AUSTRALIAN PRODUCT INFORMATION

HIBERIX (Haemophilus influenzae type b (Hib) vaccine) powder and diluent for solution for injection

1 NAME OF THE MEDICINE

Haemophilus influenzae type b (Hib) vaccine.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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 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.

List of excipients with known effect

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Powder and diluent for solution for injection.

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.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

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

4.2 DOSE AND METHOD OF ADMINISTRATION

HIBERIX is supplied as a white lyophilised powder for reconstitution with sterile 0.9% saline diluent. HIBERIX is prepared as detailed below (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION, 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 Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

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.

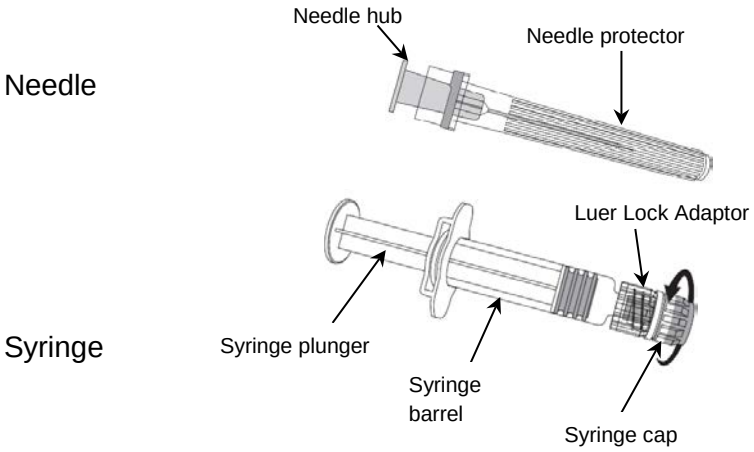
Directions for Reconstitution

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

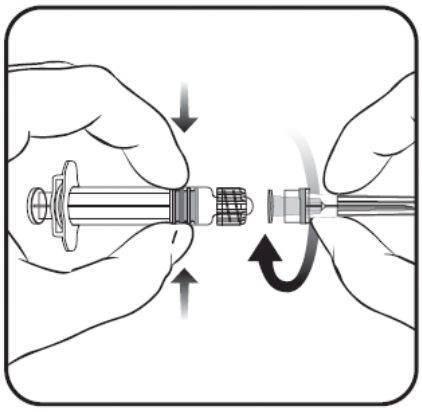
<u>Instructions for reconstitution of the vaccine with the diluent presented in pre-filled syringe:</u>

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

To attach a needle to the syringe, carefully read the instructions given with pictures 1 and 2. However, the syringe provided with HIBERIX might be slightly different than the syringe illustrated.



Picture 1



Picture 2

Always hold the syringe by the barrel, not by the syringe plunger or the Luer Lock Adaptor (LLA), and maintain the needle in the axis of the syringe (as illustrated in picture 2). Failure to do this may cause the LLA to become distorted and leak.

During assembly of the syringe, if the LLA comes off, a new vaccine dose (new syringe and vial) should be used.

1. Unscrew the syringe cap by twisting it anticlockwise (as illustrated in picture 1).

2. Attach the needle to the syringe by gently connecting the needle hub into the LLA and rotate a quarter turn clockwise until you feel it lock (as illustrated in picture 2).

3. Remove the needle protector, which may be stiff.

4. Add the diluent to the powder. The mixture should be well shaken until the powder is completely dissolved in the diluent.

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.

5. Withdraw the entire contents of the vial.

6. A new needle should be used to administer the vaccine. Unscrew the needle from the syringe and attach an injection needle by repeating step 2.

Inject the entire contents of the syringe.

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

4.3 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.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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 Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

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 Section 4.2 DOSAGE AND METHOD OF 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 the elderly

No data available

Paediatric use

See Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE.

Effects on laboratory tests

No data available

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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 Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)

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

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available

Use in pregnancy

(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.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE 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 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE, Paediatric use 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

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

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 Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

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 ≥ 0.15 µg/mL correlates with immediate protection against Hib infection and ≥ 1.0 µg/mL correlates with long term protection.

Clinical trials

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.

5.2 PHARMACOKINETIC PROPERTIES

Not relevant to vaccines

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available

Carcinogenicity

No data available

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The reconstituted vaccine preparation contains the excipients lactose monohydrate, sodium chloride and water for injection

6.2 INCOMPATIBILITIES

See Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

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.

6.5 NATURE AND CONTENTS OF CONTAINER

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.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Not relevant to vaccines

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

8 SPONSOR

GlaxoSmithKline Australia Pty Ltd

Level 4, 436 Johnston Street,

Abbotsford, Victoria, 3067

9 DATE OF FIRST APPROVAL

15 October 1997

10 DATE OF REVISION

31 October 2019

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Reformat and editorial updates
4.2	Update to instructions for reconstitution
6.1	Update to ingredient name in line with Australian Approved Name
8	Removal of manufacturer

Version 8.0