AUSTRALIAN PRODUCT INFORMATION

PRIORIX (measles, mumps and rubella) vaccine, live, powder and diluent for solution for injection

1 NAME OF THE MEDICINE

Measles virus, mumps virus and rubella virus vaccine.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

PRIORIX is a live virus vaccine for immunisation against measles, mumps and rubella.

PRIORIX is a sterile lyophilised mixed preparation containing the attenuated Schwarz measles virus strain, the RIT 4385 strain of mumps virus (derived from the Jeryl Lynn strain) and the Wistar RA 27/3 rubella virus strain. Each virus strain is separately obtained by propagation in either chick embryo tissue cultures (mumps and measles) or MRC5 human diploid cells (rubella).

Each 0.5 mL dose of the reconstituted vaccine contains not less than $10^{3.0}$ $CCID_{50}$ (cell culture infectious dose 50%) of the Schwarz measles, not less than $10^{3.7}$ $CCID_{50}$ of the RIT 4385 mumps and not less than $10^{3.0}$ $CCID_{50}$ of the Wistar RA 27/3 rubella virus strains. The three virus strains are mixed prior to lyophilisation.

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.

PRIORIX meets the World Health Organisation requirements for manufacture of biological substances and for measles, mumps and rubella vaccines and combined vaccines (live).

List of excipients with known effect

PRIORIX also contains the excipient ingredient phenylalanine and residual amounts of neomycin sulphate, which is carried over from the manufacturing process.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Powder and diluent for solution for injection.

PRIORIX powder is presented as a whitish to slightly pink coloured cake, a portion of which may be yellowish to slightly orange. The sterile water diluent is clear and colourless. The reconstituted vaccine may vary in colour from clear peach to fuchsia pink, without deterioration of the vaccine potency.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

PRIORIX is indicated for active immunisation against measles, mumps and rubella from 12 months of age.

4.2 DOSE AND METHOD OF ADMINISTRATION

All parenteral drug and vaccine products should be inspected visually for any particulate matter and/or variation of physical aspects prior to reconstitution or administration. In the event of either being observed, do not use the vaccine.

Dosage (dose and interval)

A reconstituted dose is 0.5 mL for children and adults.

Children:

Two doses are usually given. The first dose is usually given at 12 months of age, followed by a booster dose at 4 - 6 years of age (see Section 4.1 THERAPEUTIC INDICATIONS).

Adults:

A single dose may be given to adults who do not have immunity.

Method of administration

PRIORIX is administered by subcutaneous or intramuscular injection, in the deltoid region or in the anterolateral area of the thigh. THE VACCINE SHOULD NEVER BE ADMINISTERED INTRAVASCULARLY.

The vaccine should be administered subcutaneously in subjects with bleeding disorders (e.g. thrombocytopenia or any coagulation disorder).

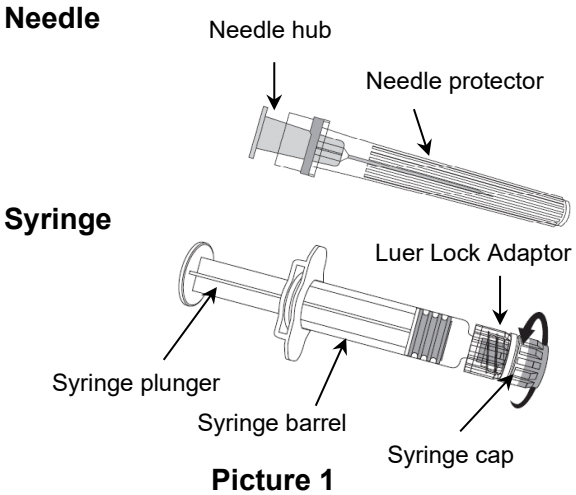
Further guidance regarding the use of vaccines is found in the Australian Immunisation Handbook.

Reconstitution

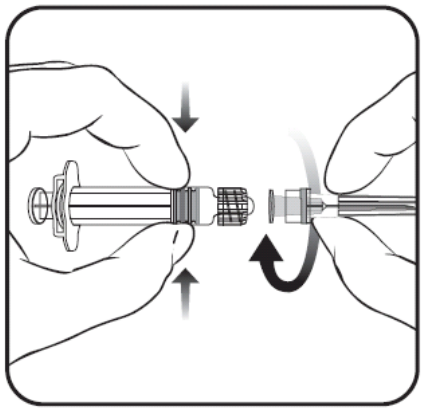
Instructions for reconstitution of the vaccine with the diluent presented in pre-filled syringe

PRIORIX must be reconstituted by adding the entire contents of the pre-filled syringe of diluent to the vial containing the powder.

To attach a needle to the syringe, carefully read the instructions given with pictures 1 and 2. However, the syringe provided with PRIORIX might be slightly different than the syringe illustrated.



Picture 1



Picture 2

Always hold the syringe by the barrel, not by the syringe plunger or the Luer Lock Adaptor (LLA), and maintain the needle in the axis of the syringe (as illustrated in picture 2). 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.

1. Unscrew the syringe cap by twisting it anticlockwise (as illustrated in picture 1).
2. Attach a needle to the syringe by gently connecting the needle hub into the LLA and rotate a quarter turn clockwise until you feel it lock (as illustrated in picture 2).
3. Remove the needle protector, which may be stiff.
4. Add the diluent to the powder. The mixture should be well shaken until the powder is completely dissolved in the diluent.

After reconstitution, the vaccine should be used promptly.

5. Withdraw the entire contents of the vial.
6. A new needle should be used to administer the vaccine. Unscrew the needle from the syringe and attach an injection needle by repeating step 2 above.

Inject the entire contents of the syringe.

The vaccine should be injected as soon as possible after reconstitution. The reconstituted vaccine can be stored between 2 and 8°C, for up to 8 hrs before use.

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

4.3 CONTRAINDICATIONS

PRIORIX is contraindicated in pregnant women. If vaccination of postpubertal women occurs, pregnancy should be avoided for one month (see Section 4.6 FERTILITY, PREGNANCY AND LACTATION, Use in Pregnancy).

PRIORIX should not be administered to children and adults with known hypersensitivity to any components of the vaccine (for egg allergy see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE). Vaccination is contraindicated in children and adults who are allergic to neomycin, although a history of contact dermatitis to neomycin is not a contraindication.

PRIORIX is contraindicated in children and adults having shown signs of hypersensitivity after previous administration of measles, mumps and/or rubella vaccines.

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

PRIORIX is contraindicated in patients with severe humoral or cellular (primary or acquired) immunodeficiency e.g. symptomatic HIV infection (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE), those receiving high dose steroids (further guidance is found in the Australian Immunisation Handbook).

PRIORIX is contraindicated in patients on current or recent immunosuppressive therapy (includes high doses of corticosteroids but not topical or inhaled corticosteroids). Further guidance can be found in the Australian Immunisation handbook.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

PRIORIX must not be administered intravascularly.

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

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.

Alcohol and other disinfecting agents must be allowed to evaporate from the skin before injection of the vaccine as they can inactivate the attenuated viruses in the vaccine.

Infants below 12 months of age may not respond sufficiently to the measles component of the vaccine due to the possible persistence of maternal measles antibodies. This should not preclude the use of the vaccine in younger infants (< 12 months) as vaccination may be indicated in certain situation such as high risk areas (see Section 4.1 THERAPEUTIC INDICATIONS). In these circumstances revaccination at or after 12 months should be considered.

Limited protection against measles may be obtained by vaccination up to 72 hours after exposure to natural measles. If the vaccination status of the child is in doubt, the vaccine should be given as there are no ill effects of vaccinating individuals who are already immune. The antibody response to the rubella and mumps components is too slow for effective post-exposure prophylaxis.

Transmission of measles and mumps virus from vaccinees to susceptible contacts has never been documented. Pharyngeal excretion of the rubella virus is known to occur about 7 to 28 days after vaccination with peak excretion around the 11th day. However there is no evidence of transmission of this excreted virus to susceptible contacts.

PRIORIX should be given with caution to persons with a history or family history of allergic disease or those with a history or family history of convulsions.

The measles and mumps components of the vaccine are produced in chick embryo cell culture and may therefore contain traces of egg protein. Persons with a history of anaphylactic, anaphylactoid, or other immediate reactions (e.g., hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) subsequent to egg ingestion should not be vaccinated with PRIORIX.

It appears that persons are not at increased risk if they have egg allergies that are not anaphylactic or anaphylactoid in nature. Such persons may be vaccinated in the usual manner. There is no evidence to indicate that persons with allergies to chickens or feathers are at increased risk of reaction to the vaccine.

As for any vaccine, immunisation with measles, mumps, rubella vaccine may not result in seroconversion in 100% of susceptible persons given the vaccine.

Cases of worsening thrombocytopenia and recurrence of thrombocytopenia in children and adults who suffered thrombocytopenia after the first dose have been reported following vaccination with live measles, mumps and rubella vaccines. In such cases, the risk-benefit of immunising with PRIORIX should be carefully evaluated.

There is limited data on the use of PRIORIX in immunocompromised patients, therefore vaccination should be considered with caution and only when, in the opinion of the physician, the benefits outweigh the risks (e.g. asymptomatic HIV subjects) further guidance is found in the Australian Immunisation Handbook.

Immunocompromised patients who have no contraindication for this vaccination (see Section 4.3 CONTRAINDICATIONS) may not respond as well as immunocompetent children and adults, therefore some of these patients may acquire measles, mumps or rubella despite appropriate vaccine administration. Immunocompromised patients should be monitored carefully for signs of measles, mumps and rubella.

Due to the potential risk of decreased vaccine response and/or disseminated diseases, consideration should be given to the time interval between PRIORIX vaccination and immunosuppressive therapy (see Section 4.3 CONTRAINDICATIONS).

Use in the elderly

No data available.

Paediatric use

See Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Clinical studies have demonstrated that PRIORIX can be given simultaneously with any of the following monovalent or combination vaccines: hexavalent vaccine (DTPa-HBV-IPV/Hib), diphtheria-tetanus-acellular pertussis vaccine (DTPa), reduced antigen diphtheria-tetanus-acellular pertussis vaccine (dTpa), *Haemophilus influenzae* type b vaccine (Hib), inactivated polio vaccine (IPV), hepatitis B vaccine (HBV), hepatitis A vaccine (HAV), meningococcal serogroup B vaccine (MenB), meningococcal serogroup C conjugate vaccine (MenC), meningococcal serogroups A, C, W-135 and Y conjugate vaccine (MenACWY), varicella vaccine and pneumococcal conjugate vaccine (PCV).

In addition, it is generally accepted that combined measles, mumps and rubella vaccines may be given at the same time as oral polio vaccine (OPV) or the combined diphtheria-tetanus and whole cell pertussis vaccines (DTPw).

If PRIORIX is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

If PRIORIX cannot be given at the same time as another live attenuated vaccine, an interval of at least 1 month should be left between the two vaccinations.

If tuberculin (Mantoux) testing is needed, it should be carried out before, or simultaneously with measles, mumps and rubella vaccination. It has been reported that live measles (and possibly mumps) vaccine may cause a temporary depression of tuberculin skin sensitivity which could last 4 to 6 weeks. Tuberculin testing is therefore unreliable (false negative) for 4 to 6 weeks after administration of measles, mumps, rubella vaccine.

In children and adults who have received human gammaglobulins or blood transfusions, vaccination should be delayed for at least 3 months because of the possibility of vaccine failure due to passively acquired measles, mumps and rubella antibodies.

PRIORIX should not be mixed with other vaccines in the same syringe.

PRIORIX can be used as a booster dose in children and adults who have previously been vaccinated with PRIORIX or another measles, mumps and rubella combined vaccine.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

(Pregnancy Category B2)

Pregnant women must not be vaccinated with PRIORIX. Pregnancy should be avoided for one month after vaccination. Women who intend to become pregnant should be advised to delay pregnancy.

Studies have not been conducted with PRIORIX in pregnant women.

In a literature review of more than 3,500 susceptible women who were unknowingly in early stages of pregnancy when vaccinated with a rubella-containing vaccine, no cases of congenital rubella syndrome were reported. Post-marketing surveillance identified congenital rubella syndrome associated with a rubella vaccine strain (Wistar RA 27/3) following inadvertent vaccination of a pregnant woman with measles, mumps and rubella vaccine.

Foetal damage has not been documented when measles or mumps vaccines have been given to pregnant women.

Women of child bearing age should be tested for rubella antibodies prior to pregnancy. All seronegative women, provided they are not pregnant, should be offered rubella vaccine.

Use in lactation

There is little human data regarding use in breastfeeding women. Persons can be vaccinated where the benefit outweighs the risk.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Clinical Trial Experience

Primary Immunisation:

A total of approximately 12,000 subjects were administered PRIORIX in clinical trials. During controlled clinical studies, the signs and symptoms were actively monitored during a 42 day follow-up. The vaccinees were also requested to report any other clinical events which manifested during the study period. Table 1 lists the pooled incidence of solicited symptoms from 9 comparative studies for children vaccinated with PRIORIX according to protocol. (The results for the comparator vaccine are based on 8 studies, n=1074).

Table 1: Pooled incidence of solicited symptoms from 9 comparative studies for children vaccinated with PRIORIX according to protocol.

Solicited Symptom	PRIORIX (% incidence)	Comparator vaccine (% incidence)
Local redness	7.2	16.3
Rash*	7.1	9.8
Fever (>39.5°C)*	6.4	11.9
Local pain	3.1	8.6
Local swelling	2.6	7.4
Parotid swelling	0.7	0.5
Febrile convulsions	0.1	0.1

* Daily incidence in two studies not recorded

Other events:

The safety profile presented below is based on a total of approximately 12,000 subjects administered PRIORIX in clinical trials. Causality has not been established. The incidence of adverse reactions described below were similar to the comparator MMR vaccine.

The events are listed within body systems and categorised by frequency according to the following definitions:

Very common: ≥ 10%
Common: ≥ 1% and < 10%
Uncommon: ≥ 0.1% and < 1%
Rare: ≥ 0.01% and < 0.1%
Very rare: < 0.01%

Body as a whole
Very common: redness at the injection site, fever ≥ 38°C (rectal) or ≥ 37.5°C (axillary/oral)
Common: pain and swelling at the injection site, fever > 39.5°C (rectal) or >39°C (axillary/oral), viral infection
Uncommon: injury, infection**,** allergy, abnormal crying, fatigue, infection bacterial, infection fungal

Skin and appendages
Common: rash
Uncommon: dermatitis**,** eczema, pruritis, herpes simplex, herpes zoster

Respiratory
Common: pharyngitis, bronchitis, coughing, respiratory disorder, other upper respiratory tract infection, rhinitis
Uncommon: pneumonia, laryngitis**,** stridor

Gastrointestinal
Common: diarrhoea
Uncommon: anorexia, gastrointestinal disorder, parotid gland enlargement, toothache, vomiting, enteritis, gastroenteritis, stomatitis, stomatitis aphthous

Central Nervous System
Common: nervousness
Uncommon: insomnia
Rare: febrile convulsions

Special Senses
Common: otitis media
Uncommon: conjunctivitis

Haematologic/ Lymphatic
Uncommon: anaemia, lymphadenopathy

Five adverse events experienced by three subjects were considered by the investigators to be serious and related or possibly related. These events were: granulocytopenia, fever, exanthema, vomiting and epididymitis.

Booster Immunisation:

In a study examining booster doses of PRIORIX administered to children aged 4-6 years, the following solicited symptoms in Table 2 were reported:

Table 2: Solicited symptoms reported in a study examining booster doses of PRIORIX administered to children aged 4-6 years

Solicited symptom	PRIORIX (n=38) % incidence	Comparator vaccine (n=37) % incidence
Pain (burning/stinging)*	13.2	32.4
Pain	10.5	18.9
Redness	10.5	8.1
Swelling	2.6	0.0
Fever > 39.5°C	5.3	0.0
Parotid gland swelling	0.0	0.0

* pain at the time of injection (burning/stinging) or within 30mins of injection

In a study examining booster doses of PRIORIX administered to children aged 11-12 years of age, the following solicited symptoms in Table 3 were reported:

Table 3: Solicited symptoms reported in a study examining booster doses of PRIORIX administered to children aged 11-12 years

Solicited symptom	PRIORIX (n=149) % incidence	Comparator vaccine (n=150) % incidence
Pain	20.1	33.3
Redness	25.5	25.3

Swelling	13.4	12.7
Fever > 39.5°C	1.3	0.7
Skin rash	0.7	1.3
Parotid gland swelling	1.3	0.7

Other events

All unsolicited events reported in this booster study, are listed below. The events are listed within body systems and categorised by frequency according to the following definitions:

Very common: ≥ 10%
Common: ≥ 1% and < 10%
Uncommon: ≥ 0.1% and < 1%
Rare: ≥ 0.01% and < 0.1%
Very rare: < 0.01%
Causality has not been established.

Booster in 4-6 year old children:

Body as a whole
Very common: pain and redness at the injection site, fever ≥ 38°C (rectal) or ≥ 37.5°C (axillary/oral)
Common: swelling at the injection site, fever > 39.5°C (rectal) or >39°C (axillary/oral), allergy

Respiratory
Common: bronchitis, coughing, pharyngitis, rhinitis
Uncommon: asthma, epistaxis, sinusitis
Gastrointestinal
Common: diarrhoea, vomiting
Uncommon: colitis, gastroenteritis, parotid gland enlargement

Central Nervous System
Common: headache
Uncommon: dysphonia

Skin and appendages disorder
Common: rash, eczema
Uncommon: dermatitis, urticaria

Vision disorders
Uncommon: conjunctivitis

Resistance mechanism disorders
Common: upper respiratory tract infection, otitis media, herpes zoster (varicella)
Uncommon: herpes simplex, infection viral

Booster in 11-12 year old children

Body as a whole
Uncommon: viral infection, lymphadenopathy

Respiratory
Common: upper respiratory tract infection, rhinitis, pharyngitis, asthma
Uncommon: coughing, epistaxis

Gastrointestinal
Uncommon: abdominal pain, gastroenteritis, diarrhoea

Central Nervous System
Common: headache
Uncommon: dizziness

Skin and appendages disorder
Uncommon: pruritis, skin exfoliation, nail disorder, injection site reaction, urticaria

Post-marketing data

During post-marketing surveillance, the following reactions have been reported additionally in temporal association with PRIORIX vaccination:

Infections and infestations
Rare: meningitis, measles-like syndrome, mumps-like syndrome (including orchitis, epididymitis and parotitis)

Blood and Lymphatic system disorders
Rare: thrombocytopenia, thrombocytopenic purpura, immune thrombocytopenia (ITP)

Immune system disorders
Rare: anaphylactic reactions

Nervous system disorders
Rare: encephalitis, cerebellitis, cerebellitis like symptoms (including transient gait disturbance and transient ataxia), Guillain Barré syndrome, transverse myelitis, peripheral neuritis

Vascular disorders
Rare: vasculitis (including Henoch Schonlein purpura and Kawasaki syndrome)

Skin and subcutaneous tissue disorders
Rare: erythema multiforme

Unknown: skin granuloma associated with vaccine derived rubella virus

Musculoskeletal and connective tissue disorders
Rare: arthralgia, arthritis

As in natural rubella infection, myalgia may occur 2 to 4 weeks after administration of live rubella vaccines.

Accidental intravascular administration may give rise to severe reactions or even shock. Immediate measures depend on the severity of the reaction. (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Cases of overdose (up to 2 times the recommended dose) have been reported during post-marketing surveillance. Adverse events reported following overdosage were similar to those reported with normal vaccine administration.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

PRIORIX induces antibodies against all vaccine components.

Clinical trials

Seroconversion has been shown to equate with protection against each of the measles, mumps and rubella viruses.

Primary Immunisation:

In clinical studies, PRIORIX has been demonstrated to be highly immunogenic.

In previously seronegative vaccinees, antibodies were detected in 98.0%, 96.1% and 99.3% of subjects against measles, mumps and rubella respectively.

In a pooled analysis of comparative studies of over 1400 children, antibodies against measles, mumps and rubella were detected in 98.7%, 95.5% and 99.5% of previously seronegative subjects (n=1094) who received PRIORIX. Antibodies against measles, mumps and rubella were detected in 96.9%, 96.9% and 99.5% of subjects (n=388) respectively, who had received a commercially available combined MMR vaccine.

Similar seroconversion rates were seen in subjects who received PRIORIX by the intramuscular route.

Seroconversion rates in a limited number of subjects (n=60) aged 9-11 months were also measured. 100% of these subjects developed antibodies against mumps and rubella. 96.6% of the subjects developed anti-measles antibodies.

Antibody levels of participants in the pooled studies have been monitored for up to 12 months following vaccination. All subjects remained seropositive for anti-measles and anti-rubella antibodies. Anti-mumps antibodies were detected in 88.4% of subjects. A similar result was observed with a commercially available MMR vaccine.

In a more recent study comparing the current formulation of PRIORIX (albumin-free) with the previous formulation containing albumin, antibodies against measles, mumps and rubella were detected in 98.4, 94.8 and 100% of previously seronegative subjects (n=191) who received the current formulation. Antibodies against measles, mumps and rubella were detected in 99.5, 94.7 and 100% of subjects (n=190) respectively, who had received the formulation used in the earlier studies containing albumin. There were no significant differences in immunogenicity between the current formulation of PRIORIX (albumin-free) and the formulation containing albumin used in the earlier studies.

Booster Immunisation:

A booster dose of PRIORIX was administered to children aged 4 - 6 years or 11-12 years, who had been primed with a different MMR vaccine. All subjects aged 4-6 years who were seronegative at the time of booster, subsequently seroconverted. In subjects aged 11 -12 years who were seronegative at the time of booster, seroconversion rates of 85.7%, 93.5% and 100% were observed for measles, mumps and rubella respectively.

5.2 PHARMACOKINETIC PROPERTIES

Not relevant to vaccines.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The lyophilised vaccine contains lactose, amino acids and sorbitol and mannitol as stabilisers. Neomycin sulphate is present as a residual from the manufacturing process.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

The vaccine should be stored between 2°C and 8°C in a refrigerator.

6.5 NATURE AND CONTENTS OF CONTAINER

The powder is presented in a glass vial. The diluent is presented in a glass prefilled syringe.

PRIORIX is available in pack sizes of 1 or 10.

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

Not all pack sizes may be distributed in Australia.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Not relevant to vaccines

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

8 SPONSOR

GlaxoSmithKline Australia Pty Ltd
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9 DATE OF FIRST APPROVAL

24 October 2003

10 DATE OF REVISION

04 June 2026

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.8	Revision of safety information to include skin granuloma

Version 16.0