• maintenance chemotherapy should be withheld one week before and one week after immunisation of patients in the acute phase of leukaemia. Patients under radiotherapy should normally not be vaccinated during the treatment phase. Generally patients are immunised when they are in complete haematological remission from the disease.

• the total lymphocyte count should be at least 1,200 per mm3 or no other evidence of lack of cellular immune competence exists.

• vaccination should be carried out a few weeks before the administration of the immunosuppressive treatment for patients undergoing organ transplantation (e.g. kidney transplant).

3.2. Posology and method of administration

### Posology

0.5 ml of reconstituted vaccine contains one immunising dose.

- **Children 9 months to 12 years**
  From the age of 9 months up to and including 12 years of age: 1 dose.

- **Children 13 years up**
  13 years and above: 2 doses with an interval of 6 to 10 weeks.

- **High risk patients**
  The same schedule described for healthy subjects should be applied for high-risk patients.

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

### Method of administration

Varilrix™ is for subcutaneous use only.

3.3. Contra-indications

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

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. 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.

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

3.6. Use during pregnancy and lactation
It is contra-indicated to administer Varilrix™ to pregnant women. Furthermore, pregnancy should be avoided for three months after immunisation (see Contraindications). There are no data regarding use in nursing women.

3.7 Effect on ability to drive and use machines
Not applicable

3.8. Undesirable effects
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 5369 doses of Varilrix™ administered in monotherapy to children, adolescents and adults. Frequencies are reported as:

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

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 ≥37.5oC or rectal temperature ≥38.0oC)*
Uncommon: fever (oral/axillary temperature >39.0oC or rectal temperature >39.5oC), fatigue, malaise

* Swelling at the injection site and fever were reported very commonly in studies conducted in adolescents and adults.

On average, the reactogenicity after the second dose was not higher than after the first dose.
No difference was 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 surveillance
Infections and infestations:
Herpes zoster**

Immune system disorders:
Hypersensitivity, anaphylactic reactions

Nervous system disorders:
Convulsions, cerebellar ataxia**

** This reaction reported after vaccination is also a consequence of wild-type varicella infection. There is no indication of an increased risk of its occurrence following vaccination compared with wild-type disease.

3.9 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.

4. Pharmacological particulars
4.1. Pharmacodynamic properties.
Varilrix™ produces an attenuated clinically inapparent varicella infection in susceptible subjects.
Some protection may be obtained by immunisation up to 72 hours after exposure to natural varicella.
The presence of antibodies is accepted to be an indication of protection.

Healthy subjects
In subjects aged 9 months to 12 years, the overall
5. Pharmaceutical particulars

5.1 List of excipients
Excipients of the vaccine are: amino acids, human albumin, lactose, neomycin sulphate and polyalcohols. Diluent is water for injection.

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

5.3. Shelf-life
The expiry date of the vaccine is indicated on the label and packaging.

5.4. Special precautions for storage
The lyophilised vaccine should be stored in a refrigerator between +2°C and +8°C and protected from light. The diluent can be stored in the refrigerator or at ambient temperatures. The lyophilised vaccine is not affected by freezing.

When supplies of Varilrix™ are distributed from a central cold store, it is necessary to arrange transport under refrigerator conditions.

5.5. Instructions for use, handling and disposal (if appropriate)
Varilrix™ is presented as a slightly cream to yellowish or pinkish coloured pellet in a glass vial. The sterile diluent is clear and colourless and presented in ampoules and prefilled syringes.

Varilrix™ must be reconstituted by adding the contents of the supplied container of diluent to the vaccine vial. The vaccine pellet should be completely dissolved in the diluent. The entire contents of the vial are to be injected.

Due to minor variations of its pH, the colour of the reconstituted vaccine may vary from clear peach to pink coloured solution.

Vaccines 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 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.

Seroconversion rate was >98% when measured at 6 weeks post-vaccination. In children vaccinated at 12-15 months of age, antibodies persisted for at least 7 years postvaccination.

In subjects aged 13 years and above, the seroconversion rate was 100% when measured 6 weeks after the second 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). In a study specifically designed to evaluate vaccine efficacy, 10 to 30-month-old children were followed up for a period of 29.3 months. The protective efficacy was 100% against common clinical cases of varicella (≥30 vesicles). Against any case of varicella (at least 1 vesicle or papule), protective efficacy was 88%.

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

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 ≥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.

Transmission of the Oka vaccine virus as shown by virus isolation and identification has been demonstrated in four cases in siblings of immuno-compromised vaccinees who had a vesicular eruption. Whenever those siblings of immuno-compromised vaccinees developed themselves a post-exposure rash, it was always very mild.

4.2 Pharmacokinetic properties
Not applicable

4.3 Preclinical safety data
Not applicable
After reconstitution, it is recommended that the vaccine be injected as soon as possible. However, 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-8°C). If not used within these timeframes, the reconstituted vaccine must be discarded. For further information, please contact the manufacturer.

Varilrix is a trademark.