Varilrix
Varicella vaccine
Powder and solvent for solution for injection

1. NAME OF THE MEDICINAL PRODUCT

VARILRIX VACCINE.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

After reconsitituion, 1 dose (0.5 mL)contains:
Varicella virus[1] Oka strain (live, attenuated) not less than $10^{3.3}$ PFU[2]
[1] produced in human diploid cells (MRC-5); [2] plaque forming units

The powder is slightly cream to yellowish or pinkish. The solvent is clear and colourless.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Varilrix is indicated for active immunisation against varicella:
- In healthy individuals from the age of 9 months (see *section 5.1*);
- For post-exposure prophylaxis if administered to healthy, susceptible individuals exposed to varicella within 72 hours of contact (see *sections 4.4* and *5.1*);
- In individuals at high risk of severe varicella (see *sections 4.3, 4.4 and 5.1*).

Vaccination of susceptible healthy close contacts of individuals at risk of severe varicella is recommended, in order to reduce the risk of transmission of wild-type virus to these individuals. Close contacts include parents and siblings of high-risk individuals, and medical and paramedical personnel.

Limited data from clinical trials are available for Varilrix in individuals at high risk of severe varicella. If vaccination is considered, it is advised that:

- maintenance chemotherapy is withheld 1 week before and 1 week after immunisation of patients in the acute phase of leukaemia. Patients under radiotherapy should normally not

be vaccinated during the treatment. Generally, patients are immunised when they are in complete haematological remission from their disease.
- the total lymphocyte count is at least 1,200 per mm^3 or no other evidence of lack of cellular immune competence exists.
- vaccination is carried out a few weeks before the administration of the immunosuppressive treatment for patients undergoing organ (e.g. kidney) transplantation .

4.2 Posology and method of administration

A single dose of the reconstituted vaccine is 0.5 mL.

Posology

The immunisation schedules for Varilrix should be based on official recommendations.

Healthy individuals
Children from the age of 9 months, adolescents and adults receive 2 doses of Varilrix to ensure optimal protection against varicella (see *section 5.1*). The second dose should generally be given at least 6 weeks after the first dose. Under no circumstances should the interval between the doses be less than 4 weeks.

Post-exposure prophylaxis susceptible individuals exposed to varicella should receive 1 dose of Varilrix within 72 hours of contact.

Individuals at high risk of severe varicella

The same schedule should be applied for individuals at high risk of severe varicella (see *section 5.1*). Periodic measurement of varicella antibodies after vaccination may be indicated in order to identify those who may benefit from re-vaccination. In these individuals, additional doses of vaccine might be required. Under no circumstances should the interval between the doses be less than 4 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 is to be injected subcutaneously (SC) or intramuscularly (IM) in the deltoid region or in the anterolateral area of the thigh.
Varilrix should be administered subcutaneously in individuals with bleeding disorders (e.g. thrombocytopenia or any coagulation disorder).
For instructions on reconstitution of the medicinal product before administration see *section 6.6*.

4.3 Contraindications

Varilrix is contraindicated in individuals with severe humoral or cellular immunodeficiency such as (see also *section 4.4)*:

- primary or acquired immunodeficiency states with a total lymphocyte count less than 1,200 per mm^3;
- other evidence of lack of cellular immune competence (e.g. patients with leukaemias, lymphomas, blood dyscrasias, clinically manifest HIV infection);
- current or recent immunosuppressive therapy (includes high doses of corticosteroids but not topical or low-dose parenteral corticosteroids).

Varilrix is contraindicated in individuals with known hypersensitivity to neomycin or to any other component of the vaccine. A history of contact dermatitis to neomycin is not a contraindication.

Varilrix is contraindicated in individuals having shown signs of hypersensitivity after previous administration of varicella vaccine.

Varilrix is contraindicated in pregnant women. Pregnancy should be avoided for 1 month after vaccination (see *section 4.6*).

4.4 Special warnings and precautions for use

As with other vaccines, the administration of Varilrix should be postponed in individuals suffering from acute severe febrile illness. In healthy individuals 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.

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 (see *section 5.1*).

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

The mild nature of the rash in the healthy contacts indicates that the virus remains attenuated after passage through human hosts.

