Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Hiberix. Haemophilus Type b (Hib) vaccine.Powder and Solvent for Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Hiberix is a lyophilized vaccine of purified polyribosyl-ribitol-phosphate capsular polysaccharide (PRP) of Haemophilus type b covalently bound to tetanus toxoid.

Each 0.5 ml dose of the vaccine contains 10 micrograms of purified capsular polysaccharide of Haemophilus type b covalently bound to approximately 25 micrograms tetanus toxoid.

Excipients with a known effect:
This product contains sodium 77 micromol per dose (see section 4.4).

For the full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Powder and Solvent for Solution for Injection.
Powder: white powder
Solvent: Clear colourless aqueous solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Hiberix is indicated for active immunisation against disease caused by *Haemophilus influenzae* type b in infants from the age of two months.

Hiberix does not protect against disease caused by other types of *H. influenzae* or against meningitis caused by other organisms.

4.2 Posology and method of administration

Posology
The primary immunisation course should start at two months of age, and consists of three doses with an interval of two months between each dose.

Each dose consists of 0.5 ml of the vaccine by intramuscular injection.

A single dose of Hib vaccine is recommended if the child presents after age 13 months and has had no previous Hib vaccine.

Booster dose

A fourth, booster dose of vaccine should be administered, if this is in accordance with official recommendations. Children who were primed with Hiberix may be boosted with Hiberix or with another Hib conjugate vaccine (monovalent or combined). Similarly, Hiberix may be used to boost children who were primed with other Hib conjugate vaccines (monovalent or combined).

Method of administration

Intramuscular injection. (For patients with thrombocytopenia or bleeding disorders the injection should be given subcutaneously, see Section 4.4, Special warnings and precautions for use)

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

Hiberix should not be administered to individuals that have shown any signs of hypersensitivity after previous administration of Hib vaccines.

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

4.4 Special warnings and precautions for use

It is good clinical practice that immunisation should be preceded by a review of the medical history (especially with regard to previous immunisation and possible occurrence of undesirable events) and a clinical examination.

As with all vaccinations, appropriate medical treatment should be available for injection should an anaphylactic reaction occur. Recipients of the vaccine should remain under observation until they have been seen to be in good health and not to be experiencing an immediate adverse reaction. It is not possible to specify an exact length of time.

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.

Hiberix should be administered with caution to individuals with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these individuals. In these individuals Hiberix may be administered by deep subcutaneous injection, see Section 4.2, Posology and method of administration.

The potential risk of apnoea and the need for respiratory monitoring for 48-72 h should be considered when administering the primary immunization series to very premature infants (born ≤ 28 weeks of gestation) and particulary 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.

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

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

Excretion of capsular polysaccharide antigen in the urine has been described following receipt of the Hib vaccine and therefore antigen detection may not have a diagnostic value in suspected Hib disease within one to two weeks of vaccination.

Hiberix should under no circumstances be administered intravascularly.

The solvent of the vaccine contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially "sodium-free".

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 (see section 5.1).

Different injectable vaccines should 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.

4.6 Fertility, pregnancy and lactation

Pregnancy
As Hiberix is not intended for use in adults, human data on use during pregnancy and animal reproduction studies are not available. There is no accurate information on the safety of this vaccine in pregnancy; therefore this vaccine should not be used in pregnancy.

Lactation
As Hiberix is not intended for use in adults, human data on use during lactation and animal reproduction studies are not available. There is no accurate information on the safety of this vaccine in lactation; therefore this vaccine should not be administered to breastfeeding mothers

4.7 Effects on ability to drive and use machines

Hiberix has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Clinical trial data

The following frequencies were based on the analysis of approximately 3000 infants enrolled in study Hib-097 and of approximately 1200 infants enrolled in study DTPa-HBV-IPV-011.

Adverse reactions reported are listed according to the following frequency:
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

Metabolism and nutrition disorders
Very common: loss of appetite

Psychiatric disorders
Very common: crying, irritability, restlessness

Nervous system disorders
Very common: somnolence
Rare: convulsions (including febrile convulsions)

Gastrointestinal disorders
Very common: diarrhoea
Common: vomiting

General disorders and administration site conditions
Very common: fever, swelling, pain and redness at the injection site

Post-marketing surveillance
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, syncope or vasovagal responses to injection

Respiratory, thoracic and mediastinal disorders
Very rare: Apnoea in very premature infants (≤ 28 weeks of gestation) (see section 4.4)

Skin and subcutaneous tissue disorders
Very rare: urticaria, rash (including local and generalised)

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

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via HPRA Pharmacovigilance, Website: www.hpra.ie

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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Bacterial vaccines, ATC code J07AG01
Primary vaccination
Table 1 presents the immunogenicity results from 4 clinical trials in which infants in the United States, Europe, South America and South-East Asia received a 3-dose primary vaccination with Hiberix in the first 6 months of life starting from 6 weeks of age. Varying vaccination schedules were evaluated and Hiberix was co-administered with other routinely recommended vaccines.

Hiberix was immunogenic in all 3-dose schedules studied. Anti- PRP concentration of > 0.15 µg/mL (a level indicative for short-term protection) was obtained in 96.6 - 99.4% of infants one month after the completion of the vaccination course.

