	180 days after the first dose

B. Special dosage recommendations:

B1 To neonates born to HBV infected mothers the recommended paediatric dose schedule:

1 st dose	On selected date
2 nd dose	30 days after the first dose
3 rd dose	60 days after the first dose
Booster dose	1 year after the first dose

HBIG may also be given to compromised neonates on advice from the medical practitioner.

B2 To person involuntarily exposed by accident to HBV infection:

The schedule of the immunization stated at B1 is recommended at paediatric dosage level for children and as adult dose for others.

B3 Immuno-compromised patients will require additional dosage as per schedule given:

1 st dose of 40 mcg (2mL)	- On the first day
2 nd dose of 40 mcg (2mL)	- 30 days after the first dose
3 rd dose of 40 mcg (2mL)	- 60 days after the first dose
4 th dose of 40 mcg (2mL)	- 180 days after the first dose

4.3 Contraindication

Revac-*Bmcf* 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.

4.4 Special warning and precautions for use

It is suggested that the medical practitioners ascertain the pre-immunization hypersensitive status of the subject. In general, biologicals are known to cause reactions occasionally. Sympathomimetic drugs, such as adrenalin, may be kept readily available in case of any anaphylactic reactions due to the vaccine.

Before use, Revac-*Bmcf* should be well-shaken to obtain a uniform, whitish, translucent suspension. Vaccine 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.

NOTE: Because of the long incubation for hepatitis-B virus to manifest the symptoms, some subjects may receive the vaccine while the infection stays unrecognized. In such cases, the vaccine may not prevent the onset of hepatitis due to hepatitis-B virus. Revac-*Bmcf* will not prevent hepatitis caused by other viruses such as hepatitis A, hepatitis C and hepatitis D and other agents known to infect the liver.

4.5 Interaction with other medicinal products and other forms of interactions

Revac-*Bmcf* can be administered at the same time as BCG, DPT, OPV and measles vaccines that are widely used in the Expanded Program of Immunization (EPI).

Revac-*Bmcf* should be administered at a different injection site in the event of its use along with EPI vaccines.

Revac- *Bmcf* should not be mixed with other vaccines.

4.6 Pregnancy and lactation

Routine vaccination of pregnant women/mothers with recombinant Hepatitis-B vaccine is not recommended due to inadequate data on its effects on the foetus. No contraindication was recorded for the use of the vaccine in the lactating 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 machine

Nil.

4.8 Undesirable effects

Revac-*Bmcf* has proven low reactogenicity and is well tolerated. Open and comparative trials did not show adverse reactions in the vaccines.

Inflammation at the site of injection or a febrile reaction may be observed in some subjects.

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, myalgia and similar associated symptoms and side effects.

Strict adherence to the above-mentioned precautions is advised to avoid untoward reactions.

4.9 Overdose

An overdose of this vaccine is unlikely to occur. In paediatric dose there is no question of overdose because it is a single dose vial of 0.5 mL. If an adult dose is given to children there is no concern as it is still safe. However there are no studies to prove it and we have not come across these cases in practice. There is no specific treatment for overdose of Hepatitis B vaccine in medical literature so far.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Not applicable

5.2 Pharmacokinetic Properties

Not applicable

5.3 Preclinical Safety Data

Hepatitis B vaccine, when tested for toxicity in mice and guinea pigs at different dosage levels, including at much higher levels used for administration into humans, was found to be safe.

IMMUNOLOGICAL PROPERTIES:

In clinical trials, Revac-*Bmcf* induced specific antibodies in the vaccinees against hepatitis B virus. Three doses of Revac-*Bmcf* immunization elicited high protective humoral antibody levels in 92 to 98 percent of the recipients.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminum Hydroxide and buffer solution containing Disodium Hydrogen Orthophosphate, Sodium Dihydrogen Orthophosphate, Sodium Chloride and water for injection.

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

3 years from the date of manufacture at recommended storage temperature of +2°C to +8°C.

6.4 Special precautions for storage

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.

6.5 Nature and contents of container

Revac- *Bmcf* is presented in USP Type 1 glass vial. The content upon storage may present a fine white deposit with a clear colourless supernatant. Once shaken the vaccine is slightly opaque.

Paediatric Single Dose: 0.5 ml

6.6 Special precautions for disposal and other handling

SHAKE WELL BEFORE USE.

DO NOT FREEZE. DISCARD IF FROZEN.

KEEP OUT OF REACH OF CHILDREN.

7. MARKETING AUTHORIZATION HOLDER

BioNet-Asia Co., Ltd.

8. MARKETING AUTHORIZATION NUMBER(S)

1C 27/54(B)

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORISATION

October 31, 2011

10. DATE OF REVISION OF THE TEXT