

1. NAME OF THE MEDICINAL PRODUCT

Haemophilus influenzae Type b Conjugate Vaccine I.P. (Freeze-Dried).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Haemophilus influenzae Type b Conjugate Vaccine (Sii HibPRO) is a freeze-dried vaccine of purified polyribosyl ribitol phosphate capsular polysaccharide (PRP) of Hib, covalently bound to tetanus toxoid (carrier protein). The Hib polysaccharide is prepared from capsular polysaccharide of *H influenzae* type b strain and after activation is coupled to tetanus toxoid.

The Tetanus toxoid is prepared by extraction, ammonium sulfate purification and formalin inactivation of the toxin from cultures of *Clostridium tetani*. The vaccine meets the requirements of WHO and I.P. when tested by the methods outlined in WHO, TRS 897 (2000) and I.P.

Each dose of 0.5 ml contains:

Purified capsular polysaccharide (PRP) conjugated	10 mcg
Tetanus Toxoid (carrier protein)	19 to 33 mcg

Diluent: Reconstitute with diluent for *Haemophilus influenzae* Type b Conjugate Vaccine I.P.

3. PHARMACEUTICAL FORM

Haemophilus influenzae Type b Conjugate Vaccine I.P. is a freeze-dried vaccine of purified polyribosyl ribitol phosphate capsular polysaccharide (PRP) of Hib, covalently bound to tetanus toxoid (carrier protein).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Sii HibPRO (*Haemophilus influenzae* Type b Conjugate Vaccine I.P.) is indicated for the active immunization against *Haemophilus influenzae* type b infections of all children from the age of 6 weeks to 5 years.

Sii HibPRO (*Haemophilus influenzae* Type b Conjugate Vaccine I.P.) does not protect against disease due to other types of *H. influenzae* nor against meningitis caused by other organisms.

4.2 Posology and method of administration

Dosage

Sii HibPRO (*Haemophilus influenzae* Type b Conjugate Vaccine I.P.) is indicated for children 6 weeks to 60 months of age for the prevention of invasive disease caused by *Haemophilus influenzae* type b. For infants 6 weeks to 6 months of age, the immunizing dose is three separate injections of 0.5 ml given at approximately 4 weeks intervals. Previously unvaccinated infants from 7 through 11 months of age should receive two separate injections, approximately 2 months apart. Children from 12 through 14 months of age who have not been vaccinated previously should receive one injection. All vaccinated children should receive a single booster dose at 12-18 months of age, but not less than 2 months after the previous dose. Previously unvaccinated children 15 to 60 months of age receive a single

injection of Sii HibPRO (*Haemophilus influenzae* Type b Conjugate Vaccine I.P.). Preterm infants should be vaccinated according to their chronological age, from birth.

Recommended Immunisation schedule:

Age at first immunization (month)	No. of doses	Booster
6 weeks	3	Yes
7-11	2	Yes
12-14	1	Yes
15 and over	1	No

Interruption of the recommended schedules with a delay between doses does not interfere with the final immunity achieved nor does it necessitate starting the series over again regardless of the length of time elapsed between doses.

Method of Administration

The reconstituted vaccine is for intramuscular injection.

Sii HibPRO (*Haemophilus* Type b Conjugate Vaccine I.P.) can be used as follows: -

To use Sii HibPRO as monovalent Hib vaccine: Sii HibPRO (*Haemophilus influenzae* Type b Conjugate Vaccine I.P.) is presented as a white Hib pellet in a vial, with a clear and colourless sterile diluent in a separate container. The vaccine must be reconstituted by adding the entire contents of the supplied container of diluent (0.5 ml) to the vial containing the pellet. After the addition of the diluent to the pellet, the mixture should be well shaken until the pellet is completely dissolved in the diluent.

