health
Department:
Health
REPUBLIC OF SOUTH AFRICA

MEDICINES CONTROL COUNCIL
The Registrar of Medicines, Private Bag X828, PRETORIA, 0001
Tel 012 395 8000 Fax 012 395 9201
Tel: 012 395 8778
Fax: 012 395 8505
Enquiries: **BIOLOGICAL MEDICINES UNIT**
Reference: (N2/6/1/320468
(637121RT)
2017-04-05

THE RESPONSIBLE PHARMACIST
GLAXOSMITHKLINE SOUTH AFRICA (PTY) LIMITED
P O BOX 44
HOWARD PLACE
7450
CAPE TOWN, SOUTH AFRICA

E-mail: michelle.a.hertwick@gsk.com

Dear Sir/Madam

RE: APPLICATION FOR BIOLOGICAL AMENDMENT: [VARILRIX- 32/30.1/0468]

After evaluation of the Package Insert (PI) and Patient Information leaflet (PIL) safety update, dated 2017/02/21 in terms of safety, quality and efficacy, the following are approved;

1. Update of the information provided in the "Pharmacodynamic Properties" section of the PI with recent data of long-term efficacy against varicella disease after a follow-up period of 6 years in study OKAH-182.
2. Amendment of route of administration section under "Dosage and Directions for Use" to include subcutaneous injection into anterolateral area of the thigh.
3. Reformatting of the clinical trial side effects sections into a tubular format

Yours faithfully

K.P MUTOTI
BIOLOGICAL MEDICINES
FOR AND ON BEHALF OF THE REGISTRAR OF MEDICINES SOUTH AFRICA

Page **1** of **1**

VARILRIX®

SCHEDULING STATUS:
S4

PROPRIETARY NAME AND DOSAGE FORM:
VARILRIX®
Lyophilised virus vaccine. Powder for solution and injection.

COMPOSITION:
VARILRIX is a lyophilised preparation of the live attenuated OKa strain of the varicella-zoster virus, obtained by propagation of the virus in MRC_5 human diploid cell culture.
Each 0,5 ml of the reconstituted vaccine contains not less than 2 000 plaque forming units (PFU) of the live attenuated varicella-zoster (OKa strain) virus.

Excipients:
Powder: amino acids, human albumin, lactose, mannitol and sorbitol.
Diluent: water for injections.
Residues: neomycin sulphate.

PHARMACOLOGICAL CLASSIFICATION:
A 30.2 Biologicals, Antigens

PHARMACOLOGICAL ACTION:
Pharmacodynamic properties:
VARILRIX produces an attenuated clinically inapparent varicella infection in susceptible subjects. The presence of antibodies is accepted to be an indication of protection.
The efficacy of GlaxoSmithKline (GSK)'s Oka/RIT varicella vaccines in preventing confirmed varicella disease (by PCR or exposure to 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 the Table below.

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).
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 hospitalisations and ambulatory visits among children were respectively 81 % and 87 % overall.
Effectiveness data suggest a higher level of protection and a decrease in breakthrough varicella following two doses of vaccine than following one dose.

Pharmacokinetic properties:
Evaluation of pharmacokinetic properties is not required for vaccines.

INDICATIONS:
Healthy subjects: VARILRIX is indicated for active immunisation against varicella of healthy infants (from the age of 9 months), children and adolescents.

High-risk patients and healthy close contacts: VARILRIX is also indicated for active immunisation against varicella of susceptible high-risk patients and their susceptible healthy close contacts.

Patients with acute leukaemia: Patients suffering from leukaemia have been recognised to be at special risk when they develop varicella and should therefore receive the vaccine if they have no history of the disease or are found to be seronegative.

When immunising patients in the acute phase of leukaemia: Maintenance chemotherapy should be withheld one week before and one week after immunisation. Patients under radiotherapy should normally not be immunised during the treatment phase.

Patients under immunosuppressive treatment: Patients under immunosuppressive treatment (including corticosteroid therapy) for malignant solid tumours or for serious chronic diseases (such as chronic renal failure, auto-immune diseases, collagen diseases, severe bronchial asthma) are predisposed to severe varicella.
Generally patients are immunised when they are in complete haematological remission from the disease. It is advised that the total lymphocyte count should be at least 1 200/mm^3 or no other evidence of lack of cellular immune competence exists.

