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# VARILRIX™

**1. Name of the medicinal product**
*Varilrix™*

**2. Qualitative and quantitative composition**
*Varilrix™* is a lyophilised preparation of the live attenuated Oka strain of varicella-zoster virus, obtained by propagation of the virus in MRC5 human diploid cell culture.
*Varilrix™* meets the World Health Organisation requirements for biological substances and for varicella vaccines.
Each dose of the reconstituted vaccine contains not less than $10^{3.3}$ plaque-forming units (PFU) of the attenuated varicella-zoster virus.

**3. Clinical particulars**
**3.1. Therapeutic indications**
Healthy subjects
*Varilrix™* is indicated for active immunisation against varicella of healthy subjects from the age of 9 months onwards.
Vaccination of susceptible healthy close contacts of subjects at risk of severe varicella is recommended, in order to reduce the risk of transmission of wild-type virus to these patients. Close contacts include parents and siblings of high-risk patients, and medical and paramedical personnel.
Patients at high risk of severe varicella
Patients suffering from 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.
There is only limited data from clinical trials available for *Varilrix™* in patients at high risk of severe varicella; should vaccination be considered, it is advised that :
- 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 $mm^3$ 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 presence of a minor infection, however, is not a contra-indication for immunisation.
*Varilrix™* is contra-indicated in subjects with a total lymphocyte count less than 1200 per $mm^3$ or presenting other evidence of lack of cellular immune competence.
*Varilrix™* is contra-indicated in subjects with known systemic hypersensitivity to neomycin, but a history of contact dermatitis to neomycin is not a contra-indication.
*Varilrix™* is contra-indicated during pregnancy. Furthermore, pregnancy should be avoided for three months after vaccination (see **Pregnancy and lactation**).

**3.4. Special warnings and special precautions for use**
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 and cough with respect to cases in unvaccinated individuals.
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. For this reason, the vaccinee should remain under medical supervision for 30 minutes after immunisation.
*Varilrix™* should not be administered intradermally.
***Varilrix™* must under no circumstances be administered intravenously.**

**3.5. Interactions with other medicaments and other forms of interaction**
In subjects who have received immune globulins or a blood transfusion, immunisation 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.
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.
Frequencies are reported as:
Very common: ≥ 10%

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

- Children (aged from 9 months to 12 years)

The most frequently observed adverse effects were injection site reactions (mild pain, redness and swelling), reported following 21% of all doses administered to children.
Other events reported were:
Body as a whole:
Very common: fever (oral/axillary temperature ≥ 37.5°C or rectal temperature ≥ 38.0°C)
Common: fever (oral/axillary temperature > 39°C or rectal temperature > 39.5°C)
Skin and appendages:
Uncommon: varicella-like (papulo-vesicular) rash
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.
- Adolescents (≥ 13 years and adults)

The most frequently observed adverse effects were injection site reactions (mild pain, redness and swelling), reported following 26% of all doses administered to adolescents or adults.
Other events reported were:
Body as a whole:
Very common: fever (oral/axillary temperature ≥ 37.5°C )
Rare: fever (oral/axillary temperature > 39.0°C)
Skin and appendages:
Common: rash
Uncommon: varicella-like (papulo-vesicular) rash
On average, the reactogenicity after the second dose was not higher than after the first dose.
In two placebo-controlled studies enrolling a total of 315 individuals, there was no significant differences in the nature of incidence of fever and rash in subjects receiving vaccine or placebo.
No differences were seen between the reactogenicity in 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.

**3.9. Overdose**
Not applicable

**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 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

**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 pinkinsh 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.
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.

**International Data Sheet** version 4.0 (27/09/2005)


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