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

There are limited data on the use of Varilrix in immunocompromised patients, therefore vaccination should be considered with caution and only when, in the opinion of the physician, the benefits outweigh the risks.
Immunocompromised patients who have no contraindication for this vaccination (see *section 4.3*) may not respond as well as immunocompetent individuals, therefore some of these individuals may acquire varicella despite appropriate vaccine administration. Immunocompromised individuals 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*).

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

Encephalitis has been reported during post-marketing use of live attenuated varicella vaccines including Varilrix. Fatal outcomes have been observed, especially in patients who were immunocompromised (see Contraindications). Vaccinees or parents should be instructed to seek prompt medical attention if they or their child experience, after vaccination, symptoms suggestive of encephalitis such as loss or reduced levels of consciousness, convulsions or ataxia accompanied by fever and headache.

Varilrix must not be administered intravascularly or intradermally.

4.5 Interactions with other medicinal products and other forms of interactions

If tuberculin testing is needed, it should be done before or simultaneously with vaccination. Live viral vaccines may cause a temporary depression of tuberculin skin sensitivity. As this anergy may last up to 6 weeks, tuberculin testing should not be performed within that period after vaccination to avoid false negative results.

In individuals who have received immune globulins or a blood transfusion, immunisation should be delayed for at least 3 months because of the likelihood of vaccine failure due to passively acquired varicella antibodies.

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

Healthy individuals

Varilrix can be given concomitantly with: measles-mumps-rubella vaccine (MMR), 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), hexavalent vaccine (DTPa-HBV-IPV/Hib), hepatitis A vaccine (HAV), meningococcal serogroup B vaccine (Bexsero), meningococcal serogroup C conjugate vaccine (MenC), meningococcal serogroups A, C, W and Y conjugate vaccine (MenACWY) and pneumococcal conjugate vaccine (PCV).

Different injectable vaccines should always be administered at different injection sites.

If a measles containing vaccine cannot be given at the same time as Varilrix, an interval of at least 1 month should be respected. Measles vaccination may lead to short-lived suppression of the cell mediated immune response.

Individuals at high risk of severe varicella

Varilrix should not be administered at the same time as other live attenuated vaccines. Inactivated vaccines may be administered in any temporal relationship to Varilrix, given that no specific contraindication has been established.

4.6 Fertility, pregnancy, and lactation

Fertility: No data are available.

Pregnancy

Pregnant women must not be vaccinated with Varilrix. Pregnancy should be avoided for 1 month after vaccination. Women who intend to become pregnant should be advised to delay pregnancy.

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

Lactation: No data are available.

4.7 Effects on ability to drive and use machines

No studies have been performed.

4.8 Undesirable effects

Clinical trial data

Healthy subjects
More than 7,900 subjects have participated in clinical trials evaluating the reactogenicity profile of the vaccine administered subcutaneously either alone or concomitantly with other vaccines.

The safety profile presented below is based on a total of 5,369 doses of Varilrix administered alone to children, adolescents and adults.

Frequencies are reported as:

Very common (≥1/10) /Common (≥1/100 to <1/10) /Uncommon (≥1/1,000 to <1/100) /Rare (≥1/10,000 to <1/1,000) /Very rare (<1/10,000)

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[a], fever (oral/axillary temperature ≥ 37.5°C or rectal temperature ≥ 38.0°C)[a]
	Uncommon	fever (oral/axillary temperature > 39.0°C or rectal temperature > 39.5°C), fatigue, malaise

[a] 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. No difference was seen in the reactogenicity profile between initially seropositive and initially seronegative subjects.

In a clinical trial, 328 children aged 11 to 21 months received GSK's combined measles, mumps, rubella and varicella vaccine (containing the same varicella strain as Varilrix) either subcutaneously or intramuscularly. A comparable safety profile was observed for both administration routes.

Individuals at high risk of severe varicella
Limited data from clinical trials are available in subjects 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.

Post-marketing data

The following additional adverse reactions have been identified in rare occasions during post-marketing surveillance. Because they are reported voluntarily from a population of unknown size, a true estimate of frequency cannot be provided:

System Organ Class	Adverse reactions
Infections and infestations	herpes zoster
Blood and lymphatic system disorders	thrombocytopenia
Immune system disorders	hypersensitivity, anaphylactic reactions
Nervous system disorders	Encephalitis (see *section 4.4*), cerebrovascular accident, cerebellitis, cerebellitis like symptoms (including transient gait disturbance and transient ataxia), convulsions
Vascular disorders	vasculitis (including Henoch Schonlein purpura and Kawasaki syndrome)
Skin and subcutaneous tissue disorders	erythema multiforme

Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

Cases of accidental overdose 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

Varilrix produces an attenuated clinically inapparent varicella infection in susceptible individuals.
The presence of antibodies is accepted to be an indication of protection.