Patients with planned organ transplantation: If organ transplantation (e.g. kidney transplant) is being considered, immunisation should be carried out a few weeks before the administration of the immunosuppressive treatment.

Patients with chronic diseases: Other chronic diseases, such as metabolic and endocrine disorders, chronic pulmonary and cardiovascular diseases, mucoviscidosis and neuromuscular abnormalities may also predispose to severe varicella.

Healthy close contacts: Susceptible healthy close contacts should be immunised in order to reduce the risk of transmission of the virus to high-risk patients. These include parents and siblings of high-risk patients and medical, paramedical personnel and other people who are in close contact with varicella patients or high-risk patients.

CONTRA-INDICATIONS:
VARILRIX is contra-indicated in subjects with severe humoral or cellular immunodeficiency such as:

- subjects with primary or acquired immunodeficiency states, with a total lymphocyte count less than 1 200 per mm^3
- subjects presenting other evidence of lack of cellular immune competence (e.g. subjects with leukaemias, lymphomas, blood dyscrasias, clinically manifest HIV infection
- subjects receiving immunosuppressive therapy, including high dose corticosteroids (see WARNINGS AND SPECIAL PRECAUTIONS).

VARILRIX is contra-indicated in subjects with known hypersensitivity to neomycin, or to any component of the vaccine. A history of contact dermatitis to neomycin is not a contra-indication.
VARILRIX is contra-indicated in pregnant women. Pregnancy should be avoided for one month after immunisation (see PREGNANCY AND LACTATION).
In high-risk patients, 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 contra-indication has been established.

WARNINGS AND SPECIAL PRECAUTIONS:
The administration of VARILRIX should be postponed in patients suffering from acute severe febrile illness. In healthy subjects, the presence of minor infection, however, is not a contra-indication for immunisation.
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.
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.
It is advised that contact of vaccinees with persons who may be immunocompromised due to HIV infection or other immunodeficiency should be avoided for at least 14 days post immunisation.
There is limited data on the use of VARILRIX in immunocompromised subjects, therefore vaccination should be considered with caution and only when, in the opinion of the physician, the benefits outweigh the risks.
Immunocompromised subjects who have no contra-indication for this vaccination (see CONTRA-INDICATIONS) may not respond as well as immunocompetent subjects, therefore some of these subjects may acquire varicella despite appropriate vaccine administration. Immunocompromised subjects should be monitored carefully for signs of varicella.
Very few reports exist on disseminated varicella with internal organ involvement following vaccination with Oka varicella vaccine strain mainly in immunocompromised subjects.
In high-risk patients VARILRIX should not be administered at the same time as other live attenuated vaccines.
VARILRIX must not be administered intravascularly or intradermally.
Appropriate medical treatment should always be readily available including adrenaline in case of rare anaphylactic reactions following administration of the vaccine. For this reason, the vaccinee should remain under medical supervision for 30 minutes after immunisation.

It must be expected that the reactogenicity following co-administration of VARILRIX and more reactogenic vaccines will be determined by the reactions of the latter.

Excipient Warnings:
VARILRIX contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not be given VARILRIX (see COMPOSITION).
VARILRIX contains traces of neomycin. VARILRIX should not be used in patients with a known hypersensitivity to this antibiotic.

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

INTERACTIONS:
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 subjects who have received immune globulin or a blood transfusion, immunisation should be delayed for at least three months because of likelihood of vaccine failure 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.

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

High-risk patients:
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 contra-indication has been established. However, different injectable vaccines should always be administered at different injection sites (see CONTRA-INDICATIONS).

PREGNANCY AND LACTATION:
Fertility: No data available.
Pregnancy: VARILRIX is contra-indicated during pregnancy. Pregnant women must not be vaccinated with VARILRIX. Pregnancy should be avoided for one month after immunisation (see CONTRA-INDICATIONS). 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.
Lactation: Administration of VARILRIX is not advised during breastfeeding.

DOSAGE AND DIRECTIONS FOR USE:
0,5 ml of reconstituted vaccine contains one immunising dose.

Healthy Subjects:

- **Children 9 months up to and including 12 years of age:**
  Children from the age of 9 months up to and including 12 years of age should receive 2 doses of VARILRIX to ensure optimal protection against varicella.
  It is preferable to administer the second dose at least 6 weeks after the first dose but in no circumstances less than 4 weeks.
- **Adolescents and adults from 13 years of age and above:**
  From 13 years of age and above: 2 doses. It is preferable to administer the second dose at least 6 weeks after the first dose but in no circumstances less than 4 weeks.

