	Serum Institute of India Pvt. Ltd.	Haemophilus influenzae type b Conjugate Vaccine (Lyophilized) (Hib Vaccine)	Summary of Product Characteristics
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1. NAME OF THE MEDICINAL PRODUCT

Haemophilus influenzae type b Conjugate Vaccine (Freeze-Dried)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 0.5 ml contains:

Purified capsular polysaccharide (PRP) 10 mcg

Tetanus Toxoid (carrier protein) 19 to 33 mcg

Diluent: Reconstitute with Diluent for *Haemophilus influenzae* type b Conjugate Vaccine

3. PHARMACEUTICAL FORM

Lyophilized powder for injection

4. CLINICAL PARTICULARS

4.1 Therapeutic indications


Haemophilus influenzae type b Conjugate Vaccine is indicated for active immunization against Haemophilus influenzae type b infection for all children from the age of 6 weeks to 5 years.

Haemophilus influenzae type b Conjugate Vaccine 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

Posology:

Haemophilus influenzae type b Conjugate Vaccine 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 received one injection. All vaccinated children 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 haemophilus influenzae type b conjugate vaccine. Preterm infants should be vaccinated according to their chronological age, from birth.

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Recommended Immunisation schedule

Age at first immunisation (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.

If Hib vaccine is given as a separate injection at the same time as other vaccines, it should be administered at a different site. It should not be mixed in the vial or syringe with any other vaccine unless it is manufactured by Serum Institute of India Pvt. Ltd. (e.g. DTP, DTPHB) Hib vaccine can be given safely and effectively at the same time as BCG, DTP, measles, polio vaccines (OPV or IPV), Hepatitis B vaccine, yellow fever vaccines and vitamin A supplementation.

Method of administration:

The reconstituted vaccine is for Intramuscular injection.

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 or adults.

The vaccine should be reconstituted only with the diluent supplied using a sterile syringe and needle. With gentle shaking the dried cake is easily dissolved.


Sii Haemophilus influenzae type b Conjugate Vaccine can be used as follows:

To use Sii Hib as monovalent Hib vaccine:

Sii Hib 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 Hib as Pentavalent (Sii DTP-HB-Hib) vaccine:

Sii Hib vaccine may be reconstituted with Sii DTP-HB vaccine for simultaneous administration via single injection. Sii DTP-HB 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.

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To use Sii Hib as Quadravalent (Sii DTP-Hib) vaccine:

Sii Hib vaccine may be reconstituted with Sii DTP Vaccine for simultaneous administration via single injection. Sii DTP Vaccine 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 (Sii DTP-Hib) vaccine should be injected promptly.

It is recommended that the vaccine be used as soon as possible after reconstitution. Store reconstituted vaccine in the vaccine vial at 2- 8°C and discard if not used within 6 hours. Agitate prior to injection. Parenteral drug products should be inspected visually for extraneous particulate matter and discoloration prior to administration. The vaccine vial monitor (see figure), for this type of vaccine is attached to the vial cap and should be discarded when the vaccine is being reconstituted.

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

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. All vaccines can be administered to persons with minor illness such as diarrhoea, or other low grade febrile illness; persons 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

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 reaction occurs. For this reason the vaccinee should remain under medical supervision for 30 minutes after immunisation.

Human immunodeficiency Virus (HIV) infection is not considered as a contra- indication for Haemophilus influenzae type b Conjugate Vaccine. Although limited immune response to the tetanus toxoid component may occur. Vaccination with Haemophilus influenzae type b Conjugate Vaccine 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 Haemophilus influenzae type b Conjugate Vaccine should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection, however, is not a contraindication for vaccination.

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Haemophilus influenzae type b Conjugate Vaccine should under no circumstances be administered Intravenously.

4.5 Interaction with other medicinal products and other forms of interaction

Individuals receiving immunosuppressive therapy (e.g. corticotropin, corticosteroids, alkylating agents, antimetabolites, radiation therapy) may have a diminished antibody response to immunization with Hib polysaccharide conjugate vaccine.

As with other vaccines it may be expected that in patients receiving immuno-suppressive therapy or patients with immunodeficiency an adequate response may not be achieved.

4.6 Fertility, pregnancy and lactation

Adequate human data on use during pregnancy or lactation and adequate animal reproduction studies are not available. Hib vaccine is not recommended for use in a pregnant woman.

4.7 Effects on the ability to drive and use machines

No studies have been performed

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 were mild and 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.

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

ATC code: J07AG01

Hib polysaccharide conjugate (tetanus toxoid conjugate) vaccine is used to stimulate active immunity to Haemophilus influenzae type b (Hib) infection by inducing production of specific antibodies. Hib capsular polysaccharide present in the vaccines promotes the production of Hib anticapsular antibody; evidence indicates that this antibody provides the protection against infection with H. influenzae type b.

Vaccines composed of Hib capsular polysaccharide combined with other protein antigens (e.g. tetanus toxoid) generally produce greater immunity against Hib infection than that produced by nonconjugated Hib polysaccharide vaccine. This increased immunogenicity generally occurs because the protein carries or antigens confer thymus-dependent features to the polysaccharide. Thymus-dependent antigens induce an immune response that is predominantly IgG and potentially boostable. Twofold or greater increases in Hib anticapsular antibody levels compared with prevaccination levels have been observed in 2-17 months of age following administration of 1-3 doses if carries Hib capsular polysaccharide /protein antigen combinations. Booster responses have been observed following administration of Hib polysaccharide vaccine in children of this age group who previously received primary immunization with Hib capsular polysaccharide/protein antigen combinations.