Pharmacodynamic effects

Efficacy and effectiveness

Healthy subjects

The efficacy of GSK's Oka varicella vaccines in preventing confirmed varicella disease (by Polymerase Chain Reaction (PCR) or exposure to varicella case) has been evaluated in a large active controlled multi-country clinical trial, which included the combined measles-mumps-rubella vaccine (Priorix) as active control.
Children aged 12-22 months received 1 dose of Varilrix or 2 doses of the combined measles, mumps, rubella and varicella (Oka) vaccine (Priorix-Tetra). Vaccine efficacy against

confirmed varicella of any severity and against moderate or severe confirmed varicella was observed after a primary follow-up period of 2 years (median duration 3.2 years). Persistent efficacy was observed during the long-term follow-up periods of 6 years (median duration 6.4 years) and 10 years (median duration 9.8 years). See table below.

Group	Timing	Efficacy against confirmed varicella of any severity	Efficacy against moderate or severe confirmed varicella
Monovalent varicella (Oka) vaccine **(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)
	Year 10(1)	67.2% (95% CI: 62.3;71.5)	89.5% (95% CI: 86.1;92.1)
Combined measles, mumps, rubella and varicella (Oka) vaccine **(Priorix-Tetra)** **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)
	Year 10(1)	95.4% (95% CI: 94.0;96.4)	99.1% (95% CI: 97.9;99.6)

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

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).

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

Effectiveness data, deriving from observation in different contexts (epidemic onset, case-control studies, observational studies, databases, models) suggest a higher level of protection and a decrease in the occurrence of cases of chickenpox following 2 doses of vaccine compared to a single dose.

The impact of 1 dose of Varilrix in reducing varicella hospitalisations and ambulatory visits among children were respectively 81% and 87% overall.

Post-Exposure Prophylaxis

In a randomised, double-blind, placebo-controlled study including 42 children aged between 1 and 13 years, 22 children received 1 dose of Varilrix and 20 children received 1 dose of placebo within 3 days after exposure. Similar percentages (41% and 45%, respectively) of children contracted varicella, but the risk of developing a moderate to severe form of the disease was 8 times higher in the placebo group compared with the vaccinated group (relative risk = 8.0; 95% CI: 1.2; 51.5; P=0.003).

In a controlled study including 33 children aged between 1 and 12 years, 15 received varicella vaccine (Varilrix: 13 subjects; another Oka strain varicella vaccine: 2 subjects) up to 5 days after exposure and 18 subjects were not vaccinated. In 12 children vaccinated within 3 days after exposure, vaccine effectiveness was 44% (95% CI: -1; 69) in preventing any disease and 77% (95% CI: 14; 94) in preventing moderate or severe disease.

In a prospective cohort study (with historic attack rates as control), 67 children, adolescents or adults received varicella vaccine (Varilrix: 55 subjects; another Oka strain varicella vaccine: 12 subjects) within 5 days after exposure. Vaccine effectiveness was 62.3% (95% CI: 47.8; 74.9) in preventing any type of disease and 79.4% (95% CI: 66.4; 88.9) in preventing moderate and severe disease.

Individuals at high risk of severe varicella

Patients with leukaemia, patients under immunosuppressive treatment (including corticosteroid therapy) for malignant solid tumour, for serious chronic diseases (such as chronic renal failure, auto-immune diseases, collagen diseases, severe bronchial asthma) or following organ transplantation, are predisposed to severe natural varicella. Vaccination with the Oka-strain has been shown to reduce the complications of varicella in these patients.

Immune response after subcutaneous administration

Healthy subjects
In children aged 11 to 21 months the seroconversion rate, when measured by Enzyme-linked Immunosorbent Assay (ELISA) 6 weeks after vaccination, was 89.6% after 1 dose and 100% after the second dose.