High risk patients:
In high risk patients additional doses of vaccine might be required.

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 for **subcutaneous** administration in the deltoid region or in the anterolateral area of the thigh.
VARILRIX should **not** be administered intradermally.
Note: VARILRIX must under no circumstances be administered intravenously.

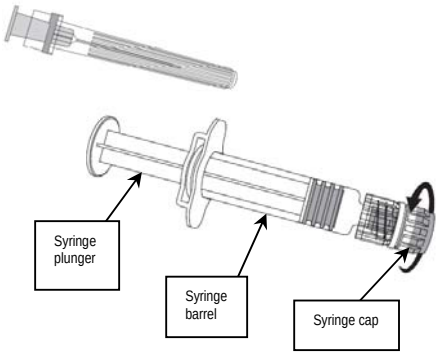
Use and handling:
The diluent and the reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the diluent or the reconstituted vaccine.
VARILRIX must be reconstituted by adding the contents of the supplied container of diluent to the vial containing the powder. After the addition of the diluent to the powder, the mixture should be well shaken until the powder is completely dissolved in the diluent. Due to minor variations of its pH, the colour of the reconstituted vaccine may vary from clear peach to pink coloured solution.

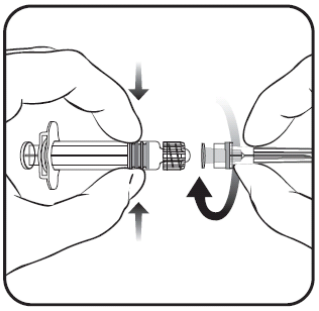
Instructions for reconstitution of the vaccine with diluent presented in ampoules:
VARILRIX must be reconstituted by adding the entire contents of the supplied ampoule of diluent to the vial containing the powder. After the addition of the diluent to the powder, the mixture should be well shaken until the powder is completely dissolved in the diluent.
After reconstitution, the vaccine should be used immediately.
A new needle should be used to administer the vaccine. The administration needle should be suitable in size (e.g. 25 gauge 5/8 inch (0,5 x 16 mm)) for subcutaneous injection.
Withdraw the entire contents of the vial.

Instructions for reconstitution of the vaccine with diluent presented in pre-filled syringe:
VARILRIX must be reconstituted by adding the entire content of the pre-filled syringe of diluent to the vial containing the powder.
To attach the needle to the syringe, refer to the below drawing. However, the syringe provided with VARILRIX might be slightly different than the syringe described in the drawing.

Needle:

Syringe:





1. Holding the syringe barrel in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.
2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock (see picture).
3. Remove the needle protector, which on occasion can be a little stiff.

Add the diluent to the powder. After the addition of the diluent to the powder, the mixture should be well shaken until the powder is completely dissolved in the diluent.
After reconstitution, the vaccine should be used immediately.
A new needle should be used to administer the vaccine. The administration needle should be suitable in size (e.g. 25 gauge 5/8 inch (0,5 x 16 mm)) for subcutaneous injection.
Withdraw the entire contents of the vial.
Any unused product or waste material should be disposed of in accordance with local requirements.

SIDE EFFECTS:
Clinical trial data:
Healthy subjects:
More than 7 900 individuals have participated in clinical trials evaluating the reactogenicity profile of the vaccine administered alone or concomitantly with other vaccines.
The safety profile presented below is based on a total of 5 369 doses of VARILRIX administered in monotherapy to children, adolescents and adults.
Frequencies are reported as follows:
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, including isolated reports.

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

High-risk patients: 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.

Post-marketing data:
During post-marketing surveillance, the following additional reactions have been reported after varicella vaccination:
Infections and infestations: herpes zoster
Blood and lymphatic disorders: thrombocytopenia
Immune system disorders: hypersensitivity, anaphylactic reactions
Nervous system disorders: encephalitis, 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.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
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.
See SIDE EFFECTS. Treatment is symptomatic and supportive.

IDENTIFICATION:
Vaccine: Cream to yellowish or pinkish coloured cake or powder of lyophilised vaccine.
Diluent: Clear and colourless liquid.
Reconstituted vaccine: Clear peach to pink coloured solution, free from visible particles.

