

## **HIBERIX® PRODUCT INFORMATION**

*Haemophilus influenzae* type b (Hib) vaccine

### **DESCRIPTION**

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 pellet for reconstitution with sterile 0.9% saline solution. Each 0.5mL dose contains 10mcg of purified capsular polysaccharide of Hib covalently bound to approximately 30mcg of tetanus toxoid. The reconstituted vaccine preparation also contains lactose, sodium chloride and water for injection.

The HIBERIX Hib polysaccharide is extracted from a culture of *Haemophilus influenzae* type b strain 20,752. After activation with cyanogen bromide and derivatisation with an adipic hydrazide spacer, the Hib polysaccharide is coupled to tetanus toxoid via carbodiimide condensation. After purification, the Hib conjugate is lyophilised in the presence of a lactose stabiliser.

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.

HIBERIX meets the World Health Organization requirements for the manufacture of biological substances and Hib conjugate vaccines.

### **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  $\geq 0.15$  mcg/mL correlates with immediate protection against Hib infection and  $\geq 1.0$  mcg/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% ( $\geq 0.15$  mcg/mL) and 87-90% ( $\geq 1.0$  mcg/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  $\geq 0.15$  mcg/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  $\geq 0.15$  mcg/mL and  $\geq 1.0$  mcg/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 never 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).

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 immunization series to very premature infants (born  $\leq$  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**

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 REACTIONS**

### **Clinical Trial Data**

In controlled clinical trials, 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 was 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.

Events are listed within body systems and categorised by frequency according to the following definitions: very common events reported at a frequency of greater or equal to 1/10 patients; common events reported at a frequency of less than 1/10 but greater or equal to 1/100 patients; uncommon events reported at a frequency of less than 1/100 but greater or equal to 1/1,000 patients; rare events reported at a frequency of less than 1/1,000 patients.

Local reactions: *Very common*: redness (>2.0cm) ; *Common*: 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*: restlessness, unusual crying; *Common*: nervousness, somnolence; *Uncommon*: insomnia, emotional lability

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**

Undesirable effects reported are listed according to the following frequency:

Very rare <1/10000

### 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 PRECAUTIONS].

### 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 pellet for reconstitution with sterile 0.9% saline diluent. HIBERIX is prepared by adding the entire contents of the diluent container to the vial containing the Hib vaccine pellet. The reconstituted solution must be shaken well before use, and must not be injected prior to complete dissolution of the Hib pellet. All parenteral drug and vaccine products should be inspected visually prior to administration for foreign particulate matter and/or discolouration. If either are observed, discard the diluent or reconstituted vaccine. After reconstitution HIBERIX 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.

The recommended dose is 0.5mL.

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.

## **STORAGE**

HIBERIX must be stored between +2°C to +8°C, and protected from light. Lyophilised Hib vaccine is not affected by freezing. The sterile 0.9% saline diluent may be refrigerated 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.

## **PRESENTATIONS**

HIBERIX is presented as a white lyophilised pellet in a glass vial. The sterile 0.9% saline diluent is clear and colourless and presented in a single dose glass vial or prefilled syringe.

The vials and prefilled syringes are made of neutral glass type 1, which conforms to European Pharmacopoeia requirements.

## **MANUFACTURER**

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## **DISTRIBUTED IN AUSTRALIA BY**

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