NEW ZEALAND DATA SHEET

1. PRODUCT NAME

VARILRIX (human albumin-free) live attenuated varicella vaccine

Each dose of the reconstituted vaccine contains not less than $10^{3.3}$ plaque-forming units (PFU) of the varicella-zoster virus.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 mL) contains:

Live attenuated Oka strain of varicella-zoster virus, obtained by propagation of the virus in MRC_5 human diploid cell culture.

VARILRIX meets the World Health Organisation requirements for biological substances and for varicella vaccines.

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

3. PHARMACEUTICAL FORM

Lyophilised powder: slightly cream to yellowish or pinkish colour.

Sterile diluent: clear and colourless.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

VARILRIX is indicated for active immunisation and prophylaxis against varicella in healthy infants (from the age of 9 months), children, adolescents and adults.

There are socioeconomic benefits for the more extensive use of VARILRIX in the community eg. health workers, school teachers and others exposed to children should be vaccinated with VARILRIX if there is no history of varicella. Working mothers should have their children vaccinated.

4.2 Dose and method of administration

0.5 mL of reconstituted vaccine contains one immunising dose.

Dose

Paediatric population: children from the age of 9 months up to 12 years of age: two doses of VARILRIX administered at least six weeks apart is recommended for the benefit of enhanced immune response against varicella virus.

13 years and above: two doses with an interval between doses of a minimum of 6 weeks.

Interchangeability

- A single dose of VARILRIX may be administered to those who have already received a single dose of another varicella-containing vaccine.

- A single dose of VARILRIX may be administered followed by a single dose of another varicella-containing vaccine.

Method of administration

VARILRIX SHOULD NEVER BE ADMINISTERED INTRAVENOUSLY.

VARILRIX should be administered by subcutaneous injection only. The upper arm (deltoid region) is the preferred site of injection.

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

4.3 Contraindications

VARILRIX is contraindicated in people with severe humoral or cellular immunodeficiency such as:

- people with primary or acquired immunodeficiency states with a total lymphocyte count less than 1,200 per mm^3;
- people presenting other evidence of lack of cellular immune competence (e.g. people with leukaemias, lymphomas, blood dyscrasias, clinically manifest HIV infection);
- people on current or recent immunosuppressive therapy (includes high doses of corticosteroids but not topical or low-dose parenteral corticosteroids).
  See also section 4.4 Special warnings and precautions for use.

VARILRIX is contraindicated in people with known hypersensitivity to neomycin or to any other component of the vaccine (see section 6.1 List of excipients). A history of contact dermatitis to neomycin is not a contraindication.

VARILRIX is contraindicated in people having shown signs of hypersensitivity after previous administration of varicella vaccine.

VARILRIX is contraindicated in pregnant women. Pregnancy should be avoided for one month after vaccination (see section 4.6 Fertility, pregnancy and lactation).

4.4 Special warnings and precautions for use

As with other vaccines, the administration of VARILRIX should be postponed in people suffering from acute severe febrile illness. In healthy people the presence of a minor infection, however, is not a contraindication for vaccination.

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

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

Limited protection against varicella may be obtained by vaccination up to 72 hours after exposure to natural disease.

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

As for other varicella vaccines, cases of varicella disease have been shown to occur in persons who have previously received VARILRIX. These breakthrough cases are usually mild, with a fewer number of lesions and less fever as compared to cases in unvaccinated individuals.

Transmission of the Oka vaccine virus has been shown to occur at a very low rate in seronegative contacts of vaccinees with rash. Transmission of the Oka vaccine from a vaccinee who does not develop a rash to seronegative contacts cannot be excluded.

The mild nature of the rash which developed in the healthy contacts indicates that the virus remains attenuated after passage through human hosts. Vaccine recipients should attempt to avoid contact with susceptible high risk individuals for up to 6 weeks, where possible.

There is limited data on the use of VARILRIX in immunocompromised people, therefore vaccination should be considered with caution and only when, in the opinion of the physician, the benefits outweigh the risks.

Immunocompromised people who have no contraindication for this vaccination (see section 4.3 Contraindications) may not respond as well as immunocompetent people, therefore some of these people may acquire varicella despite appropriate vaccine administration. Immunocompromised people should be monitored carefully for signs of varicella.

Due to the potential risk of decreased vaccine response and/or disseminated disease, consideration should be given to the time interval between VARILRIX vaccination and immunosuppressive therapy (see section 4.3 Contraindications).

Very few reports exist on disseminated varicella with internal organ involvement following vaccination with Oka varicella vaccine strain mainly in immunocompromised people.

Vaccinees who develop papulo-vesicular eruptions within the first 4 weeks post vaccination should avoid contact with patients known to be immune suppressed for the duration of the rash.

Care should be exercised in patients with serious chronic diseases (such as chronic renal failure, autoimmune diseases, collagen diseases, severe bronchial asthma).

VARILRIX must not be administered intravascularly or intradermally.

4.5 Interactions with other medicines and other forms of interaction

If tuberculin testing has to be done it should be carried out before or simultaneously with vaccination since it has been reported that live viral vaccines may cause a temporary depression of tuberculin skin sensitivity. As this anergy may last up to a maximum of 6 weeks, tuberculin testing should not be performed within that period after vaccination to avoid false negative results.

In people who have received immune globulins or a blood transfusion, vaccination should be delayed for at least three months because of the likelihood of vaccine failure due to passively acquired varicella antibodies.

Salicylates should be avoided for 6 weeks after varicella vaccination as Reye's Syndrome has been reported following the use of salicylates during natural varicella infection.

VARILRIX can be administered at the same time as any other vaccine. Different injectable vaccines should always be administered at different injection sites.

Inactivated vaccines can be administered in any temporal relationship to VARILRIX.

Should a measles containing vaccine not be given at the same time as VARILRIX, it is recommended that an interval of at least one month should be respected since it is recognised

that measles vaccination may lead to short lived suppression of the cell mediated immune response.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Adequate human data on the use of VARILRIX during pregnancy are not available and animal studies on reproductive toxicity have not been conducted.

Breast-feeding

There are no data regarding use in breastfeeding women.

Fertility

No data available.

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

VARILRIX is a vaccine of low overall reactogenicity in all age groups.

The safety profile presented below is based on a total of 5369 doses of VARILRIX administered in monotherapy to children, adolescents and adults.

Undesirable effects reported are listed according to the following frequency:

Very common: $\geq$ 1/10

Common: $\geq$ 1/100 *and* < 1/10

Uncommon: $\geq$ 1/1000 *and* < 1/100

Rare: $\geq$ 1/10000 *and* < 1/1000

Very rare: < 1/10000

System organ class	Frequency	Adverse reactions
Infections and infestations	Uncommon	upper respiratory tract infection, pharyngitis
Blood and lymphatic system disorders	Uncommon	lymphadenopathy
Psychiatric disorders	Uncommon	irritability
Nervous system disorders	Uncommon	headache, somnolence
Eye disorders	Rare	conjunctivitis

Respiratory, thoracic and mediastinal disorders	Uncommon	cough, rhinitis
Gastrointestinal disorders	Uncommon	nausea, vomiting
	Rare	abdominal pain, diarrhoea
Skin and subcutaneous tissue disorders	Common	rash
	Uncommon	varicella-like rash, pruritus
	Rare	urticaria
Musculoskeletal and connective tissue disorders	Uncommon	arthralgia, myalgia
General disorders and administration site conditions	Very common:	pain, redness
	Common	swelling at the injection site*, fever (oral/axillary temperature ≥ 37.5°C or rectal temperature ≥ 38.0°C)*
	Uncommon	fever (oral/axillary temperature > 39.0°C or rectal temperature > 39.5°C), fatigue, malaise

* Swelling at the injection site and fever were reported very commonly in studies conducted in adolescents and adults. Swelling was also reported very commonly after the second dose in children under 13 years of age.