PRESENTATION:
The vaccine is presented in a 3 ml clear glass vial with a rubber stopper.
The diluent is presented in a clear glass ampoule or a pre-filled syringe.

STORAGE INSTRUCTIONS:
Store in refrigerator between +2 °C and +8 °C. Protect from light.
Discard any unused portion.

Keep all medicines out of reach of children.

REGISTRATION NUMBER:
32/30.1/0468

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE REGISTRATION CERTIFICATE:
GlaxoSmithKline South Africa (Pty) Ltd
39 Hawkins Avenue
Epping Industria 1, 7460

DATE OF PUBLICATION OF THIS PACKAGE INSERT:
05 April 2017

GDS-12

Botswana: Reg No BOT0400676 S2

Namibia: Reg No 04/30.1/0879 NS2

VARILRIX®
Patient Information Leaflet

SCHEDULING STATUS:
S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM:
VARILRIX®
Lyophilised virus vaccine. Powder for solution and injection.

Read all of this leaflet carefully before you are vaccinated.
VARILRIX is not for self-medication and must be administered by a healthcare professional.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- VARILRIX has been prescribed for you personally and you should not share your medicine with other people. It may harm them even if their symptoms are the same.

This leaflet has been written assuming the person receiving the vaccine is reading it, but it can be given to adults and children so you may be reading it for your child.

WHAT VARILRIX CONTAINS:
After reconstitution, 1 dose (0,5 ml) of vaccine contains not less than 2 000 plaque forming units (PFU) of the live attenuated varicella-zoster (OKa strain) virus.
The other ingredients are amino acids, human albumin, lactose, mannitol, sorbitol and water for injections. Neomycin sulphate is present in trace amounts.

WHAT VARILRIX IS USED FOR:
VARILRIX is a vaccine for use from 9 months of age to protect against illness caused by the varicella (chickenpox) virus. When a person is vaccinated with VARILRIX, the immune system (the body's natural defence system) will make antibodies to protect the person from being infected by varicella (chickenpox) virus.

BEFORE YOU ARE GIVEN VARILRIX:
VARILRIX should not be given, if you:
- have any severe illness that weakens the immune system (such as blood disorders, cancer or infections)
- have recently received or are still taking treatment that weakens the immune system (including high dose corticosteroids)
- have previously had an allergic reaction to VARILRIX, neomycin (an antibiotic) or any component contained in this vaccine. However, if you have a skin rash (dermatitis) after treatment with neomycin, you can still be vaccinated with VARILRIX.

VARILRIX must not be given during pregnancy. Pregnancy should be avoided for one month following vaccination.
Check with your doctor if you think any of these apply to you.

Take special care with VARILRIX:
Your doctor needs to know before you receive VARILRIX if:
- you have a severe infection with a high temperature. It might be necessary to postpone the vaccination until recovery. A minor infection such as a cold should not be a problem, but talk to your doctor first
- you have a history of family history of allergies
- you have a weakened immune system. You should be closely monitored as the responses to the vaccine may not be sufficient to ensure a protection against the illness

- you are due to have a skin test for possible tuberculosis. If this test is done within 6 weeks after receiving VARILRIX, the result may not be reliable.

Fainting can occur following, or even before, any needle injection, therefore tell the doctor or nurse if you fainted with a previous injection.
VARILRIX cannot completely protect you against catching chicken pox. However, people who have been vaccinated and catch chicken pox usually have a very mild disease, compared with people who have not been vaccinated.
In rare cases the weakened virus can be passed on from a vaccinated person to others. This has only occurred when the person vaccinated had some spots or blisters. Healthy people who become infected in this way only develop a mild rash, which is not harmful.
People injected with VARILRIX should avoid contact for at least 14 days after vaccination with persons who have a poor immune system (e.g. due to HIV infection or other immune system disorder).

Pregnancy and Breastfeeding:
If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice, before you are given VARILRIX.
VARILRIX **must not** be given to pregnant women.
If you are pregnant, think you may be pregnant or are trying to become pregnant, tell your doctor before VARILRIX is given.
It is also important that you do not become pregnant **within one month** after being vaccinated with VARILRIX**.** During this time you should use an effective method of birth control to avoid pregnancy.
Ask your doctor for advice about breastfeeding before receiving VARILRIX.