To use Sii HibPRO as Pentavalent (DTP-HB+Hib) vaccine: Sii HibPRO vaccine may be reconstituted with Sii Q-VAC (DTP-HB Vaccine) for simultaneous administration via single injection. Sii Q-VAC is presented as a suspension. The vaccine should be well shaken in order to obtain a homogenous turbid white suspension. After reconstitution the combined pentavalent (DTP-HB-Hib) vaccine should be injected promptly.

Discard the sterile diluent provided with Sii HibPRO.

To use Sii HibPRO as Quadravalent (DTP-Hib) vaccine: Sii HibPRO vaccine may be reconstituted with Sii Triple Antigen (DTP Vaccine) for simultaneous administration via single injection. Sii Triple Antigen is presented as a suspension. The vaccine should be well shaken in order to obtain a homogenous turbid white suspension. After reconstitution the combined quadravalent (DTP-Hib) vaccine should be injected promptly.

Discard the sterile diluent provided with Sii HibPRO.

The diluent and reconstituted vaccine should be inspected visually for any foreign particular matter and/or variation of physical aspects prior to administration. In the event of either being

observed, discard the diluent or reconstituted vaccine. A new sterile needle should be used to administer the vaccine.

After reconstitution, the vaccine should be injected promptly.

The vaccine should be well shaken before use. One single human dose of 0.5 ml should be injected intramuscularly into the anterolateral aspect of the thigh in infants, or into the deltoid muscles of older children.

The monovalent vaccine should be reconstituted only with the diluent supplied using a sterile syringe and needle. With gentle shaking the dried cake is easily dissolved. Agitate prior to injection. Parenteral drug products should be inspected visually for extraneous particulate matter and discoloration prior to administration.

4.3 Contraindications

Known hypersensitivity to any component of the vaccine, or a severe reaction to a previous dose. The vaccine will not harm individuals previously infected with the Hib bacteria. Children infected with Human Immunodeficiency Virus (HIV) both asymptomatic and symptomatic, should be immunized with Hib vaccine according to standard schedules. All vaccines can be administered to children with minor illness such as diarrhoea, or other low grade febrile illness; children with moderate or severe febrile illness should be vaccinated as soon as they have recovered from the acute phase of the illness.

4.4 Special warnings and precautions for use

Warnings

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available. Since anaphylactoid or other allergic type reactions are possible following administration of Hib vaccine, 1:1000 adrenaline should be available for immediate treatment if such reactions occur. For this reason the vaccinee should remain under medical supervision for 30 minutes after immunization.

Human Immunodeficiency Virus (HIV) infection is not considered as a contraindication for Sii HibPRO (*Haemophilus influenzae* Type B Conjugate Vaccine I.P). Although limited immune response to the tetanus toxoid component may occur, vaccination with Sii HibPRO (*Haemophilus influenzae* Type b Conjugate Vaccine I.P) alone does not substitute for routine tetanus vaccination. Excretion of capsular polysaccharide antigen in the urine has been described following receipt of Hib vaccines and therefore antigen detection in urine may not have a diagnostic value in suspected Hib disease within 1-2 weeks of vaccination.

As with other vaccines the administration of Sii HibPRO (*Haemophilus influenzae* Type b Conjugate Vaccine I.P) should be postponed in subject's suffering from acute severe febrile illness. The presence of a minor infection, however, is not a contra-indication for vaccination.

Sii HibPRO (*Haemophilus influenzae* Type b Conjugate Vaccine I.P) should under no circumstances be administered intravenously.

4.5 Interaction with other medicinal products and other forms of Interaction

Drug Interactions

Individuals receiving immunosuppressive therapy (e.g. corticotropin, corticosteroids, alkylating agents, antimetabolites, and radiation therapy) may have a diminished antibody response to immunization with Sii HibPRO (*Haemophilus influenzae* Type b Conjugate Vaccine I.P.). As with other vaccines it may be expected that in patients receiving immunosuppressive therapy or patients with immunodeficiency an adequate response may not be achieved. Hib vaccine can be given safely and effectively at the same time as BCG, DTP, measles, polio vaccines (OPV or IPV), and HBV or yellow fever vaccines.