Table 1: Percentage of subjects with antibody concentration ≥ 0.15 µg/mL one month after primary vaccination with Hiberix

Study	**Age at primary vaccination**	**N**	**Co-administered vaccines**	**% subjects with anti-PRP ≥ 0.15 µg/mL (95% CI)**
Hib-097	2-4-6 months	1590	DTPa-HBV-IPV PCV13 HRV	96.6 (95.6;97.4)
DTPw-HBV-Hib-008 PRI	2-4-6 months	171	DTPw-HBV	99.4 (96.8;100)
DTPa-HBV-IPV-005	3-4-5 months	410	DTPa-HBV-IPV or DTPa-HBV-IPV + OPV (at 3rd dose)	99.0 (97.5;99.7)
DTPw-HBV=Hib Kft-001	6-10-14 weeks	175	DTPw-HBV	99.4 (96.9;100)

CI: Confidence Interval
DTPw-HBV: combined Diphtheria, Tetanus, Pertussis (whole cell) and Hepatitis B Vaccine
DTPa-HBV-IPV: combined Diphtheria, Tetanus, Pertussis (acellular), Hepatitis B and Poliomyelitis Vaccine
HRV: Human Rotavirus Vaccine
N: number of subjects in the according to protocol (ATP) cohort
OPV: Oral Polio Vaccine
PCV13: 13-valent Pneumococcal Conjugate Vaccine
PRP: Polyribosylribitol phosphate

In addition, in unprimed toddlers aged 22-26 months (study Hib-036) who received a single dose of Hiberix co-administered with DTPa, 100% of subjects [N= 54, 95 % CI (93.4;100)] achieved anti-PRP concentrations ≥ 1.0 µg/mL one month after vaccination. These data support a single dose of Hiberix in children aged from 1 year and above.

Booster vaccination:
Antibody responses to booster vaccination with Hiberix after a 3 dose priming schedule are presented in Table 2. One month after the booster dose, all children had anti-PRP concentrations ≥ 0.15 µg/mL and at least 99.1% had anti-PRP concentrations ≥ 1.0 µg/mL, a concentration correlated with long term immunity to Hib (Table 2).

Table 2: Percentage of subjects with antibody concentration ≥ 1.0 µg/mL one month after booster vaccination with Hiberix

Study	**N**	**Age at primary vaccination**	**Age at booster vaccination**	**Co-administered vaccines at booster**	**% of subjects with anti-PRP ≥ 1.0 µg/mL (95% CI)**
Hib-097	336	2-4-6 months	15-18 months	DTPa	99.1 (97.4;99.8)
DTPw-HBV-Hib-008 BST	161	2-4-6 months	18 months	DTPw-HBV	99.4 (96.6;100)
DTPw-HBV=Hib Kft-003	74	6-10-14 weeks	15-18 months	DTPw-HBV	100% (95.1;100)

CI: Confidence Interval
N: number of subjects in the ATP cohort
DTPa: combined Diphtheria, Tetanus, Pertussis (acellular) vaccine
DTPw-HBV: combined Diphtheria, Tetanus, Pertussis (whole cell) vaccine and Hepatitis B Vaccine
PRP: Polyribosylribitol phosphate

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
Solvent: Sodium chloride, Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, the vaccine must not be mixed with other medicinal products.

6.3 Shelf life

The shelf-life of the Hiberix vacine is three years when stored as packaged for sale at 2^0C to 8^0C.

Once reconstituted the vaccine should be used within 1 hour.

6.4 Special precautions for storage

Store in a refrigerator (2°C to 8°C).
Store in the original package in order to protect from light.
Do not freeze.

6.5 Nature and contents of container

Powder for 1 dose in a vial (type I glass) with a stopper (butyl rubber) and solvent in a pre-filled syringe (type I glass) with a plunger stopper (butyl rubber) and a rubber tip cap.

The tip cap and rubber plunger stopper of the pre-filled syringe and the stopper of the vial are not made with natural rubber latex.

Pack sizes of 1 with or without needles.

6.6 Special precautions for disposal and other handling

The solvent and reconstituted Hiberix 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 solvent or the reconstituted vaccine.

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

Hiberix must be reconstituted by adding the entire contents of the pre-filled syringe of solvent to the vial containing the powder using a suitable needle (21G to 25G).

To attach the needle to the syringe, carefully read the instructions.

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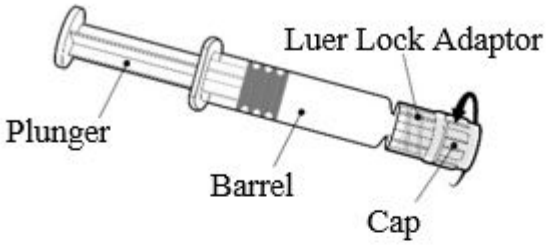
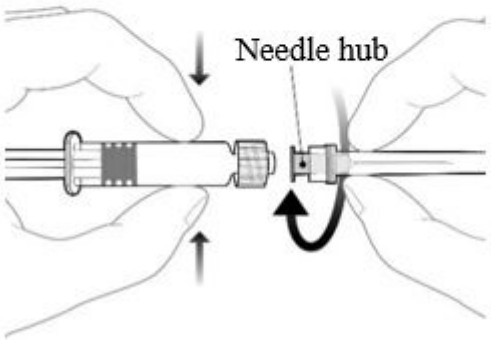


Hold the syringe by the barrel, not by the plunger or by the Luer Lock Adaptor (LLA).

Unscrew the syringe cap by twisting it anticlockwise.



To attach the needle, gently connect the hub to the LLA and rotate a quarter turn clockwise until you feel it lock.

Maintain the needle in the axis of the syringe. 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.

Reconstitute the vaccine as described below.

Do not pull the syringe plunger out of the barrel. If it happens, do not administer the vaccine.

1. Add the solvent to the powder. Shake well until the powder is completerly dissolved in the solvent. After reconstitution, use the vaccine promptly.

2. Withdraw the entire contents of the vial.

3. A new needle should be used to administer the vaccine. Unscrew the needle from the syringe and attach the injection needle by repeating steps above.

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

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

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1077/027/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 June 1999
Date of last renewal: 11 June 2009

10 DATE OF REVISION OF THE TEXT

May 2026