SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT (GENERIC NAME):

Name of the product: Hepatitis-B Vaccine (r-DNA)I.P.
Brand Name: Revac – B$^{+®}$

Strength:
a) Each pediatric dose of 0.5 mL contains
Hepatitis B surface Antigen (HBsAg)…….. ≥10 µg
b) Composition: Each adult dose of 1.0 mL contains
Hepatitis B surface Antigen (HBsAg)……... ≥20 µg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition: Each pediatric dose of 0.5 mL contains
Hepatitis B surface Antigen (HBsAg)…….. ≥10 µg
Aluminum Hydroxide Gel equivalent to Aluminum (Al^{+++})….. 0.25 mg
Thiomersal IP ……..…….. 0.025 mg
Phosphate Buffered Saline ……..…… q.s. to 0.5 mL

b) Composition: Each adult dose of 1.0 mL contains
Hepatitis B surface Antigen (HBsAg)……... ≥20 µg
Aluminum Hydroxide Gel equivalent to Aluminum (Al^{+++})…… 0.5 mg
Thiomersal IP…….. 0.05 mg
Phosphate Buffered Saline…….…… q.s. to 1.0 mL

3. PHARMACEUTICAL FORM (DOSAGE FORM AND STRENGTH)

Suspension for injection. White or almost white, transparent liquid. Free from particulate matter by visual observation.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Revac-B$^{+®}$ is indicated for the active immunization against infection caused by Hepatitis-B viruses.

Revac-B$^{+®}$ is indicated for the immunization of persons against infection by Hepatitis B virus and its common subtypes. It can also be administered to hepatitis C and D virus-infected patients to protect them against co-infection with hepatitis B virus.

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

- Healthcare personnel
- Patients prone to infection due to unscreened or improperly tested blood transfusions
- Hemophiliacs and patients on hemodialysis.
- 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 or hostels
- Household contacts of persons with acute or chronic HBV infection
- Infants born to HBV carrier mothers.
- Organ transplant recipients
- Others: Police, armed forces and other regimented personnel.

4.2 Posology and Method of Administration

20µg/mLor the adult dose formulation is the recommended dose for adults and children above 10 years of age. 10µg/0.5mL or the pediatric dose formulation is the recommended dose for neonates, infants, and children below 10 years of age.

A. Primary immunization schedule:
Indian Academy of Pediatrics recommends the following for children:

1. At Birth
2. At 6 weeks of age
3. At 6 months: The final (3rd or 4th) dose is administered no earlier than age 24 weeks and at least 16 weeks after the first dose.

As per the Universal Immunisation Program, the hepatitis B vaccine is provided as part of the pentavalent vaccine at 6. 10 & 14 weeks apart from the birth dose.

Adults: 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.

B. 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

Hepatitis B Immunoglobulins may also be given to comprised neonates on advice from a medical practitioner.

- To persons involuntarily exposed by accident to HBV infection:
  The schedule of immunization stated above is recommended at the pediatric dose level for children and at the adult dose for others.

C. Method of Administration

Revac-B+® should be injected intramuscularly into the deltoid region in adults and in the Antero-lateral aspect of the thigh in neonates, infants and young children.

Revac-B+® should not be injected into the gluteal muscle. This route of administration may result in lower immune response. Under no circumstance **Revac-B+®** should be given intravenously.

4.3 Contraindications

Revac-B+® is generally well tolerated. However, the vaccine should not be administered or repeated to persons known to be hypersensitive to any of the vaccine's components. Avoid immunization during severe febrile illness.

4.4 Special warning and Precautions for use

- Do not administer intravenously, intradermally, or subcutaneously.
- Like all other vaccines, supervision and appropriate medical treatment should always be available to treat anaphylactic reactions following immunization.
- Epinephrine injection (1:1000) must be immediately available in case of an acute anaphylactic reaction or any allergic reaction due to any vaccine component.
- 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 a separate sterile syringe and needle to administer every dose. Used multi-dose vial that contains the remaining vaccine must be stored at the recommended storage temperature and reexamined carefully before reuse. A multi-dose vial of **Revac-B+®** 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 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
- An aseptic technique has been used to withdraw all doses

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

Revac-B+ ® can be administered simultaneously with BCG, DTP, OPV and measles vaccines that are extensively used in the Universal Immunization Program (UPI). **Revac-B+ ®** should always administered at a different injection site in the event of its use along with UPI vaccines.