Substantially increased immunogenicity of Hib polysaccharide conjugate vaccine compared with nonconjugated Hib polysaccharide vaccine also has been observed in children 15-24 months of age. In addition, Hib conjugate vaccines appear to be more immunogenic than nonconjugated Hib polysaccharide vaccine in children at high risk of Hib infection secondary to underlying disease (e.g. sickle cell anemia). Although the duration of immunity following a single dose of the conjugate vaccine currently is not known, it is expected to persist for at least 1.5-3 years in children vaccinated with the conjugate at 18 months of age or older.

5.2 Pharmacokinetic properties

Pharmacokinetic studies are not required for vaccines.

5.3 Preclinical safety data

Acute intramuscular study of Haemophilus Influenzae Type B Conjugate Vaccine in Rat and Mouse reveals no abnormal clinical signs during 14 days of post dosing. There was no mortality in the treated male and female animals. No gross pathological alteration was encountered in the treated animal at terminal necroscopy.

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Subacute (28 days) intramuscular toxicity study in Mouse and Rat shown no abnormal clinical signs of toxicity. All animals were survived with no adverse effect on hematological and biochemical parameters. No significant or gross histopathological changes were observed in either of the animal.

Repeated (90 days) intramuscular toxicity study shown no incidence of significant and treatment related clinical abnormalities, no neurotoxicity and mortality.

Each batch of Haemophilus Influenzae Type B Conjugate Vaccine is tested for abnormal toxicity to assure that the product is safe and does not produce any abnormal reactions in animals.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sucrose

Trometamol (TRIS BUFFER)

Water for Injection

6.2 Incompatibilities

If Hib vaccine is given as a separate injection at the same time as other vaccines, it should be administered at different site. It should not be mixed in the vial or syringe with any other vaccine unless it is manufactured by Serum Institute of India Ltd. (e.g. DTP, DTPHB).

Hib vaccine can be given safely and effectively at the same time as BCG, DTP, measles, polio vaccines (OPV or IPV), HBV or yellow fever vaccines


6.3 Shelf-life

36 months from date of manufacture.

6.4 Special precautions for storage

The Lyophilised vaccine should be stored and transported at +2°C to +8°C, protected from light. The Lyophilised 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.

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6.5 Nature and contents of container

1 dose vial of vaccine - Clear white tubular type I glass vial; sealed with rubber stopper and flip off seal

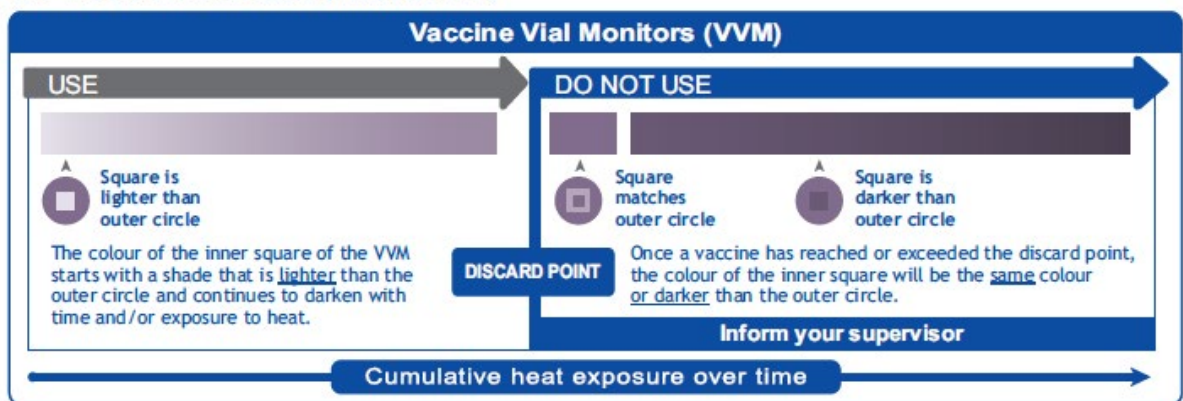
1 dose ampoule of diluent - Clear white tubular type I glass ampoule with one point cut mechanism

6.6 Special precautions for disposal and other handling

It is recommended that the vaccine be used as soon as possible after reconstitution. Store reconstituted vaccine in the vial at 2-8° C and discard if not use within 6 hours. Agitate prior to injection. Parental drug products should be inspected visually for extraneous particulate matter and discoloration prior to administration.


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

THE VACCINE VIAL MONITOR (VVM) (Optional)



Vaccine Vial Monitors (VVMs) are on the cap of *Haemophilus influenzae* type b Conjugate Vaccine supplied through Serum Institute of India Pvt. Ltd. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the outer circle, then the vaccine can be used. As soon as the colour of the central square is the same colour as the outer circle or of a darker colour than the outer circle, then the vial should be discarded.

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7. MARKETING AUTHORISATION HOLDER

SERUM INSTITUTE OF INDIA PVT. LTD

Regd. Office and Laboratories:
212/2, Hadapsar, Pune-411028.
India.

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT
