NEW ZEALAND DATA SHEET

1. PRODUCT NAME

BOOSTRIX Combined diphtheria-tetanus-acellular pertussis (dTpa) suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

BOOSTRIX dTpa vaccine is a sterile suspension which contains diphtheria toxoid, tetanus toxoid and three purified antigens of Bordetella pertussis [pertussis toxoid (PT), pertussis filamentous haemagglutinin (FHA) and pertussis 69 kilodalton (kDa) outer membrane protein (OMP)] adsorbed onto aluminium salts.

1 dose (0.5 mL) contains:

Diphtheria toxoid[1]	not less than 2 International Units (IU) (2.5 Lf)
Tetanus toxoid[1]	not less than 20 International Units (IU) (5 Lf)
Bordetella pertussis antigens	
Pertussis toxoid[1]	8 micrograms
Filamentous Haemagglutinin[1]	8 micrograms
Pertactin[1]	2.5 micrograms
[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$)	0.3 milligrams Al^{3+}
and aluminium phosphate ($AlPO_4$)	0.2 milligrams Al^{3+}

The diphtheria toxoid, tetanus toxoid and acellular pertussis vaccine (dTpa) components are adsorbed on 0.5 mg aluminium and suspended in isotonic sodium chloride.

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

3. PHARMACEUTICAL FORM

BOOSTRIX is a turbid white suspension for injection.

Upon storage a white deposit and clear supernatant can be observed. This is a normal finding.

4. CLINICAL PARTICULARS

4.1 Indications

BOOSTRIX is indicated for booster vaccination against diphtheria, tetanus and pertussis of individuals aged four years and older (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

BOOSTRIX is also indicated for passive protection against pertussis in early infancy following maternal immunisation during pregnancy (see Section 4.2 Dose and method of administration, Section 4.6 Fertility, Pregnancy and Lactation and 5.1 Pharmacodynamic properties).

The use of BOOSTRIX should be in accordance with official recommendations.

4.2 Dose and method of administration

Dose

Each dose consists of a 0.5 mL ready to use sterile suspension.

BOOSTRIX can be administered to pregnant women during the second or the third trimester in accordance with official recommendations (see Section 4.1 Therapeutic indications, 4.6 Fertility, Pregnancy and Lactation and 5.1 Pharmacodynamic properties).

Method of administration

BOOSTRIX is administered by deep intramuscular injection, preferably in the deltoid region. THE VACCINE SHOULD NEVER BE ADMINISTERED INTRAVENOUSLY.

Immunisation Schedule

BOOSTRIX can be given in accordance with the current local medical practices for booster vaccination with adult-type combined diphtheria-tetanus vaccine, when a booster against pertussis is desired.

BOOSTRIX may also be administered to adolescents and adults with unknown vaccination status or incomplete vaccination against diphtheria, tetanus and pertussis as part of an immunisation series against diphtheria, tetanus and pertussis (see Section 5.1 Pharmacodynamic properties). Based on data in adults, two additional doses of a diphtheria and tetanus containing vaccine are recommended one and six months after the first dose to maximize the vaccine response against diphtheria and tetanus.

Repeat vaccination against diphtheria, tetanus and pertussis should be performed at intervals as per official recommendations (generally 10 years).

BOOSTRIX can be used in the management of tetanus prone injuries in persons who have previously received a primary vaccination series of tetanus toxoid vaccine. Tetanus immunoglobulin should be administered concomitantly in accordance with official recommendations.

4.3 Contraindications

BOOSTRIX 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 diphtheria, tetanus or pertussis vaccines.

As with other vaccines, the administration of BOOSTRIX should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection, however, is not a contraindication.

BOOSTRIX is contraindicated if the subject has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis-containing vaccine. In these circumstances, pertussis vaccination should be discontinued and the vaccination course should be continued with diphtheria and tetanus vaccines.

BOOSTRIX should not be administered to subjects who have experienced transient thrombocytopenia or neurological complications following an earlier immunisation against diphtheria and/or tetanus (for convulsions or hypotonic-hyporesponsive episodes see section 4.4 Special warnings and precautions for use).

4.4 Special warnings and precautions for use

BOOSTRIX should under no circumstances be administered intravenously.

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.

If any of the following events have occurred in temporal relation to receipt of pertussis containing vaccines, the decision to give doses of pertussis containing vaccines, should be carefully considered. There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks, particularly since these events are not associated with permanent sequelae.

- Temperature of ≥40.0°C within 48 hours of vaccination, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours of vaccination.
- Persistent, inconsolable crying lasting ≥3 hours, occurring within 48 hours of vaccination.
- Convulsions with or without fever, occurring within 3 days of vaccination.

In children with progressive neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is better to defer pertussis (Pa or Pw) immunisation until the condition is corrected or stable. However, the decision to give pertussis vaccine must be made on an individual basis after careful consideration of the risks and benefits.

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

BOOSTRIX should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects. If in accordance with official recommendations, the vaccine may need to be administered subcutaneously to these subjects. With both routes of administration, firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

A history or a family history of convulsions and a family history of an adverse event following DTP vaccination do not constitute contraindications.

Human Immunodeficiency Virus (HIV) infection is not considered a contraindication for diphtheria, tetanus and pertussis (whole-cell or acellular) immunisation. However in patients with immunodeficiency or in patients receiving immunosuppressive therapy, an adequate immunologic response may not be achieved. In these patients, when tetanus vaccine is needed for tetanus prone wound, plain tetanus vaccine should be used.

Extremely rare cases of collapse or shock-like state (hypotonic-hyporesponsiveness episode) and convulsions within 2 to 3 days of vaccination have been reported in DTPa and DTPa combination vaccines.

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.

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

4.5 Interaction with other medicines and other forms of interaction

BOOSTRIX can be given concomitantly with any of the following monovalent or combination vaccines: unadjuvanted inactivated seasonal influenza vaccines, human papilloma virus vaccines, meningococcal serogroups A, C, W-135 and Y (MenACWY) conjugate vaccines and adjuvanted

recombinant zoster vaccine. Data have shown no clinically relevant interference in the antibody response to each of the vaccine antigens.

Clinical data from co-administration of BOOSTRIX with a trivalent inactivated influenza vaccine in subjects aged between 19 and 64 years demonstrated that the immune responses to the tetanus, diphtheria, pertussis toxoid (PT) and influenza antigens were unaffected. Lower geometric mean concentrations (GMCs) were observed for the pertussis filamentous haemagglutinin (FHA) and pertactin (PRN) antigens; however, these data do not suggest clinically relevant interference. No differences were observed in a predefined exploratory cohort when the vaccines were given concomitantly or separately to subjects aged 65 years and older.

Clinical data from co-administration of BOOSTRIX with non-live herpes zoster vaccine in subjects aged 50 years and older demonstrated that the immune responses to the tetanus, diphtheria, PT, FHA and herpes zoster antigens were unaffected. Lower GMCs were observed for the PRN antigen; however, these data do not suggest clinically relevant interference.

Clinical data from co-administration of BOOSTRIX with MenACWY conjugate vaccines in subjects aged 9 to 25 years demonstrated that the immune responses to the tetanus, diphtheria and meningococcal antigens were unaffected. Lower GMCs were observed for the pertussis antigens; however, these data do not suggest clinically relevant interference.

Concomitant use with other inactivated vaccines and with immunoglobulin is unlikely to result in clinically relevant interference with the immune responses.

If BOOSTRIX is to be given at the same time as another injectable vaccine or immunoglobulin, the products should always be administered at different sites.

BOOSTRIX must not be mixed with other vaccines.

4.6 Fertility, pregnancy and lactation

Pregnancy

(Category B1)

BOOSTRIX can be used during the second or third trimester of pregnancy in accordance with official recommendations.For data relating to the prevention of pertussis disease in infants born to women vaccinated during pregnancy (see section 5.1 Pharmacodynamic properties).

Safety data from a randomised controlled clinical trial (341 pregnancy outcomes) and from a prospective observational study (793 pregnancy outcomes) where BOOSTRIX was administered to pregnant women during the third trimester have shown no vaccine related adverse effect on pregnancy or on the health of the foetus/newborn child.

Safety data from prospective clinical studies on the use of BOOSTRIX or BOOSTRIX-IPV during the first and second trimester of pregnancy are not available.

Data from post-marketing surveillance where pregnant women were exposed to BOOSTRIX or to BOOSTRIX-IPV (dTpa-inactivated poliovirus vaccine) in the 3rd and 2nd trimester have shown no vaccine related adverse effect on pregnancy or on the health of the foetus/newborn child.

As with other inactivated vaccines, it is not expected that vaccination with BOOSTRIX harms the foetus at any trimester of pregnancy. The benefits versus the risks of administering BOOSTRIX during pregnancy should be carefully evaluated.

Non-clinical data obtained with BOOSTRIX reveal no specific hazard for humans based on conventional studies of embryo-foetal development in rats and rabbits, and also of parturition and postnatal toxicity in rats (up to the end of the lactation period).

When protection against tetanus is sought, consideration should be given to tetanus or combined diphtheria-tetanus vaccines.

Breast-feeding

The safety of BOOSTRIX when administered to breast-feeding women has not been evaluated.

It is unknown whether BOOSTRIX is excreted in human breast milk.

BOOSTRIX should only be used during breast-feeding when the possible advantages outweigh the potential risks.

Fertility

No human data available. Non-clinical data obtained with BOOSTRIX reveal no specific hazard for humans based on conventional studies of female fertility in rats and rabbits.

4.7 Effects on ability to drive and use machines

The vaccine is unlikely to produce an effect on the ability to drive and use machines.

4.8 Undesirable effects

Tabulated list of adverse reactions

Clinical trial data

The safety profile below is based on data from clinical trials where BOOSTRIX was administered to 839 children (from 4 to 9 years of age) and 1931 adults, adolescents and children (above 10 years of age).

Adverse reactions reported are listed according to the following frequency:

Very common: ≥1/10

Common: ≥1/100 and <1/10

Uncommon: ≥1/1000 and <1/100

Rare: ≥1/10,000 and <1/1000

Very rare: <1/10,000

Children from 4 to 9 years of age

Infections and infestations

Uncommon: upper respiratory tract infection

Metabolism and nutrition disorders

Common: anorexia

Psychiatric disorders

Very common: irritability

Nervous system disorders

Very common: somnolence

Common: headache

Uncommon: disturbances in attention

Eye disorders

Uncommon: conjunctivitis

Gastrointestinal disorders

Common: diarrhoea, vomiting, gastrointestinal disorders

Skin and subcutaneous tissue disorders

Uncommon: rash

General disorders and administration site conditions

Very common: injection site reactions (including pain, redness and swelling), fatigue

Common: fever ≥ 37.5 °C (including fever > 39 °C),

Uncommon: other injection site reactions (such as induration), pain

Adults, adolescents and children from the age of 10 years onwards

Infections and infestations

Uncommon: upper respiratory tract infection, pharyngitis

Blood and lymphatic system disorders

Uncommon: lymphadenopathy

Nervous system disorders

Very common: headache

Common: dizziness

Uncommon: syncope

Respiratory, thoracic and mediastinal disorders

Uncommon: cough

Gastrointestinal disorders

Common: nausea, gastrointestinal disorders

Uncommon: diarrhoea, vomiting

Skin and subcutaneous tissue disorders

Uncommon: hyperhidrosis, pruritus, rash

Musculoskeletal and connective tissue disorders

Uncommon: arthralgia, myalgia, joint stiffness, musculoskeletal stiffness

General disorders and administration site conditions

Very common: injection site reactions (including pain, redness and swelling), fatigue, malaise

Common: fever ≥ 37.5 °C, injection site reactions (such as injection site mass and injection site abscess sterile)

Uncommon: fever > 39 °C, influenza like illness, pain

Reactogenicity after repeat dose of BOOSTRIX

Data on 146 subjects suggest a small increase in local reactogenicity (pain, redness, swelling) with repeated vaccination according to a 0, 1, 6 months schedule in adults (> 40 years of age).

Subjects fully primed with 4 doses of INFANRIX followed by a BOOSTRIX dose around 10 years of age show an increase of local reactogenicity after an additional BOOSTRIX dose administered 10 years later.

Post-marketing experience

Blood and lymphatic system disorders

Rare: angioedema

Immune system disorders

Very rare: allergic reactions, including anaphylactic and anaphylactoid reactions

Nervous system disorders

Rare: convulsions (with or without fever)

Skin and subcutaneous tissue disorders

Rare: urticaria

General disorders and administration site conditions

Rare: extensive swelling of the vaccinated limb, asthenia

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

Cases of overdose have been reported during post-marketing surveillance. Adverse events following overdosage, when reported, were similar to those reported with normal vaccine administration.

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 combined, ATC code: J07AJ52.

Mechanism of action

BOOSTRIX (dTpa vaccine), induces antibodies against all vaccine components.

Clinical efficacy and safety

Immune response

Immune response results to the diphtheria, tetanus and acellular pertussis components in clinical studies are presented in the table below. Approximately one month following booster vaccination with BOOSTRIX, the following seroprotection / seropositivity rates were observed:

Antigen	**Seroprotection / Seropositivity**	**Adults and adolescents from the age of 10 years onwards, at least 1690 subjects (% vaccinees)**	**Children from 4 to 9 years of age, at least 415 subjects (% vaccinees)**
Diphtheria	≥ 0.1 IU/ml*	97.2%	99.8%
Tetanus	≥ 0.1 IU/ml*	99.0%	100.0%
Pertussis:			
- Pertussis toxoid	≥ 5 EL.U/ml	97.8%	99.0%
- Filamentous haemagglutinin	≥ 5 EL.U/ml	99.9%	100.0%
- Pertactin	≥ 5 EL.U/ml	99.4%	99.8%

*cut-off accepted as indicative of protection

Results of the comparative studies with commercial dT vaccines indicates that the degree and duration of protection would not be different from those obtained with these vaccines.

Efficacy in protecting against pertussis

There is currently no correlate of protection defined for pertussis; however, the protective efficacy of GlaxoSmithKline Biologicals' DTPa (INFANRIX) vaccine against WHO-defined typical pertussis (≥ 21 days of paroxysmal cough with laboratory confirmation) was demonstrated in the following 3-dose primary studies:

- a prospective blinded household contact study performed in Germany (3, 4, 5 months schedule). Based on data collected from secondary contacts in households where there was an index case with typical pertussis, the protective efficacy of the vaccine was 88.7%. Protection against laboratory confirmed mild disease, defined as 14 days or more of cough of any type was 73% and 67% when defined as 7 days or more of cough of any type; and

- an NIH sponsored efficacy study performed in Italy (2, 4, 6 months schedule). The vaccine efficacy was found to be 84%. When the definition of pertussis was expanded to include

clinically milder cases with respect to type and duration of cough, the efficacy of INFANRIX was calculated to be 71% against >7 days of any cough and 73% against >14 days of any cough.
In a follow-up of the same cohort, the efficacy was confirmed up to 5 years after completion of primary vaccination without administration of a booster dose of pertussis.
The study assessed duration of protection of INFANRIX given in a 3 dose schedule to infants. A similar duration of protection cannot be assumed to apply to older children or adults given a single dose of BOOSTRIX, regardless of previous vaccination against pertussis.

Although the protective efficacy of BOOSTRIX has not been demonstrated in adolescents and adult age groups, vaccinees in these age groups who received BOOSTRIX achieved anti-pertussis antibody titres greater than those in the German household contact study where the protective efficacy of INFANRIX was 88.7%.

There are currently no data which demonstrate a reduction of transmission of pertussis after immunisation with BOOSTRIX. However, it could be expected that immunisation of immediate close contacts of newborn infants, such as parents, grandparents healthcare workers and childcare workers would reduce exposure of pertussis to infants not yet adequately protected through immunisation.

Passive protection against pertussis in infants (below 3 months of age) born to mothers vaccinated during pregnancy

In a randomised, cross-over, placebo-controlled study, higher pertussis antibody concentrations were demonstrated at delivery in the cord blood of babies born to mothers vaccinated with BOOSTRIX (N=291) versus placebo (N=292) during the third trimester of pregnancy. The concentrations of antibodies against the pertussis antigens PT, FHA and PRN were respectively 8, 16 and 21 times higher in the cord blood of babies born to vaccinated mothers versus controls. These antibody titres may provide passive protection against pertussis, as shown by observational effectiveness studies.

Immunogenicity in infants and toddlers born to mothers vaccinated during pregnancy

In follow-up trials in more than 500 infants and toddlers born to vaccinated mothers, clinical data did not show clinically relevant interference between maternal vaccination with BOOSTRIX and the infant and toddler response to diphtheria, tetanus, hepatitis B, inactivated polio virus, haemophilus influenzae type b or pneumococcal antigens. Although lower concentrations of antibodies against some pertussis antigens were observed post primary and post booster vaccination, 92.1 - 98.1% of subjects born to vaccinated mothers showed a booster response against all pertussis antigens. Current epidemiological data on pertussis disease do not suggest any clinical relevance of this immune interference.

Effectiveness in the protection against pertussis disease in infants born to women vaccinated during pregnancy

BOOSTRIX or BOOSTRIX-IPV vaccine effectiveness (VE) was evaluated in three observational studies in UK, Spain and Australia. The vaccine was used during the third trimester of pregnancy to protect infants below 3 months of age against pertussis disease, as part of a maternal vaccination programme.

Details of each study design and results are provided in the table below.

VE against pertussis disease for infants below 3 months of age born to mothers vaccinated during the third trimester of pregnancy with BOOSTRIX/BOOSTRIX-IPV:

Study Location	**Vaccine**	**Study design**	**Vaccination Effectiveness (VE)**

UK	BOOSTRIX-IPV	Retrospective, screening method	88% (95% CI: 79, 93)
Spain	BOOSTRIX	Prospective, matched case-control	90.9% (95% CI: 56.6, 98.1)
Australia	BOOSTRIX	Prospective, matched case-control	69% (95% CI: 13, 89)

CI: confidence interval

If maternal vaccination occurs within two weeks before delivery, VE in the infant may be lower than the figures in the table.

Persistence of the immune response

The following seroprotection / seropositivity rates were observed 3 to 3.5 years, 5 to 6 years and 10 years following vaccination with BOOSTRIX:

Antigen	Seroprotection/ seropositivity	Adults and adolescents from the age of 10 years onwards (% vaccinees)						Children from the age of 4 years onwards (% vaccinees)	
		3-3.5 years persistence		5 years persistence		10 years persistence		3-3.5 years persistence	5 to 6 years persistence
		Adult	Adole-scent	Adult	Adole-scent	Adult	Adole-scent		
Diphtheria	≥ 0.1 IU/ml*	71.2%	91.6%	84.1%	86.8%	64.6%	82.4%	97.5 %	94.2 %
	≥ 0.016 IU/ml*	97.4%	100%	94.4%	99.2%	89.9%	98.6%	100 %	Not determined
Tetanus	≥ 0.1 IU/ml	94.8%	100%	96.2%	100%	95.0%	97.3%	98.4 %	98.5 %
Pertussis									
Pertussis toxoid		90.6%	81.6%	89.5%	76.8%	85.6%	61.3%	58.7 %	51.5 %
Filamentous haemagglutinin	≥ 5 EL.U/ml	100%	100%	100%	100%	99.4%	100%	100 %	100 %
Pertactin		94.8%	99.2%	95.0%	98.1%	95.0%	96.0%	99.2 %	100 %

