

Registration No. 1C 23/45

Importer / Manufacturer: Pharmaland(1982) Co., Ltd./

Centro De Ingenleria Genetica Biotecnologia (CIGB)

1. NAME OF THE MEDICAL PRODUCT

Heberbiovac HB

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Components	Composition per 0.5 mL/dose	Composition per 1.0 mL/dose
Hepatitis B virus recombinant surface antigen (HBsAg)	10 µg	20 µg
Aluminum hydroxide gel (Al ³⁺)	0.25 mg	0.50 mg
Thiomersal	0.025 mg	0.050 mg
Sodium chloride	4.0 mg	8.0 mg
Sodium phosphate dibasic (anhydrous)	0.56 mg	1.12 mg
Sodium phosphate monobasic (dihydrate) or	0.62 mg	1.24 mg
Sodium phosphate monobasic (monohydrate)	0.55 mg	1.10 mg
Water for injection qs	0.5 mL	1.0 mL

3. PHARMACEUTICAL FORM

Suspension for injection

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For active immunization against infection by HBV and prevention of its potential consequences such as acute or chronic hepatitis, liver cirrhosis and primary carcinoma. Specially recommended for the following high-risk population groups:

- Health workers in direct contact with patients. Morgue, funeral parlor and forensic-service staff.
- Students in medical and nursing schools and related technical schools in contact with patients.
- Persons who work with blood and blood derivatives.
- Travelers going to or coming from high-risk countries or regions.
- Household contacts with positive cases.
- Handicapped persons receiving social service, persons living in institutions and community homes, and the staff of these institutions.
- Patients who have received a number of blood transfusions or those affected with oncological

disorders, nephropathies, cirrhosis or receiving hemodialysis or plasmapheresis, among others.

- New-born children of infected mothers or all new-born children in high or medium-risk countries or regions.
- Patients who will undergo elective surgery with sufficient time for seroconversion.
- Receptors of transplanted organs.
- Hemophiliacs and other systematic blood receptors.
- Soldiers and other military personnel on active duty.
- Prisoners, prison guards and other prison employees.
- Persons at risk of sexual contamination (e.g. promiscuous persons, male homosexuals, prostitutes and venereal-disease patients) and drug addicts.

4.2 Posology and method of administration

DOSAGE

- Adults and children of 10 years and older: A dose of 20 µg.
- Neonates, and children under 10 years : A dose of 10 µg.

There are two different schedules:

- 2 doses at 1 month interval, followed by a third dose 6 months after the first (0-1-6).
- 3 doses at 1 month interval, followed by a reactivation booster dose a year later (0-1-2+12). This schedule is recommended in cases where there is an immediate risk of infection.

The preparation should be administered by deep intramuscular injection in the deltoid region, or in the anterolateral region of the thigh in neonates. Other forms of administration are not recommended. In immunodepressed patients, protective levels of antibodies may not be attained and higher doses (usually twice the normal dose) could be necessary.

Patients with renal insufficiency including patients undergoing haemodialysis 16 years of age and above

The primary immunisation schedule for patients with renal insufficiency including patients undergoing haemodialysis is four doses of 40 µg (2 ml) at 0, 1, 2 and 6 months from the date of the first dose. The immunisation schedule should be adapted in order to ensure that the anti-HBs antibody titre remains equal to or higher than the accepted protective level of 10 IU/L.

SHAKE WELL BEFORE USE.

4.3 Contraindication

The vaccine should not be administered to persons with feverish states due to severe infections or to persons allergic to any of its components.

4.4 Special warnings and precautions for use

Vaccination of pregnant is not recommended but in case of high risk or other special situations, the physician could consider it justified. Abortion is not required in the case of unconscious vaccination.

As with any type of vaccine, a 1:1000 adrenaline solution must be immediately available ready for use in an unexpected and rare case of anaphylactic reaction.

WARNING

Due to long incubation period of Hepatitis B (up to 6 months or more). If the disease is being incubated when the vaccine is administered, vaccination may not be effective.

DO NOT ADMINISTER INTRAVENOUSLY

4.5 Interaction with other medical products and forms of interaction

Heberbiovac HB can be administered safely and effectively at the same time than BCG, DPT, *Haemophilus influenzae* type B, Va-Mengoc BC, measles, and oral or injectable Poliovirus (OPV or IPV) and yellow fever vaccines as well as Vitamin A supplements. In case of simultaneous administration with other vaccines, it should be applied in different sites of injection and with independent syringes. *It should not be mixed in the same vial or syringe with any other vaccine, unless it has been produced with a combined product (example: DTP-HB).*

It is interchangeable with other Hepatitis B vaccines of plasmatic or recombinant nature.

4.6 Pregnancy and lactation

Vaccination for pregnant women is not recommended, but in case of high-risk or other special situations, the physician may determine its administration. Pregnancy interruption is not required in case of non-deliberate vaccination of the pregnant woman.

As well as with any type of vaccine, an epinephrine solution (1:1 000) should be available, ready for its immediate use, in an unexpected and rare case of occurrence of an anaphylactic reaction or any other acute hypersensitiveness reaction.

