HIBERIX®

PRODUCT INFORMATION

NAME OF THE MEDICINE

HIBERIX

Haemophilus influenzae type b (Hib) vaccine

DESCRIPTION

Powder and diluent for solution for injection.

After reconstitution, 1 dose (0.5 ml) contains:

Haemophilus influenzae type b polysaccharide	10 micrograms
conjugated to tetanus toxoid as carrier protein	approximately 25 micrograms

HIBERIX is a non-infectious vaccine containing purified polyribosyl-ribitol-phosphate capsular polysaccharide (PRP) of *Haemophilus influenzae* type b covalently bound to tetanus toxoid.

HIBERIX is supplied as a white lyophilised powder for reconstitution with a diluent (sterile 0.9% saline solution). The diluent is supplied as a clear and colourless liquid. The reconstituted vaccine preparation contains the excipients lactose, sodium chloride and water for injection.

The manufacture of this product includes exposure to bovine derived materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

CLINICAL PHARMACOLOGY

The protective efficacy of HIBERIX has not been studied in field trials. HIBERIX has however been shown to induce anti-PRP antibodies above the level known to be protective against invasive disease due to *Haemophilus influenzae* type b. An anti-PRP antibody titre $\geq$ 0.15 µg/mL correlates with immediate protection against Hib infection and $\geq$ 1.0 µg/mL correlates with long term protection.

The immunogenicity of HIBERIX has been investigated in clinical studies involving over 300 infants (over 2 months of age) using a 3 dose primary vaccination schedule. Protective anti-

PRP antibody titres were demonstrated in 95-100% (≥ 0.15 µg/mL) and 87-90% (≥ 1.0 µg/mL) of infants one month after completion of the primary schedule.

Clinical trials have demonstrated the immunogenicity of HIBERIX is unaltered by administration of different primary vaccination schedules. One month after completion of a 2, 4, 6 month or 3, 4, 5 month primary schedule, over 95% of infants in each group obtained anti-PRP titres ≥ 0.15 µg/mL.

A boosting dose of HIBERIX was given either separately (n=19) or in combination with DTPa (n=56) to infants aged between 15 and 18 months who had previously received primary immunisation with HIBERIX and DTPa given at separate sites. One month after administration of this booster dose, an anamnestic response was observed with anti-PRP antibody titres of ≥ 0.15 µg/mL and ≥ 1.0 µg/mL being obtained in 100% and greater than 94% of infants respectively.

INDICATIONS

HIBERIX is indicated for active immunisation against *Haemophilus influenzae* type b infection in children aged from 2 months to 5 years.

CONTRAINDICATIONS

HIBERIX should not be administered to subjects with known hypersensitivity to any component of the vaccine, or to subjects having shown signs of hypersensitivity after previous administration of Hib vaccines.

As for any vaccine, HIBERIX should not be administered to subjects suffering from acute severe febrile illness. However, the presence of minor infection does not contraindicate vaccination.

PRECAUTIONS

HIBERIX should under no circumstances be administered intravenously.

It is good clinical practice that any vaccination be preceded by a review of medical history (especially with regard to previous vaccinations and possible adverse events) and a clinical examination.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of anaphylactic reactions following the administration of the vaccine.

Native populations (native Alaskans, native American Indians) with a high incidence of *Haemophilus influenzae* type b disease have shown a reduced antibody response to conjugated *Haemophilus influenzae* type b vaccines. The immunogenicity of HIBERIX has not been studied in the Australian aboriginal population and the possibility of a lower antibody response than that seen in clinical studies should be borne in mind.

Human Immunodeficiency Virus (HIV) infection is not a contraindication to vaccination. However an adequate antibody response may not be obtained in patients with an immunodeficiency disorder or in patients receiving immunosuppressive therapy (see INTERACTIONS WITH OTHER MEDICINES).

HIBERIX should be administered subcutaneously in patients with thrombocytopenia or bleeding disorders (eg. haemophiliacs) since bleeding after intramuscular injection may occur in these patients (see DOSAGE AND ADMINISTRATION).

Urinary excretion of the capsular polysaccharide antigen has been reported following Hib vaccination. Therefore antigen detection within 1-2 weeks of vaccination may not be of diagnostic value in suspected Hib disease.

An immune response to the tetanus toxoid component may occur following HIBERIX vaccination, however this does not substitute for routine tetanus vaccination.

HIBERIX will not protect against diseases caused by other types of *Haemophilus influenzae,* or meningitis caused by other organisms.