Important information about some of the ingredients of VARILRIX:
Patients who are intolerant to lactose should note that VARILRIX contains a small amount of lactose. If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before you are given VARILRIX.
VARILRIX contains traces of neomycin. Tell your doctor if you have had an allergic reaction to this antibiotic.

Taking other medicines with VARILRIX:
Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)
If you have recently had a blood transfusion, or been given human immunoglobulin, your doctor may delay vaccination with VARILIX for at least 3 months.
Aspirin or aspirin-type products (also known as salicylates) should not be taken for 6 weeks after vaccination with VARILRIX as this may cause a serious disease called Reye's Syndrome which can affect all your body organs.
If another vaccine is due to be given at the same time as VARILRIX, your doctor or nurse will advise you whether this can be given or whether it must be delayed.
A different place for the injection will be used for each vaccine.

HOW TO RECEIVE VARILRIX:
Your doctor or nurse will inject the recommended dose of vaccine. If more than one dose is necessary, the doctor will tell you.
VARILRIX will be given as an injection under the skin, either in the upper arm or in the outer thigh. The vaccine must never be injected into a vein. Your doctor may wipe the skin with alcohol or other disinfecting agents and will let the skin dry before the injection.

POSSIBLE SIDE EFFECTS:
VARILRIX can have side effects.

As with all injectable vaccines, there is a small risk of allergic reactions. The signs of allergy may include symptoms such as difficulty in breathing or swallowing, itchy rash of the hands and feet, swelling of the eyes and face. Such reactions will usually occur before leaving the doctor's surgery, but in any event you should seek immediate treatment.

Frequent side effects include:

- pain and redness at the injection site.
- rash (spots and/or blisters)
- swelling at the injection site
- fever of 38 °C or more (rectal).

Less frequent side effects include:

- upper respiratory tract infection
- sore throat and discomfort when swallowing
- swollen glands in the neck, armpit or groin
- irritability
- headache
- sleepiness
- cough
- runny or blocked nose, sneezing (rhinitis)
- nausea
- vomiting
- chickenpox-like rash
- itching
- painful, swollen joints
- aching muscles, muscle tenderness or weakness, not caused by exercise
- fever greater than 39,5 ºC (rectal)
- tiredness (fatigue)
- generally feeling unwell.

Other side effects include:

- discharge with itching of the eyes and crusty eyelids (conjunctivitis)
- stomach pain or discomfort
- diarrhoea
- hives (urticaria).

The following side effects have also been reported:

- shingles (herpes zoster)
- bleeding or bruising more easily than normal, due to a drop in a type of blood cells called platelets
- allergic reactions
- fits or seizures
- infection or inflammation of the brain, spinal cord and peripheral nerves, resulting in temporary difficulty when walking (unsteadiness) and/or temporary loss of control of body movements
- stroke
- narrowing or blockage of blood vessels. This may include unusual bleeding or bruising under the skin (Henoch Schonlein purpura) or fever which lasts for more than five days, associated with a rash on the trunk sometimes followed by a peeling of the skin on the hands and fingers, red eyes, lips, throat and tongue (Kawasaki disease)
- severe condition of the skin that may affect the mouth and other parts of the body.

If you or your child develops any other symptom within days following the vaccination, tell the doctor as soon as possible.
Not all side effects reported for this vaccine are included in this leaflet. Should your general health worsen while taking this vaccine, please consult your doctor, pharmacist or health care professional for advice.

STORING AND DISPOSING OF VARILRIX:
Store your vaccine in a refrigerator between +2 °C and +8 °C.
Keep in the original packaging to protect from light.
Discard any unused portion.
Store all medicines out of reach of children.
The expiry date is indicated on the packaging. The vaccine should not be used after this date.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

PRESENTATION OF VARILRIX:
The vaccine is presented in a 3 ml clear glass vial with a rubber stopper.
The diluent is presented in a clear glass ampoule or a pre-filled syringe.

IDENTIFICATION OF VARILRIX:
Vaccine: cream to yellowish or pinkish coloured cake or powder.
Diluent: clear and colourless liquid.
Reconstituted vaccine: clear peach to pink coloured solution.

REGISTRATION NUMBER:
32/30.1/0468

NAME AND ADDRESS OF REGISTRATION HOLDER:
GlaxoSmithKline South Africa (Pty) Ltd
39 Hawkins Avenue
Epping Industria 1, 7460

DATE OF PUBLICATION:
05 April 2017