Sii HibPRO (*Haemophilus influenzae* Type b Conjugate Vaccine I.P.) can be administered either simultaneously or at any time before or after a different inactivated or live vaccine but separately at different sites.

Sii HibPRO Vaccine can be mixed in the same syringe with Serum Institute of India Pvt. Ltd's, Sii Triple Antigen (DTP vaccine) or Sii Q-VAC (DTP-HB vaccine). Other injectable vaccines should always be administered at different injection sites.

4.6 Pregnancy and lactation

Adequate human data on use during pregnancy or lactation and animal reproduction / developmental toxicity studies are not available. **Sii HibPRO** is not recommended for use in a pregnant woman.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

The vaccine is very well tolerated, localized reactions may occur within 24 hours of vaccination, when recipients may experience pain and tenderness at the injection site. These reactions are generally mild and transient. In most cases, they spontaneously resolve within two to three days and further medical attention is not required. Mild systemic reactions, including fever, rarely occur following administration of Hib vaccine. More serious reactions are very rare; a causal relationship between more serious reactions and the vaccine has not been established.

The general symptoms which have been solicited and reported within the first 48 hours are mild and get resolved spontaneously. These include fever, loss of appetite, restlessness, vomiting, diarrhoea and unusual crying. As for all Hib vaccines, these general symptoms have also been reported when administered concomitantly with other vaccines. Very rarely allergic reactions, including anaphylactoid reactions, have been reported.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines,

Haemophilus influenzae B, purified antigen conjugated, ATC code J07AG01.

Hib vaccine provides immunity against *Haemophilus influenzae* b infections.

Immunological Data:

Various clinical trials performed to assess Immunogenicity and reactogenicity of the vaccine proved that the vaccine is immunogenic.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Following pre-clinical studies were conducted by Serum Institute of India Ltd, Pune:

1. Acute Intramuscular Toxicity Study in Swiss Albino Mice.
2. Acute Intramuscular Toxicity Study in Sprague Dawley Rats.
3. Subacute Intramuscular Toxicity Study in Swiss Albino Mice.
4. Subacute Intramuscular Toxicity Study in Sprague Dawley Rats.
5. Repeated Dose Intramuscular Toxicity Study in Sprague Dawley Rat.

From the acute studies in rats and mice, the median lethal dose (LD₅₀) after intramuscular injection was more than 120 µg/kg body weight (i.e. more than 30 times the human dose). From subacute and repeated dose toxicity studies, it was concluded that the 'No Observable Adverse Effect Level' (NOAEL) of Hib in rats and mice following intramuscular administration is more than 40 µg/kg body weight (i.e. more than 10 times the human dose). The safety of *Haemophilus influenzae* type b conjugate vaccine was established in these preclinical studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sucrose
- Trometamol (Tris buffer)

6.2 Incompatibilities

This product must not be mixed with other medicinal products other than that specified by the manufacturer.

6.3 Shelf life

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

6.4 Special precautions for storage

The freeze-dried vaccine should be stored +2°C to 8°C, protected from light. The freeze-dried vaccine is not affected by freezing. The diluent can be stored in the refrigerator (+2°C to 8°C) or at ambient temperatures (up to 25° C) and should not be frozen.

6.5 Nature and contents of container

Lyophilised Hib vaccine is a white dry cake in vials (Type I glass)

1 Dose vial plus diluent (0.5 ml)

2 Dose vial plus diluent (1 ml)

5 Dose vial plus diluent (2.5 ml)

10 Dose vial plus diluent (5 ml)

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

Serum Institute of India Pvt Ltd,

212/2, Hadapsar, Off Soli Poonawalla Road,

Pune – 411028, Maharashtra, INDIA.

Telephone: + 91-20- 26993900, + 91-20-26602379

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Website: www.seruminstitute.com

8. MARKETING AUTHORISATION NUMBER(S)

Manufacturing permission number: MF-7100.

Manufacturing License number: 10.

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of First Authorization: 12.01.2007.

Date: 31 December 2022