NEW ZEALAND DATA SHEET

1. PRODUCT NAME

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

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

For the full list of excipients, see section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

HIBERIX is a lyophilised vaccine, presented as a powder and diluent for solution for injection.

The lyophilised vaccine is presented as a white powder in a glass vial, and the sterile diluent (saline) is presented as a clear and colourless liquid in a pre-filled syringe.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HIBERIX is indicated for active immunisation of all infants from the age of 6 weeks against disease caused by Hib.

HIBERIX does not protect against diseases due to other types of *H. influenzae,* nor against meningitis caused by other organisms.

4.2 Dose and method of administration

Dose

The primary vaccination schedule consists of three doses in the first 6 months of life and can start from the age of six weeks. 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.

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.

For instructions on reconstitution of the medicine before administration, see section 6.6 Special precautions for disposal and other handling.

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.

4.4 Special warnings and precautions for use

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 contraindication for vaccination.

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 contraindication for 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 Hib vaccines, and therefore antigen detection may not have a diagnostic value in suspected Hib disease within 1-2 weeks of vaccination.

HIBERIX should under no circumstances be administered intravenously.

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.

4.5 Interactions with other medicines 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 GlaxoSmithKline vaccine INFANRIX (DTPa 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).

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.

Breast-feeding

As HIBERIX is not intended for use in adults, human data on use during lactation and animal reproduction studies are not available.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Tabulated list of adverse reactions

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.

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 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 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: e*xtensive swelling of vaccinated limb, injection site induration

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via: https://nzphvc.otago.ac.nz/reporting.

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 advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Bacterial vaccines, ATC code: J07AG01.

Clinical efficacy and safety

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 (except for DTPw-HBV-Hib-008: Total Vaccinated 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 monohydrate

Diluent: sterile saline solution (sodium chloride and water for injection)

6.2 Incompatibilities

This medicine must not be mixed with other medicines except those mentioned in section 6.6 Special precautions for disposal and other handling.

6.3 Shelf life

When stored under prescribed conditions, the shelf life is 3 years.

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

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 (at 2°C to 8°C) or at ambient temperatures (up to 25°C) and should not be frozen.

6.5 Nature and contents of container

Pack of one vial of lyophilised vaccine and one pre-filled syringe of diluent

or

Pack of 10 vials of lyophilised vaccine and 10 pre-filled syringes of diluent.

The vials and pre-filled syringes are made of neutral glass type I.

Not all pack sizes may be distributed in New Zealand.

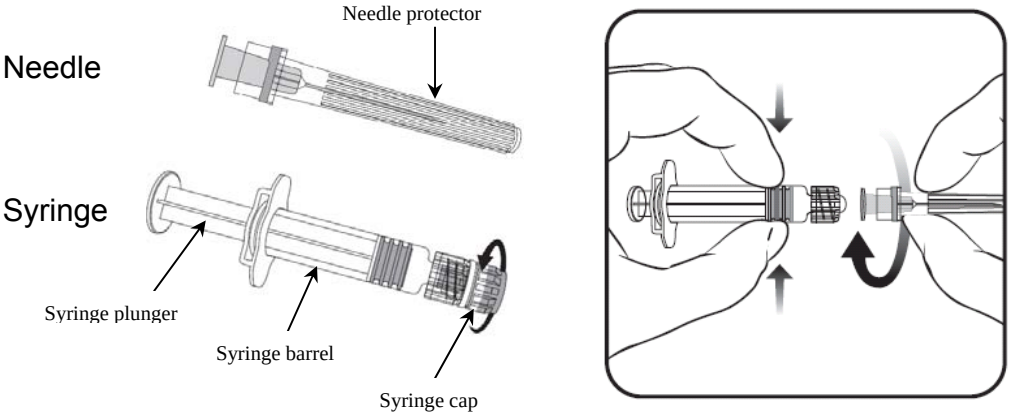
6.6 Special precautions for disposal and other handling

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.

<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 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.



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.

A new needle should be used to administer the vaccine.

Withdraw the entire contents of the vial.

As stated in section 4.5 Interactions with other medicines and other forms of interaction, HIBERIX may be mixed with INFANRIX vaccine. In this case, the diluent supplied in the HIBERIX package is replaced by the liquid INFANRIX vaccine.

- Make sure the container of the vaccine intended for mixing with HIBERIX is a monodose container. From the HIBERIX package, discard the pre-filled syringe 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 powder.

- This extemporaneously combined vaccine should be handled in the same way as the monocomponent reconstituted HIBERIX vaccine.

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

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

GlaxoSmithKline NZ Ltd
Private Bag 106600
Downtown
Auckland
NEW ZEALAND

Phone: (09) 367 2900
Facsimile: (09) 367 2910

9. DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine: 15 June 2000

10. DATE OF REVISION OF THE TEXT

18 September 2018

Summary table of changes:

Section changed	**Summary of new information**
All	Data Sheet re-format and editorial changes
2	Added cross reference to section 6.1 for excipients
4.2	Added cross reference to section 6.6 for reconstitution instructions
4.5	Relocated Interactions with other medicines and other forms of interaction section
4.6	Added Fertility section
4.8	Added mandatory information on reporting of suspected adverse reactions
4.9	Added mandatory statement regarding overdose management
5.3	Added Preclinical safety data section
6.2	Added Incompatibilities section
6.5	Relocated vial and pre-filled syringe container details

6.5	Added statement regarding available pack sizes in New Zealand
6.6	Relocated instructions for handling to Special precautions for disposal and other handling section
9	Added date of first approval
End of document	Updated trade mark statement and copyright statement

Version 9.0