In children aged 9 months to 12 years, the overall seroconversion rate when measured by Immunofluorescence Assay (IFA) 6 weeks after vaccination was >98% after 1 dose.

In children aged 9 months to 6 years, the seroconversion rate when measured by IFA 6 weeks after vaccination was 100% after the second dose. A marked increase of antibody titres was observed following the administration of a second dose (5 to 26-fold of geometric mean titres increase).

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

Individuals at high risk of severe varicella
Limited data from clinical trials are available in subjects at high risk of varicella. The overall seroconversion rate in these subjects was found to be ≥ 80%.

Immune response after intramuscular administration

The immunogenicity of Varilrix administered intramuscularly is based on a comparative study where 283 healthy children aged 11 to 21 months received Priorix-Tetra (containing the same varicella strain as Varilrix) subcutaneously or intramuscularly. Comparable immunogenicity was demonstrated for both administration routes.

5.2 Pharmacokinetic properties

Not applicable.

Clinical Studies:

See *section 5.1*.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on general safety tests performed in animals.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder: Amino acids, Lactose, Mannitol, Sorbitol.
Solvent: Water for injections.

Residues: Neomycin sulphate.

6.2 Incompatibilities

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

6.3 Shelf life

The expiry date is indicated on the packaging.

6.4 Special precautions for storage

Store at 2°C - 8°C (in a refrigerator) and protected from light. The solvent can be stored in the refrigerator or at ambient temperature.

During transport, recommended conditions of storage should be respected, particularly in hot climates.

6.5 Nature and contents of container

- *Vial/ampoule presentation*

  Powder for 1 dose in a vial (type I glass) with a stopper (butyl rubber) and solvent in an ampoule (type I glass).

- *Vial/pre-filled syringe presentation*

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

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

Not all presentations are available in every country.

6.6 Special precautions for disposal and handling

Due to minor variations of its pH, the colour of the reconstituted vaccine may vary from clear peach to 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 solvent 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 solvent or the reconstituted vaccine.

After reconstitution, the vaccine should be injected immediately. 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-8°C).

Instructions for reconstitution of the vaccine with the solvent presented in ampoules (*vial/ampoule presentation*)

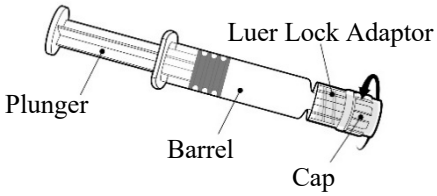
Varilrix must be reconstituted by adding the entire contents of the supplied ampoule of solvent to the vial containing the powder using a suitable needle (21G to 25G).
Shake well until the powder is completely dissolved in the solvent.
After reconstitution, use the vaccine promptly.

Withdraw the entire contents of the vial.

A new needle should be used to administer the vaccine.

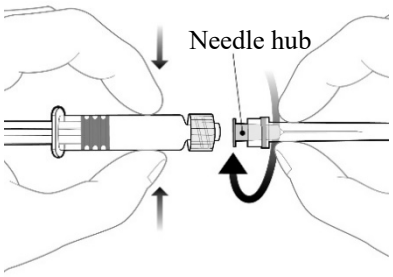
Instructions for reconstitution of the vaccine with the solvent presented in pre-filled syringe (*vial/pre-filled syringe presentation*)

Varilrix must be reconstituted by adding the entire contents of the pre-filled syringe of solvent to the vial containing the powder using a suitable needle (21G to 25G).
To attach the needle to the syringe, carefully read the instructions.



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

Unscrew the syringe cap by twisting it anticlockwise.



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

Maintain the needle in the axis of the syringe. Failure to do this may cause the LLA to become distorted and leak.

During assembly of the syringe, if the LLA comes off, a new vaccine dose (new syringe and vial) should be used.

Reconstitute the vaccine as described below.

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

- Add the solvent to the powder.

  Shake well until the powder is completely dissolved in the solvent. After reconstitution, use the vaccine promptly.

- Withdraw the entire contents of the vial.

- A new needle should be used to administer the vaccine.

  Unscrew the needle from the syringe and attach the injection needle by repeating steps above.

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

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESSES

Manufacturer:

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut, 89
B-1330 Rixensart, Belgium

8. MARKETING AUTHORISATION NUMBER(S)

11928

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF TEXT

Date of issue: 15 September 2025