The potential risk of apnoea and the need for respiratory monitoring for 48 to 72 hours should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

Use in Pregnancy (Category B2)

The effect of HIBERIX on foetal development is unknown. Therefore, vaccination of pregnant women cannot be recommended.

Use in Lactation

The effect of HIBERIX in lactation has not been assessed, as the vaccine is not intended for adult use.

INTERACTIONS WITH OTHER MEDICINES

HIBERIX may be administered either simultaneously, or at any time before or after different live or inactivated vaccines. However, different injectable vaccines administered concurrently should always be given in separate sites using separate syringes.

Clinical trials have shown concomitant administration of HIBERIX and the diphtheria-tetanus-pertussis (acellular or whole-cell) combination vaccines does not affect the immunogenicity of either vaccine, provided the vaccines are given at separate sites and NOT mixed prior to administration.

As with other vaccines, it may be expected patients receiving immunosuppressive therapy (eg high-dose steroids or cyclosporin) or patients with an immunodeficiency may not achieve an adequate immune response. (see PRECAUTIONS)

HIBERIX must not be mixed with other vaccines in the same syringe.

ADVERSE EFFECTS

Clinical Trial Data

In the initial controlled clinical trials for registration, signs and symptoms were actively monitored for the first 4-8 days following HIBERIX vaccination and recorded on diary cards. The vaccine was generally well tolerated and most local adverse events were considered to be mild and transient. The incidence of local adverse events did not increase with subsequent vaccine doses. As HIBERIX has been co-administered with either a diphtheria-tetanus-

acellular pertussis vaccine or a diphtheria-tetanus-whole cell pertussis vaccine, systemic adverse events cannot be specifically attributed to either vaccine. Most systemic events were mild and resolved spontaneously.

Data are also available from two large studies, Hib-097 and DTPa-HPV-IPV-011, in which children were vaccinated with HIBERIX.

The following frequencies were based on the analysis of the initial clinical studies as well as studies Hib-097 and DTPa-HPV-IPV-011.

Events are listed within body systems and categorised by frequency according to the following definitions:

Very common:	≥1/10
Common:	≥1/100 to <1/10
Uncommon:	≥1/1000 to <1/100
Rare:	≥1/10000 to < 1/1000
Very rare	<1/10000

Local reactions: *Very common*: redness (>2.0cm); pain, swelling (>2.0cm)

Body as a whole: *Very common*: fever; *Common*: viral infection; *Uncommon*: asthenia, fatigue, injury; *Rare*: allergic reactions, including anaphylactoid reactions

Dermatological: *Common*: rash erythematous, injection site reaction; *Uncommon*: sweating increased, purpura

Gastrointestinal: *Very common*: loss of appetite, vomiting, diarrhoea; *Common*: gastroenteritis; *Uncommon*: abdominal pain

Musculoskeletal: *Uncommon*: spastic paralysis

Nervous System: *Very common:* irritability, restlessness, unusual crying; somnolence; *Common*: nervousness; *Uncommon*: insomnia, emotional lability; *Rare: convulsions (including febrile convulsions)*

Respiratory: *Common*: rhinitis, coughing, respiratory disorder, upper respiratory tract infection, bronchitis

Special Senses: *Common*: conjunctivitis, otitis media

No serious adverse event was considered by investigators to be related to HIBERIX alone. In two serious adverse events considered related or possibly related to vaccination, HIBERIX was administered simultaneously with an acellular DTP vaccine.

Post-marketing data

Immune system disorders
Very rare: allergic reactions (including anaphylactic and anaphylactoid reactions), angioedema

Nervous system disorders
Very rare: hypotonic-hyporesponsive episode, convulsion (with or without fever), syncope or vasovagal responses to injection, somnolence

Respiratory, thoracic and mediastinal disorders
Very rare: apnoea [see section "PRECAUTIONS" for apnoea in very premature infants (≤ 28 weeks of gestation)].

Skin and subcutaneous tissue disorders
Very rare: urticaria, rash

General disorders and administration site conditions
Very rare: extensive swelling of vaccinated limb, injection site induration

DOSAGE AND ADMINISTRATION

HIBERIX is supplied as a white lyophilised powder for reconstitution with sterile 0.9% saline diluent. HIBERIX is prepared as detailed below (see *Directions for Reconstitution*).

The recommended dose is 0.5 mL.

HIBERIX vaccine must be administered by intramuscular injection. In infants and children under 12 months of age it is preferable to inject the vaccine in the anterolateral thigh because of the small size of their deltoid muscle. In children over 12 months of age the injection can alternatively be given in the deltoid region. The vaccine should be administered subcutaneously in patients with thrombocytopenia or bleeding tendencies, eg. haemophiliacs (see PRECAUTIONS).

