Registration No. 1C 7/61 (B)

Importer / Manufacturer: Biogenetech Co. Ltd. / Biological E. Limited

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICAL PRODUCT
BEVAC®

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

COMPOSITION	Paediatric Dose	Adult Dose
Volume	0.5 mL	1.0 mL
Purified HBsAg	10 μg	20 μg
Aluminium hydroxide gel equivalent to Al+++	0.25 mg	0.50 mg
Thiomersal BP	0.025 mg	0.050 mg

3. PHARMACEUTICAL FORM
BEVAC® is a sterile suspension containing highly purified, non-infectious major surface antigen of the Hepatitis-B virus produced by recombinant DNA technology. The antigen is adsorbed onto high affinity aluminium hydroxide gel particles and hence the suspension appears almost white and translucent. BEVAC® is available in paediatric dose vials (containing 10 μg HBsAg/dose) as well as adult dose vials (containing 20 μg HBsAg/dose). The vaccine meets the requirements of WHO and BP.

Recombinant technology: The hepatitis-B surface antigen (HBsAg) has been developed 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 (HBV). 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 20-24 nm containing non-glycosylated polypeptides in a lipid matrix. An extensive and rigorous in-house R&D processes characterized and confirmed that these 20-24 nm spherical particles resemble that natural HBsAg protein in their antigenic properties. The efficacy and safety of the formulated BEVAC® 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**

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BEVAC® is indicated for immunization of persons exposed to infection by hepatitis B virus and its common sub-types. It can also be given to hepatitis C and D virus infected patients to protect them against co-infection with hepatitis B virus. BEVAC® is recommended primarily for neonates, infants, children and adults not only for the prevention of the disease but also to protect them from probable hepatitis B virus – induced carrier state, cirrhosis and hepato-cellular carcinoma. In addition, for various groups of individuals as listed below, BEVAC® immunization is an essential requirement:

- Healthcare personnel.
- Patients prone to infection due to unscreened or improperly tested blood transfusions.
- Hemophiliacs and patients on haemodialysis.
- Travelers to specified high endemic areas.
- Residents in high endemic areas.
- Persons in contact with infected sexual partners.
- Drug addicts.

- Personnel and residents of community homes and hostels.
- Household contacts of persons with acute or chronic hepatitis B virus infection.
- Infants born to hepatitis B virus carrier mothers.
- Organ transplant receivers.
- Others: Police, Armed forces and such other regimented personnel.

4.2 Posology and method of administration

The liquid vaccine vial should be shaken before use to homogenize the suspension. BEVAC® should be injected deep intramuscularly into the deltoid muscle region in adults and in the antero-lateral aspect of the upper/mid thigh in neonates, infants and children. BEVAC® should not be injected into the gluteal muscles. It is not recommended for intradermal administration. These routes of administration may result in lower immune response. Under no circumstances BEVAC® should be given intravenously.

As indicated in the composition an adult dose is formulated for adults and children above 10 years of age. Paediatric dose is recommended for neonates, infants and children at and below 10 years of age.

Immunization Schedule:

A. Primary immunization schedule:

Any one of the following is recommended as a Primary Schedule (IAP Guideline) for Routine Immunization

AGE	**Schedule-1 (IAP & WHO)**	**Schedule-2 (IAP & WHO)**	**Schedule-3 (IAP)**
Birth	NA*	1st dose**	At Birth-1st dose**
6 weeks	1st dose	2nd dose	1 month-2nd dose
10 weeks	2nd dose	NA*	6 months-3rd dose
14 weeks	3rd dose	3rd dose	-------
Booster	Booster doses are not recommended.		

*Not applicable; ** Monovalent hepatitis B vaccine MUST BE USED for the birth dose.

In order to prevent HBV transmission from mother to infant, the first dose of hepatitis B vaccine needs to be given as soon as possible after birth (preferably within 24 hours). This must be followed by a second and third dose at the time of the first and third diphtheria-tetanus-pertussis (DTP) vaccination.

Temporary immunity may be obtained using hepatitis B immune globulin (HBIG) for post-exposure prophylaxis. As a rule, HBIG should be used as an adjunct to hepatitis B vaccine when given at birth, but at a different injection site. However, in full-term newborns, the protection against perinatally acquired infection achieved by immediate (<24 hours) hepatitis B vaccination is not significantly improved by the addition of HBIG.

B. Schedule for preterm infants

AGE	**Alternate Schedule (WHO) (For Preterm Infants With <2000 g Birth Weight)**
Birth	1st dose**
6 weeks	2nd dose
10 weeks	3rd dose
14 weeks	4th dose

** Monovalent hepatitis B vaccine MUST BE USED for the birth dose.

Alternatively for preterm infants, to prevent perinatal transmission, a four-dose schedule may be used; if the birth weight is <2000 grams, the vaccine dose at birth should not be counted towards the primary series, and three additional doses should be given. These doses may be given either as monovalent vaccine or as a combination (e.g. with DTP and/or Hib) following the schedules commonly used for DTP vaccines. These schedules will prevent most perinatally acquired infection.

Primary immunization schedule recommended by Pediatric Infectious Disease Society of Thailand (PIDST)

AGE	PIDST Schedule
Birth	1st dose
1-2 months	2nd dose
6 months	3rd dose

Booster Doses:

In immunocompetent individuals hepatitis B vaccine induces an effective immunological memory that lasts life-long and protects against symptomatic acute illness and development of chronic infection on exposure to the virus. Boosters of hepatitis B vaccine are, therefore, not necessary under usual circumstances.

Catch-up Vaccination:

Catch-up vaccination with hepatitis B vaccine of older age groups, including adolescents and adults should be considered only if the continuity of the infant vaccination programme can be ensured. If a higher proportion of chronic infections may be acquired among older children, adolescents and adults; catch-up immunization for these groups may be considered

C. Schedule for older children and adults:

For older children and adults the preferred schedule is 0, 1 and 6 months, 0 being the elected date for first dose.

D. Immunization in special situations:

1) Immunocompromised Individuals It is recommended (by Advisory Committee on Immunization Practices-ACIP) that adults with HIV infection receive hepatitis B vaccination (3 doses). Immunosuppressive illnesses such as advanced HIV infection, chronic liver disease, chronic renal failure and diabetes are associated with reduced immunogenicity of the vaccine.

2) Unresponsive Individuals

Persons unresponsive to the primary series of hepatitis B (serum anti-HBsAg concentration less than 10 mlU/L), may require revaccination of a fourth or fifth dose, or a new complete course of immunization at the discretion of the medical practitioner.

3) Interactions with other vaccines and other forms of interactions

Hepatitis B vaccine can be administered safely and effectively at the same time as BCG, DTP, measles, polio (OPV or IPV), Haemophilus influenzae type b, or yellow fever vaccines that are extensively used in the Expanded Programme on Immunization (EPI), worldwide or vitamin A supplementation. If hepatitis B vaccine is given at the same time as other vaccines, it should be administered at a separate site. It should not be mixed in the vial or syringe withany other vaccine unless it is licensed for use as a combined product (e.g. DTP Hep B/DTP Hep B-Hib).

4.3 Contraindication

BEVAC® 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 warnings and precautions for use

It is suggested that the medical practitioners ascertain the pre-immunization hypersensitivity status of the subject. In general, biologicals are known to cause reactions occasionally. Sympathomimetic drug like adrenalin may be kept readily available in case of rare anaphylactic reactions due to the vaccine. While using the multi-dose vial, care must be taken to use separate sterile syringe and needle for the administration of every dose.

Before use, BEVAC® 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. BEVAC® 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 medical products and forms of interaction

N/A

4.6 Pregnancy and lactation

Routine vaccination of pregnant women 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 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 the ability to drive and use machines

N/A

4.8 Undesirable effects

BEVAC® has proven for low reactogenicity and is well tolerated. Open and comparative trials did not show adverse reactions in the vaccinees. Soreness 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, pruritus, urticaria, arthralgia, myalgias and similar associated symptoms and side effects.

4.9 Overdose

N/A

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

N/A

5.2 Pharmacokinetic properties

N/A

5.3 Preclinical safety data

N/A

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium hydroxide gel equivalent to Al^{+++}, Thiomersal BP

6.2 Incompatibilities

N/A

6.3 Shelf life

3 years from the date of manufacture.

6.4 Special precautions for storage

Store between 2°C to 8°C. Do not freeze. Discard if the vaccine has been frozen.
Shake well before use.

Handling of multi dose vial: Once opened, multi dose vials of BEVAC® 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 a maximum of 4 weeks, provided that all of the following conditions are met:

- The expiry date has not passed.
- The vaccines are stored under appropriate cold chain conditions.
- The vaccine vial septum has not been submerged in water.
- Aseptic technique has been used to withdraw all doses.
- The vaccine vial monitor (VVM) has not reached the discard point.

6.5 Nature and contents of container

Paediatric: Single dose vial of 0.5 mL
Multi dose vial of 5 mL
Adult: Single dose vial of 1 mL

6.6 Special precautions for disposal and other handling

N/A

7. MARKETING AUTHORISATION HOLDER

Biogenetech Co., Ltd.
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8. MARKETING AUTHORISATION NUMBER(S)

1C 7/61 (B)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

March 29, 2018

10. DATE OF REVISION OF THE TEXT

July 5, 2018