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

NOTE: Because of the longer incubation period, hepatitis-the hepatitis B virus takes a long time to manifest symptoms; some subjects may receive the vaccine while the infection remains unrecognized. In such cases, the vaccine may not prevent the onset of hepatitis due to the hepatitis B virus.

Revac-B+ ® 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 Interactions with Other Medicinal Products and Other Forms of Interaction (Drug interactions)

The simultaneous administration of **Revac-B+ ®** and a standard dose of HepB Ig does not result in lower anti-HBs antibody concentrations provided that they are administered at separate injection sites.

Revac-B+® can be given concomitantly with *Haemophilus influenzae* type b, BCG, hepatitis A, polio, measles, mumps, rubella, diphtheria, tetanus and pertussis vaccines, human papillomavirus (HPV)

Different injectable vaccines should always be administered at different injection sites.

Revac-B+ ® may be used to complete a primary immunization course started either with plasma-derived or with other genetically-engineered hepatitis B vaccines, or, if it is desired to administer a booster dose, it may be administered to subjects who have previously received a primary immunization course with plasma-derived or with other genetically-engineered hepatitis B vaccines.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Routine vaccination of pregnant women with recombinant hepatitis-B vaccine is not recommended due to inadequate data on its effects on the fetus. No contraindication was recorded for the use of the vaccine in lactating mothers. However, the decision to immunize pregnant and lactating mothers may be made 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^{+}®** on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Revac-B^{+}® is well tolerated.

Clinical Trial Experience

Inflammation at the injection site 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, myalgia, and similar associated symptoms and side effects. No vaccine-related SAEs were observed/reported.

Post marketing surveillance data:

Post marketing surveillance study in age groups from 1 month to 70 years showed minor local reactions like pain at the site of injection or pruritus, and systemic reactions like fever are negligible and within levels observed in similar studies. Adverse events of any kind were reported in about 4% of the vaccinees. The most commonly reported AEs are pain at the injection site, itchiness, mild fever, and fatigue. No reactions were observed among newborns.

A similar post-marketing surveillance done in infants with 2 doses of Revac-B^{+} at a 28-day interval reported most common adverse events were fever and excessive crying.

In a Phase IV post-marketing study done in children aged 3 to 6 years with a booster dose, mothers of the vaccinees did not report any reaction, nor did physicians observe any local reaction during the 30-minute observation period.

List of adverse reactions

Adverse reactions reported are listed according to the following frequency
Frequency is defined as:
Very common : (≥ 1/10)
Common : (≥ 1/100, <1/10)
Uncommon : (≥ 1/1000, <1/100)
Rare : (≥ 1/10000, <1/1000)

Clinical Trial Data
Common: Pain at the injection site, fever
Uncommon: headache, dizziness, arthralgia, pruritus, myalgia

4.9. Overdose

No data available

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of action

Revac-B+ vaccine contains hepatitis B surface antigen (HBsAg) produced using recombinant DNA technology in genetically engineered yeast cells of *Pichia pastoris*, and adsorbed onto an aluminium-based adjuvant. A vaccine produced with Pichia pastoris has been shown to be highly immunogenic. Following intramuscular administration, the indigenously developed yeast-derived Hepatitis B vaccine has high immunogenicity expressed in terms of seroprotection, seroconversion, and GMT of antibody titers. Hence, the indigenously developed recombinant Revac-B^{+} vaccine is safe, well-tolerated, and highly immunogenic.

5.2 Pharmacodynamic properties

A phase III clinical trial was conducted to study the reactogenicity and immunogenicity of the yeast-derived Hepatitis B vaccine in 196 healthy adults. Blood samples were collected, and immunogenicity was tested on Days 30, 60 and 90 Revac-B+ ® was safe & and immunogenic, comparable to other commercial Hepatitis B vaccines.

Revac-B+ was tested among 1185 subjects aged from less than 1 month to about 70- years, as part of a post-marketing surveillance for safety across India. A few minor local reactions such as pain at the injection site and a few systemic reactions, were observed as encountered in similar studies, with no reactions in the newborns. With no unexpected adverse reaction, , **Revac-B^{+}®** was shown to be safe for all age groups including neonates.

In a post-marketing study designed to study the safety and immunogenicity of 2 doses of Revac B+ 20 days

apart, in 282 infants aged 3 to 6 months. Immunogenicity among infants peaked with 99% seroconversion with local reactions among 2%. Results of the study showed Revac B+® safe and immunogenic even among infants.

A phase IV post-marketing surveillance study followed a single booster dose of Revac B+® in subjects aged 3 to 6 years. All the subjects were considered seroconverted and seroprotected; no adverse events were observed among them.

5.3 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

6. PRECLINICAL SAFETY DATA (NON-CLINICAL PROPERTIES)

6.1 Animal Toxicology or Pharmacology

A 60-day repeat dose non-clinical toxicity study in mice and guinea pigs was conducted to obtain information on the chronic toxicity of the hepatitis B vaccine in mice and guinea pigs after administration of the vaccine by intramuscular route dosing on 0, 7th and 14th day. Food consumption, body weight, biochemical, hematology parameters were estimated, and all parameters were normal. No detectable signs of pain, edema or inflammation were observed at the site of injections. Based on the results, **Revac-B$^{+®}$** was safe at the doses used in chronic toxicity studies in mice and guinea pigs.

Clinical Study Data:

Active immunization against hepatitis B:

Table 1: Patient demographics of clinical trials studying active immunization against the hepatitis B Virus infection

Study Objective	Trial design	Dosage, route of administration, and duration	Study subjects vaccinated (n)	Age/ Age Groups
To study the reactogenicity and immunogenicity of yeast-derived recombinant Hepatitis B vaccine in healthy adults.	Phase III Clinical Trial, double blind, randomized, comparative, actively controlled, multicenter in healthy adults Comparative Vaccine: Enivac-B	3 dose-schedule: 30, 60 and 90 days	196	11-45 years, Mean Age: 27.65 (± 10.15)

To determine the safety and tolerance of Revac B in healthy volunteers	Phase IV, Multi-center, Post-marketing, Open-Label study, multi-center in healthy adults	3 dose-schedule: 30, 60 and 90 days	1185	1 month to 70 years; < 1 month: 29, 1 month to 6 months: 176, 6 months to 2 years: 216, 2 years to 12 years: 389, > 12 years: 339, age not specified: 36
To determine the safety and immunogenicity of Revac B in infants receiving the first two doses of Hepatitis B vaccine by intramuscular injection	Phase IV, Multi-center, Post-marketing, Open-Label study, multi-center in infants from newborn to 1 year.	2 dose-schedule: 0 and 1 month (28-32 days).	282	Newborn: 26, First month: 11, 2nd month: 43, 3rd month :41, 4th month :36, 5th month :43, 6th month :27, 7th month: 10, 8th month :11, 9th month :6, 10th month: 7, 11th month: 7, and 12th month:14
To study the safety and booster effect to immunogenicity in children receiving the first dose at 5 years after primary immunization of 3 doses	Phase IV, Multi-center, Post-marketing safety and boosting efficacy, of a booster dose of Revac B+	Booster dose at 5 years, primary vaccination of 3 doses	75	3 years: 2; 4 years: 18, 5 years: 39 and, and 6 years: 16

A phase 3 clinical trial was conducted to study the reactogenicity and immunogenicity of yeast-derived Hepatitis B vaccine in 196 healthy adults. Blood samples were collected and immunogenicity was tested on Day 30, 60 and 90 and **Revac-B+®** was safe & and immunogenic comparable to the comparator vaccine.

A multi-center post marketing surveillance was conducted to establish the safety of **Revac-B+®** produced in *Pichia pastoris* in 1185 subjects aged from less than 1 month to about 70 years. The adverse events commonly seen were minor local reactions, such as pain at the site of injection. Pruritus and systemic reactions like fever (3.2%) within levels observed in similar studies earlier. This study thus conclusively establishes that the recombinant Hepatitis B vaccine, **Revac-B+®** produced in *Pichia pastoris* is safe for all age groups including neonates. No unexpected adverse vaccine reactions were observed during the study.

A post-marketing study evaluate safety and boosting effect in children receiving one booster dose of **Revac-B$^{+®}$** in subjects aged between 5 and 6 years. Serum samples were subjected to ELISA tests (AUSAB) and the titers were expressed as mIU/mL. An increase in the antibody titers from less than 1.0 mIU/mL to a value >1mIU /mL was considered seroconverted. A four-fold increase in the titer was considered significant. A titer of greater than 10 mIU/mL is considered seroprotective. No unexpected or untoward reactions have been reported.

Another post-marketing study evaluate the safety and immunogenicity of infants receiving their first two doses of **Revac-B$^{+®}$** on day 1 and day 30 in 282 subjects, aged between 3 and 6 months. Vaccine administration: The mean titer value increased from 0.47 mIU in the first sample to 155.24 mIU/mL. The phase 4 study in infants proved the immunogenicity of **Revac-B$^{+®}$** as high as 99% seroconversion.2% of subjects showed local reactions during the study. The results conclusively establish that the recombinant Hepatitis B vaccine (**Revac-B$^{+®}$**) produced in *Pichia pastoris* by Bharat Biotech is safe and immunogenic in children and adults.

7. DESCRIPTION

Revac-B$^{+®}$ may present a fine white with a clear colourless supernatant. Once shaken, the vaccine is slightly opaque.

8. PHARMACEUTICAL PARTICULARS

8.1 List of Excipients

- Aluminum Hydroxide Gel equivalent to Aluminium (Al^{+++})
- Thiomersal IP
- Phosphate Buffered Saline

8.2 Incompatibilities

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

8.3 Shelf Life

The expiry date of the vaccine is indicated on the label and carton of the product.

9. NATURE AND CONTENTS OF CONTAINER (PACKAGING INFORMATION)

Revac-B+ ® is presented in USP type 1 glass vial. The content, upon storage, may present a fine white with a clear colourless supernatant. Once shaken, the vaccine is slightly opaque.

Pediatric Single dose: ……. 0.5 mL
Pediatric Multi-dose: …….. 2.5 mL
Pediatric Multi dose: ……. 5 mL
Adult Single dose: ……. 1 mL
Adult Multi-dose : …… 10 mL

9.1 Storage and handling instructions

9.1.1 Special precautions for storage:

36 months at +2°C to +8°C.

9.1.2 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

10. PATIENT COUNSELLING INFORMATION

Prior to the administration of this vaccine, the healthcare professional should enquire and inform the individual and/or his parents/guardians of the following:

1. Enquire about any previous or known history of severe hypersensitivity to any component of Revac-B+ or life-threatening reactions after the previous administration of any vaccine.
2. Enquire about the presence of fever, febrile illness, or any immunocompromised condition that may affect the immune response to Revac-B+. In such cases, administration of the vaccine may be post-poned until the condition has resolved to ensure an adequate immune response
3. Enquire about any history of bleeding disorders as in the case of all invasive interventions such as intramuscular injections.
4. Enquire and inform that the antibody response in persons with endogenous or iatrogenic immunosup-pression may be insufficient, and a protective immune response may not be elicited in all vaccine recipients.
5. Vaccinated persons and their parent(s)/guardian(s) should be informed that the most common general and local adverse events of Revac-B+ were dizziness, headache, nausea, abdominal pain, rash, pruritis, urticaria, arthralgia, myalgias, and similar associated symptoms and side effects. Also, Inflammation at site of injection or febrile reaction may be observed.

6. Instruct vaccine recipients and their parent(s)/guardian(s) to report any adverse reactions if encountered to their healthcare provider and/or report by calling 1-800-102-2245 (Toll-free number) or emailing feedback@bharatbiotech.com.

11. MARKETING AUTHORISATION HOLDER (DETAILS OF MANUFACTURER)

BHARAT BIOTECH Lead Innovation

Bharat Biotech International Limited, situated

Sy. No. 230, 231 & 235, Genome Valley,

Turkapally, Shamirpet Mandal,

Medchal, Malkajgiri District, Telangana State, India, Pin: 500078.

12. DETAILS OF MARKETING AUTHORISATION NUMBER(S) (DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE)

12-30/86-DC dated 14 OCT 1998

13. DATE OF REVISION

09 July 2026

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