HIBERIX MUST NOT BE GIVEN INTRAVENOUSLY.

The recommended primary vaccination course consists of three doses at 2, 4 and 6 months of age. A booster dose is recommended at 12 months of age to ensure long term protection.
This is consistent with the National Health and Medical Research Council recommendations for *Haemophilus influenzae* type b vaccination.

Directions for Reconstitution

The diluent and reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of appearance prior to administration. If either is observed, do not administer the vaccine.

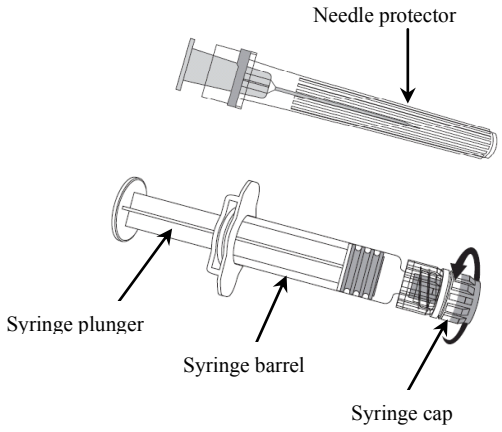
Instructions for reconstitution of the vaccine with the diluent presented in pre-filled syringe:

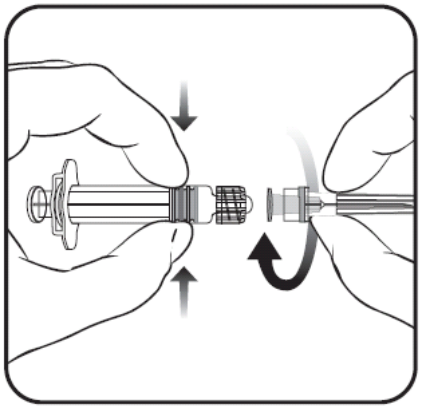
HIBERIX must be reconstituted by adding the entire content of the pre-filled syringe of diluent to the vial containing the powder.

To attach the needle to the syringe, refer to the drawing below. However, the syringe provided with HIBERIX might be slightly different than the syringe described in the drawing.

Needle

Syringe





1. Holding the syringe barrel in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.
2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock (see picture).
3. Remove the needle protector, which on occasion can be a little stiff.

Add the diluent to the powder. After the addition of the diluent to the powder, the mixture should be well shaken until the powder is completely dissolved.

The reconstituted vaccine is a clear to opalescent and colourless solution.

After reconstitution, the vaccine should be used promptly or kept in a refrigerator. If it is not used within 24 hours, it should be discarded because of the risk of contamination.

A new needle should be used to administer the vaccine.

Withdraw the entire contents of the vial.

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

OVERDOSAGE

In general, the adverse event profile reported following overdosage was similar to that observed after administration of the recommended dose of Hiberix.

For information on the management of overdose, contact the Poison Information Centre on 131 126 (Australia).

PRESENTATION AND STORAGE CONDITIONS

HIBERIX is presented as a white lyophilised powder in a glass vial. The sterile 0.9% saline diluent is clear and colourless and presented in a pre-filled syringe.
The vials and pre-filled syringes are made of neutral glass type 1.

HIBERIX is presented as a singles or tens pack.
Not all pack sizes may be distributed in Australia.

HIBERIX must be stored between 2°C to 8°C, and protected from light. The lyophilised Hib vaccine is not affected by freezing. The sterile 0.9% saline diluent may be stored in the refrigerator (at 2°C to 8°C) or stored at ambient temperatures, but must not be frozen.

The shelf-life of HIBERIX is three years from the date of manufacture when stored at temperatures between 2°C to 8°C.

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

MANUFACTURER

GlaxoSmithKline Biologicals s.a.

rue de l'Institut 89

B-1330 Rixensart, Belgium.

NAME AND ADDRESS OF THE SPONSOR

GlaxoSmithKline Australia Pty Ltd.

Level 4,

436 Johnston Street,

Abbotsford, Victoria, 3067

POISON SCHEDULE OF THE MEDICINE

Schedule 4 – Prescription Only Medicine

Date of first inclusion in the Australian Register of Therapeutic Goods (the ARTG): 15 October 1997

Date of most recent amendment: 7 November 2016

Version 7.0

HIBERIX is a registered trade mark of the GSK group of companies.