4.7 Effects on ability to drive and use machines

Even though the reactogenicity of this vaccine is very low, fever or local symptoms could appear, which if intense in persons with low threshold, could affect their capacity to drive and use machines.

4.8 Undesirable effects

The performed trials have demonstrated that Heberbiovac HB vaccine is highly safe. The adverse reactions presented temporarily associated to its administration have a low frequency of appearance, they are slight and of short duration. In a post-trading study that assessed 40 533 doses administered to children under one year, the most frequent events, according to the total administered doses, were: pain at the site of injection (0.15%), slight fever lower than 38°C (0.14%) and reddening at the site of injection (0.10%).

The previous symptoms have been also reported as the most frequent ones in controlled clinical trials performed in children, adolescents and adults, and in a low proportion, the limited induration is among the local reactions and fever, headache and weakness are among the systemic reactions.

There is no relationship between the most serious reactions and Heberbiovac HB vaccine. In other Hepatitis B vaccine types, there are reports of anaphylaxis and other types of immediate hypersensitiveness reactions in a very lower proportion, which occurs during the first hours after vaccine administration.

Up to the moment there is no confirmed scientific proof of the fact that Hepatitis B vaccines provoke peripheral or central nervous system diseases such as Guillain Barre syndrome, optic neuritis, multiple sclerosis or other demyelinating diseases, chronic fatigue syndrome, rheumatoid arthritis or autoimmune diseases. It is recommended to assess the convenience to prevent Hepatitis B and its sequelae by means of vaccination with the risk, not scientifically confirmed, of inducing any of these diseases.

4.9 Overdose

Overdose has not been described for this product.

5. Pharmacological properties

5.1 Pharmacodynamic properties

- Pharmacotherapeutic group (ATC) - JO7BC01
- Mechanism of action: immunogen
- Pharmacodynamic effect

The vaccine evokes high antibody titles against the hepatitis B virus surface antigen (anti-HBsAg) when the antigenic protein is adsorbed in aluminum hydroxide gel.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical Safety Data

This vaccine is administered in very small amounts and its safety and immunogenicity have been completely demonstrated in mice, rabbits and monkeys before being verified in controlled clinical trials in different population groups and countries.

6. Pharmaceutical particularities

6.1 List of excipients

Aluminum hydroxide gel
Thimerosal
Sodium chloride
Sodium phosphate dibasic (anhydrous)
Sodium phosphate monobasic (dihydrate) or Sodium phosphate monobasic (monohydrate)
Water for injections

6.2 Incompatibilities

There are no compatibility studies. Therefore, this vaccine should not be administered with other products.

6.3 Shelf life

3 years, at 2-8°C

6.4 Special precautions for storage

Storage conditions. Expiration.

The vaccine must be stored at 2-8°C. The expiry date for the product kept under these conditions is stated in the label and the package.

DO NOT FREEZE; WASTE THE VACCINE IF FROZEN

Vaccine stability

Heberbiovac HB, stored at 2-8°C for 48 months, preserves its immunogenic capacity in human beings. When stored at 37°C up to one month and at 45°C for a week, it keeps its quality and potency, even though these conditions are not the ones recommended for its storage.

Monodose presentations should be used immediately after opening.

Multidose vials, after an immunization session, shall be used in subsequent sessions up to 4 weeks as maximum, as long as the following conditions are fulfilled:

- The expiration date has not been expired.
- Vaccine has been stored at 2-8 °C
- Vials, once the recap has been removed, should not be submerged into water or any other solutions
- The extraction of every vial's dose is performed with a sterile syringe and needle, ensuring the strict asepsis measures to avoid contamination of the content.

6.5 Nature and content of the package

Flasks:

They are manufactured with hydrolytic glass of class 1 quality according to DIN 58.366 and 58.367 standards. The following sizes are commonly used: 2R, 6R and 15R.

Rubber stoppers:

They are manufactured of grey colored chlorobutyl material, siliconized and free of particles according to DIN 58.366 and 58.367 standards. Two sizes are commonly used: 13 and 20 mm depending on the vials.

Seals:

They are manufactured with aluminum and polypropylene-aluminum materials that can be sterilized by heat, according to DIN 58.366 standard. Two sizes: 13 and 20 mm are commonly used for 2R, 6R, and 15R flasks.

6.6 Special precautions for disposal and other handling

Instructions for use

For each injection, a sterile syringe and needle must be used.

Multidose vials, after an immunization session, shall be used in subsequent sessions up to 4 weeks as maximum, as long as the following conditions are fulfilled:

- *The expiration date has not been expired.*
- *Vaccine has been stored at 2-8 °C*
- *Vials, once the recap has been removed, should not be submerged into water or any other solutions*
- *The extraction of every vial's dose is performed with a sterile syringe and needle, ensuring the strict asepsis measures to avoid contamination of the content.*

7. Marketing authorization holder

IMPORTED BY: PHARMALAND (1982) CO, LTD.

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8. Marketing authorization number

1C 23/45

9. Date of first authorization/renewal of authorization

November 2002

10. Date of revision of the text.

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