A trend for higher incidence of pain, redness and swelling after the second dose was observed as compared to the first dose.

On average, the reactogenicity after the second dose was not higher than after the first dose.

No differences were seen in the reactogenicity profile between initially seropositive and initially seronegative subjects.

In clinical studies involving more than 2000 subjects from the age of 9 months, papulo-vesicular eruptions were reported in approximately 5% of the vaccinees. Most of them occur during the first three weeks after vaccination, and the number of lesions was generally below ten. Temperature above 37.5°C (axillary) / 38°C (rectal) was reported in approximately 5% of subjects during a six week follow-up of the vaccinees. The reactogenicity after the second dose in adolescents and adults was not higher than after the first dose. No difference was seen between the reactogenicity in initially seropositive and seronegative subjects.

In a four week follow-up double-blind placebo-controlled study including 513 children between 12-30 months of age, there was no significant difference in nature or incidence of symptoms in subjects receiving vaccine or placebo.

<u>High-risk patients</u>

There are only very limited data from clinical trials available in patients at high risk of severe varicella. However, vaccine-associated reactions (principally papulo-vesicular eruptions and fever) are usually mild. As in healthy subjects, redness, swelling and pain at the site of injection are mild and transient.

<u>Adverse reactions from spontaneous reporting</u>

During post-marketing surveillance, the following additional reactions have been reported after varicella vaccination:

System organ class	Frequency	Adverse reactions
Infections and infestations	Rare	herpes zoster
Blood and lymphatic system disorders	Rare	thrombocytopenia
Immune system disorders	Rare	hypersensitivity, anaphylactic reactions
Nervous system disorders	Rare	encephalitis, cerebrovascular accident, cerebellitis, cerebellitis like symptoms (including transient gait disturbance and transient ataxia), convulsions
Vascular disorders	Rare	vasculitis (including Henoch Schonlein purpura and Kawasaki syndrome)
Skin and subcutaneous tissue disorders	Rare	erythema multiforme

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://pophealth.my.site.com/carmreportnz/s/}

4.9 Overdose

Cases of accidental administration of more than the recommended dose of VARILRIX have been reported. Amongst these cases, the following adverse events were reported: lethargy and convulsions. In the other cases reported as overdose there were no associated adverse events.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Viral vaccines, ATC code J07BK01.

VARILRIX produces an attenuated clinically inapparent varicella infection in susceptible subjects.

The presence of antibodies is accepted to be an indication of protection.

Pharmacodynamic Effects

Efficacy studies

The efficacy of GlaxoSmithKline (GSK)'s Oka/RIT varicella vaccines in preventing confirmed varicella disease (clinical breakthrough varicella was confirmed by, polymerase chain reaction {PCR} or exposure to a varicella case) has been evaluated in a large active controlled clinical trial in which children aged 12-22 months received one dose of VARILRIX or two doses of combined measles, mumps, rubella and varicella (Oka/RIT) vaccine. Vaccine efficacy against

confirmed varicella of any severity and against moderate or severe confirmed varicella observed after a primary follow-up period of 2 years (median duration 3.2 years) and after an extended follow-up period of 6 years (median duration 6.4 years) are presented in Table 1.

Table 1: Efficacy results after one dose of VARILRIX compared to 2 doses of PRIORIX TETRA

Group	Timing	Efficacy against confirmed varicella of any severity	Efficacy against moderate or severe confirmed varicella
Varilrix (1 dose) N = 2,487	Year 2	65.4 % (97.5% CI: 57.2;72.1)	90.7% (97.5% CI: 85.9;93.9)
	Year 6(1)	67.0% (95% CI: 61.8;71.4)	90.3% (95% CI: 86.9;92.8)
Combined measles, mumps, rubella and varicella (Oka/RIT) vaccine (2 doses) N = 2,489	Year 2	94.9% (97.5% CI: 92.4;96.6)	99.5% (97.5% CI: 97.5;99.9)
	Year 6(1)	95.0% (95% CI: 93.6;96.2)	99.0% (95% CI: 97.7;99.6)

N = number of subjects enrolled and vaccinated
(1) descriptive analysis

In a previous study specifically designed to evaluate vaccine efficacy after one dose of VARILRIX, 10 to 30-month-old children were followed up for a period of approximately 2.5 years after vaccination. The protective efficacy was 100% against common clinical cases of varicella (≥ 30 vesicles) and 88% (95% CI: 71.0;95.2) against any serological confirmed case of varicella (at least 1 vesicle or papule).

Effectiveness studies

Effectiveness data suggest a higher level of protection and a decrease in breakthrough varicella following two doses of vaccine than following one dose.

The effectiveness of one dose of VARILRIX was estimated in different settings (outbreaks, case-control and database studies) and ranged from 20%-92% against any varicella disease and from 86%-100% against moderate or severe disease.

The impact of one dose of VARILRIX in reducing varicella hospitalizations and ambulatory visits among children were respectively 81% and 87% overall.

Immune Response - Healthy subjects

In children aged 11 months to 21 months the seroconversion rate, when measured by ELISA (50 mLU/mL) 6 weeks after vaccination, was 89.6% after one vaccine dose and 100% after the second vaccine dose.

In subjects aged 9 months to 12 years, the overall seroconversion rate, when measured by Immunofluorescence Assay (IFA) 6 weeks post-vaccination, was > 98% after one vaccine dose. In children vaccinated at 12-15 months of age, antibodies persisted for at least 7 years after vaccination with one dose.

In children aged 9 months to 6 years, the seroconversion rate, when measured by IFA 6 weeks

after vaccination, was 100% after a second vaccine dose. A marked increase of antibody titres was observed following the administration of a second dose (5 to 26-fold GMT increase).

In subjects aged 13 years and above, the seroconversion rate, when measured by IFA 6 weeks after vaccination, was 100% after the second vaccine dose. One year after vaccination, all subjects tested were still seropositive.

In clinical trials, the majority of vaccinated subjects who were subsequently exposed to wild-type virus were either completely protected from clinical chickenpox or developed a milder form of the disease (i.e. low number of vesicles, absence of fever).

If primary varicella infection is delayed until adolescence or adulthood, the illness is usually more severe, and may result in complications such as pneumonia, haemorrhagic varicella, encephalitis, visceral dissemination and cosmetic sequelae from superinfection of skin lesions. Complications can occur at any age but the risk increases with age.

There are insufficient data to assess the rate of protection against complications of chickenpox such as encephalitis, hepatitis or pneumonia.

Studies comparing the current formulation of VARILRIX (human albumin-free) with the previous formulation containing human albumin, demonstrated similar immune responses with both formulations. The current formulation of VARILRIX (human albumin-free) also demonstrated a similar reactogenicity and safety profile.

Immune Response - High-risk patients

There are only very limited data from clinical trials available in patients at high risk of varicella. The overall seroconversion rate in these patients was found to be $\geq$ 80%.

In high-risk patients, periodic measurement of varicella antibodies after immunisation may be indicated in order to identify those who may benefit from re-immunisation.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Appropriate safety tests have been performed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder
Amino acids
Lactose
Mannitol
Sorbitol

Diluent
Water for injection

Neomycin sulphate is present as a residual from the manufacturing process.

6.2 Incompatibilities

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

6.3 Shelf life

24 months from the date of manufacture if stored between temperatures of 2°C to 8°C.

It has been demonstrated that the reconstituted vaccine may be kept for up to 90 minutes at room temperature (25°C) and up to 8 hours in the refrigerator (2°C to 8°C).

6.4 Special precautions for storage

The lyophilised vaccine should be stored in a refrigerator between 2°C to 8°C. The diluent can be stored in the refrigerator or at ambient temperature (maximum 25°C). The lyophilised vaccine is not affected by freezing.

When supplies of VARILRIX are distributed from a central cold store, it is good practice to arrange transport under refrigerator conditions especially in hot climates.

After reconstitution, it is recommended that the vaccine be injected as soon as possible (see section 6.3 Shelf life).

6.5 Nature and contents of container

VARILRIX is supplied as:

- a single dose vial of lyophilised vaccine and diluent syringe or ampoule included,
- a box containing 10 single dose vials of lyophilised vaccine with 10 diluent syringes included,
- a box containing 10 single does vials of lyophilised vaccine, and sterile diluent in boxes of 10 ampoules is supplied separately.

Not all presentations and pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Due to minor variations of its pH, the colour of the reconstituted vaccine may vary from a clear peach to a pink coloured solution. Presence of translucent product-related particulates may be observed after reconstitution. This is normal and does not impair the performance of the vaccine. The diluent and the reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of physical appearance prior to reconstitution or administration. In the event of either being observed, do not use the diluent or the reconstituted vaccine.

Alcohol and other disinfecting agents must be allowed to evaporate from the skin before injection of the vaccine since they may inactivate the virus.

<u>Instructions for reconstitution of the vaccine with diluent presented in ampoules</u>

VARILRIX must be reconstituted by adding the entire contents of the supplied ampoule of diluent to the vial containing the powder. The mixture should be well shaken until the powder is completely dissolved in the diluent.

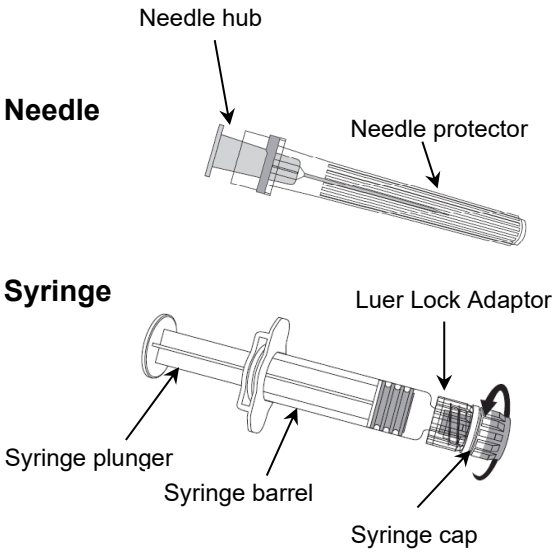
After reconstitution, the vaccine should be used promptly.

Withdraw the entire contents of the vial. Inject the entire contents of the syringe, using a new needle for administration.

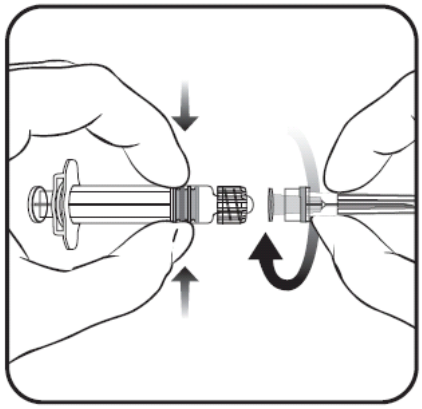
<u>Instructions for reconstitution of the vaccine with diluent presented in pre-filled syringe</u>

VARILRIX 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 VARILRIX 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.

If not used within the recommended timelines, the reconstituted vaccine must be discarded (see section 6.3 Shelf life).
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

ph (09) 367 2900
fax (09) 367 2910

9. DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine: 17 October 1996

10. DATE OF REVISION OF THE TEXT

25 July 2025

Summary table of changes:

Section changed	Summary of new information
4.3, 4.4	Revision of safety information for use with immunosuppressive therapy
4.8, 4.9	Editorial changes to align with current template

Version: 9.0