The format of this leaflet was determined by the Ministry of Health and its content was checked and approved in February 2009

1. NAME OF THE MEDICINAL PRODUCT

Hiberix™
Haemophilus influenzae type b (Hib) vaccine.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Hiberix™ is a lyophilised vaccine of purified polyribosyl-ribitol-phosphate capsular polysaccharide (PRP) of Hib, covalently bound to tetanus toxoid.

The Hib polysaccharide is prepared from Hib, strain 20,752 and after activation with cyanogen bromide and derivatisation with an adipic hydrazide spacer is coupled to tetanus toxoid via carbodiimide condensation. After purification the conjugate is lyophilised in the presence of lactose as stabiliser.

Hiberix™ meets the WHO requirements for manufacture of biological substances and of Hib conjugated vaccines.

Each single dose of vaccine is formulated to contain 10 mcg of purified capsular polysaccharide covalently bound to approximately 30 mcg tetanus toxoid.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Hiberix™ is indicated for active immunisation of all infants from the age of 2 months through 5 years against disease caused by Hib.

Hiberix™ 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

The primary vaccination schedule consists of three doses in the first 6 months of life and can start from the age of 2 months. To ensure a long-term protection, a booster dose is recommended in the second year of life.

Infants between the ages of 6 and 12 months previously unvaccinated should receive 2 injections, given with an interval of one month, followed by a booster in the second year of life. Previously unvaccinated children aged 1-5 years should be given one dose of vaccine.
As vaccination schemes vary from country to country, the schedule for each country may be used in accordance with the different national recommendations.

Method of administration
The reconstituted vaccine is for intramuscular injection. However, it is good clinical practice that in patients with thrombocytopenia or bleeding disorders the vaccine should be administered subcutaneously.

Hiberix™ should under no circumstances be administered intravascularly.

During the course of immunization, injections should not be made more than one at the same site.

As with other intramuscular injection, use with caution in patients on anti coagulant therapy.

4.3 Contra-indications

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 with other vaccines, the administration of Hiberix™ should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection, however, is not a contra-indication for vaccination.

4.4 Special warnings and special precautions for use

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

Human Immunodeficiency Virus (HIV) infection is not considered as a contra-indication for Hiberix™.

Although limited immune response to the tetanus toxoid component may occur, vaccination with Hiberix™ alone does not substitute for routine tetanus vaccination.

As reported with Haemophilus b pollysaccharide vaccines, cases of H Influenzae type b disease may occur subsequent to vaccination and prior to the onset of protective effects of the vaccine.

Excretion of capsular polysaccharide antigen in the urine has been described following receipt of Hib vaccines, and therefore antigen detection may not have a diagnostic value in suspected Hib disease within 1-2 weeks of vaccination.

Special care should be taken to ensure that the vaccine is not injected into a blood vessel.

Hiberix™ should under no circumstances be administered intravenously.

The potential risk of apnoea and the need for respiratory monitoring for 48-72h should be considered when administering the primary immunization 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.

4.5 Interaction with other medicinal products and other forms of interaction

Hiberix™ can be administered either simultaneously or at any time before or after a different inactivated or live vaccine.

Hiberix™ can be mixed in the same syringe with SmithKline Beecham vaccines Infanrix™ (DTPa vaccine), Tritanrix™ (DTPw vaccine) or Tritanrix™-HB (DTPw-HB vaccine). Other injectable vaccines should always be administered at different injection sites.

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.

Immunosopressive therapies, including irradiation, antimetabolites, alkytalin agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune response to vaccines. Short-term (< 2 weeks) of corticosteroid therapy or intra-articular, bursal or tendon injections with corticosteroids should not be immunosuppressive. Although no specific studies with pertussis vaccine are available, if immunosuppressive therapy will be discontinued shortly, it is reasonable to defer vaccination until the patient has been off therapy for one month; otherwise, the patient should be vaccinate while still on therapy.

4.6 Use during pregnancy and lactation

Adequate human data on use during pregnancy or lactation and adequate animal reproduction studies are not available.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

In controlled clinical studies, signs and symptoms were actively monitored and recorded on diary cards following the administration of the vaccine.

Of the local solicited symptoms the most frequently reported within the first 48 hours was mild redness at the injection site which resolved spontaneously. Other local solicited symptoms reported were mild swelling and pain at the injection site.

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 been also reported when administered concomitantly with other vaccines.
Very rarely allergic reactions, including anaphylactoid reactions, have been reported.

4.9 Overdose

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A titre of $\geq$ 0.15 mcg/ml was obtained in 95-100% of infants one month after the completion of the vaccination course. A titre of $\geq$ 0.15 mcg/ml was obtained in 100% of infants one month after the booster dose (94.7% with a titre of $\geq$ 10 mcg/ml).

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Vaccine : lactose
Diluent : sterile saline solution

6.2 Incompatibilities

Hiberix™ can be mixed in the same syringe with SmithKline Beecham vaccines Infanrix™ (DTPa vaccine), Tritanrix™ (DTPw vaccine) or Tritanrix™-HB (DTPw-HB vaccine). Other injectable vaccines should always be administered at different injection sites.

Hiberix™ should not be mixed with other vaccines in the same syringe (except for authorised combinations).

6.3 Shelf-life

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

When stored under prescribed conditions, the shelf-life is 36 months.

6.4 Special precautions for storage

The lyophilised vaccine has to be stored at +2°C to +8°C. The lyophilised vaccine is not affected by freezing.

The diluent can be stored in the refrigerator or at ambient temperatures (up to 25°C) and should not be frozen.

6.5 Nature and content of container

The lyophilised vaccine is presented as a white pellet in a glass vial.

The sterile diluent (saline) is clear and colourless and presented in a prefilled syringe.

The vials and syringes are made of neutral glass type I, which conforms to European Pharmacopoeia Requirements.

6.6 Instructions for us and handling, and disposal (if appropriate)

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 must be reconstituted by adding the entire contents of the supplied container of diluent 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.

After reconstitution, the vaccine should be injected promptly.

As stated in section 6.2 above, Hiberix™ may be mixed with Infanrix™, Tritanrix™, Tritanrix™ HB monodose vaccines. In this case, the diluent supplied in the Hiberix™ package is replaced by the liquid vaccine.

Make sure the container of the vaccine intended for mixing with Hiberix™ is a monodose container. From the Hiberix™ package, discard the vial containing the diluent.

The combined vaccine must be reconstituted by adding the entire contents of the other vaccine container to the vial containing the Hib white pellet.

This extemporaneously combined vaccine should be handled in the same way as the monocomponent reconstituted Hiberix™ vaccine.

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals S.A.
Rue de l'Institut 89
1330 Rixensart, Belgium

8. LICENSE HOLDER

GlaxoSmithKline (Israel) Ltd.
25 Bazel St., Petah Tikva , 49002 Israel

9. MARKETING AUTHORISATION NUMBER

Hiberix 113-64-29535