* Percentage of subjects with antibody concentrations associated with protection against disease (≥ 0.1 IU/ml by ELISA assay or ≥ 0.016 IU/ml by an in-vitro Vero-cell neutralisation assay).

Immune response after a repeat dose of BOOSTRIX

The immunogenicity of BOOSTRIX, administered 10 years after a previous booster dose with BOOSTRIX or reduced-antigen content diphtheria, tetanus and acellular pertussis vaccines has been evaluated in adults. One month after the decennial BOOSTRIX dose, >99 % of subjects were seroprotected against diphtheria and tetanus and all were seropositive for antibodies against pertussis antigens PT, FHA and PRN.

Immune response in subjects without prior or with unknown vaccination history

In adolescents aged from 11 to 18 years, without previous pertussis vaccination and no vaccination against diphtheria and tetanus in the previous 5 years, one dose of BOOSTRIX induced an antibody response against pertussis and all subjects were protected against tetanus and diphtheria.

BOOSTRIX administered in subjects ≥40 years of age with an incomplete, unknown or no history of a primary series of diphtheria and tetanus toxoid vaccination history induced an antibody response against pertussis in more than 98.5% of adults and provided seroprotection against diphtheria and tetanus in 81.5% and 93.4% of adults respectively.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety and toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium hydroxide, aluminium phosphate, sodium chloride and water for injections.

6.2 Incompatibilities

BOOSTRIX must not be mixed with other vaccines.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Store in a refrigerator (+2°C to +8°C).

DO NOT FREEZE. Discard if vaccine has been frozen.

Stability data indicate that the vaccine is stable at temperatures up to 37°C for 7 days. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

Protect from light.

6.5 Nature and contents of container

0.5 mL of suspension 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 are not made with natural rubber latex.

Pack size: 1, 10

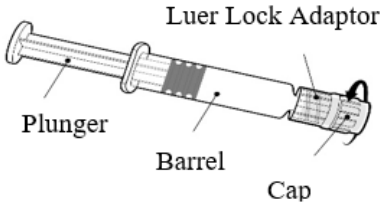
Not all pack sizes may be distributed in New Zealand.

6.6 Special precautions for disposal and other handling

All parenteral drug and vaccine products should be inspected visually for any particulate matter or discolouration prior to administration. Before use of BOOSTRIX, the vaccine should be well shaken to obtain a homogenous turbid suspension. Do not administer the vaccine if it appears otherwise.

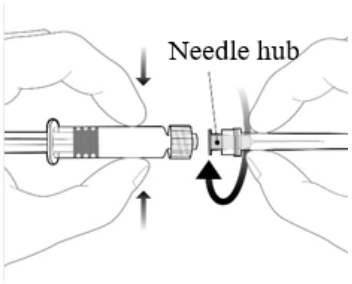
This product is for use by one patient on a single occasion.

Instructions for the pre-filled syringe



Hold the syringe by the barrel and not the plunger.

Unscrew the syringe cap by twisting it anticlockwise.



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

Do not pull the syringe plunger out of the barrel. If it happens, do not administer the 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 Limited
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: 9 November 2000

10. DATE OF REVISION OF THE TEXT

21 November 2023

Summary table of changes:

Section changed	Summary of new information
4.5	Addition of more specific information regarding concomitant administration with seasonal influenza, HPV, MenACWY and non-live herpes zoster vaccines.
6.1	Removal of residues from the Data Sheet that are not clinically relevant.

6.3	Update of shelf life
6.4	Inclusion of temperature excursion stability data

Version 14.0