(English translation of official Dutch version)

PACKAGE LEAFLET

Package leaflet: Information for the user

VariQuin 200 IU solution for injection
Human varicella immunoglobulin

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- Do you have any further questions? Please contact your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. WHAT VARIQUIN IS AND WHAT IT IS USED FOR

VariQuin is a solution for injection. The solution contains the protein "human varicella zoster immunoglobulin" (human varicella zoster antibody). Immunoglobulins are antibodies that normally occur in human blood and protect you against infections. This product contains immunoglobulin G (= IgG), an antibody that is effective against the varicella zoster virus, which can - among other things - cause chicken pox (varicella). The maximum IgA concentration is 6 g/l.

VariQuin can be used to prevent chicken pox or to reduce the symptoms of the chicken pox disease. The antibodies that are present in VariQuin and directed against the varicella zoster virus counteract the harmful effects of the virus. This prevents chicken pox or reduces its symptoms (so-called passive immunisation).

2. WHAT YOU NEED TO KNOW BEFORE YOU USE VARIQUIN

Do not use VariQuin:
If you are allergic (hypersensitive) to immunoglobulins or any of the other ingredients of this medicine (listed in section 6).

The administration of VariQuin should be stopped immediately if an allergic reaction occurs.

The product is not suitable for intravenous administration (administration into a vein).

Warnings and precautions
Thromboembolic events including myocardial infarction, stroke, deep venous thrombosis and pulmonary embolism have been associated with the use of immunoglobulins.
Contact you doctor immediately if you experience symptoms like shortness of breath, chest pain, pain and swelling of a limb, weakness or numbness on one side of your body after administration of VariQuin.

VariQuin contains a small quantity of IgA. VariQuin can cause a severe attack of hypersensitivity (anaphylactic reaction) in patients who do not have immunoglobulin A (IgA deficiency) and have antibodies against immunoglobulin A. An anaphylactic reaction can also occur in patients who have not demonstrated hypersensitivity to previous use of blood or blood products.

If you are IgA deficient and have antibodies against immunoglobulin A, or if you have demonstrated hypersensitivity to previous use of blood or a blood product, you may only receive this product if it is

absolutely necessary. In these cases, VariQuin must be administered under close supervision of a doctor. A doctor or nurse will monitor your condition for at least 20 minutes after administration of this product. Please consult section 4 of this leaflet for information about side effects.

Other medicines and VariQuin
VariQuin may not be mixed with other medicines.

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Vaccination
Tell your doctor if you have received a vaccination in the past 3 to 4 weeks or require a vaccination in the near future (within 3 months after the administration of VariQuin). VariQuin might reduce the efficacy of vaccines against measles, rubella (German measles), mumps and varicella (chicken pox). You must wait at least three months after receiving VariQuin before you can be vaccinated with any of these vaccines.

Effects on blood tests
The use of VariQuin may affect the results of certain blood tests.

VariQuin with food and drink alcohol
There are no known effects of food, drink and alcohol on the use of VariQuin.

Pregnancy and breast-feeding
The use of VariQuin during pregnancy or whilst breast-feeding has not been studied. The use of immunoglobulins – such as VariQuin – during pregnancy or the period of breast-feeding has never resulted in harmful effects in the past. Immunoglobulins are passed on to newborn children via the breast milk and contribute to the newborn's immunity.
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
No effects on the ability to drive and use machines have been observed.

Special warnings and precautions for use
When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These measures include:
- careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded
- the testing of each donation and pools of plasma for signs of virus/infections
- adding steps in the processing of the blood or plasma that can inactivate or remove viruses.

Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on an infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus and for the non-enveloped hepatitis A virus. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19.

Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections possibly because the antibodies against these infections, which are contained in the product, are protective.

It is strongly recommended that every time you receive a dose VariQuin the name and batch number of the product are recorded in order to maintain a record of the batches used.

Excipients
The product contains the following excipients: glycine and water for injections.

3. HOW TO USE VARIQUIN

Administration
Administration of VariQuin should be performed by a doctor. VariQuin must be injected in the muscle (intramuscular). The injection will generally be administered in the upper part of the arm or the buttock. The product may not be too cold when administered. We recommend bringing the product to body temperature prior to administration.

If a large dose is administered (more than 2 ml for children and more than 5 ml for adults), then it is recommended that the dose be divided over several injection sites.

Administration of VariQuin to neonates, where the mother has experienced varicella in the period from 7 days before to 7 days after delivery, should be carried out as soon as possible.
In other cases administration should be carried out as soon as possible (preferably within 3 days, but at the latest within 10 days) after the contact with a varicella patient.

If you have any further questions on the use of this medicine, ask you doctor.

In patients with a special tendency towards spontaneous, sometimes lengthy episodes of bleeding, this product may be administered under the skin (subcutaneous injection). However, the efficacy of this product cannot be guaranteed in this case.

Posology

Newborns with body weight up to 2 kg: 1 ml
Persons with body weight of 2-10 kg: 1 vial of 2 ml
Persons with body weight of 10-30 kg: 2 vials of 2 ml
Persons with body weight of more than 30 kg: 3 vials of 2 ml

Administration to neonates where the mother has experienced varicella in the period from 7 days before to 7 days after delivery should be carried out as soon as possible.
In other cases administration should be carried out as soon as possible, preferably within 3 days, but at the latest within 10 days after the contact with a varicella patient.
It is recommended that the administration be repeated if re-exposure takes place more than three weeks after the first administration.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Allergic reactions are rare. In the event of a very severe attack of hypersensitivity (anaphylactic shock), the administration must be stopped immediately and the reaction must be treated appropriately.

The following side effects can occur: pain/sensitivity, swelling, redness, hardening (induration), warmth, itching and rash at the injection site.
The following can occur in rare cases: fever, nausea, vomiting, excessively low blood pressure, increased heart rate (tachycardia), malaise, chills, hypersensitivity reactions, headache, joint pain, skin reaction and itching and redness of the skin.

The risk of transmission of pathogens through use of a blood product is very low.

Administration of VariQuin is of no use if the symptoms of chicken pox have already appeared (characterised by the typical skin rash, that is to say blisters and scabs).
VariQuin does not prevent the herpes zoster disease (shingles) from occurring in persons that have already had chicken pox or in whom antibodies against the varicella zoster virus can be demonstrated. The product has no influence upon the clinical course of shingles.

<u>Reporting of side effects</u>
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Netherlands Pharmacovigilance

Centre Lareb, website: www.lareb.nl. By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE VARIQUIN

Store in a refrigerator (2 °C – 8 °C). Do not freeze.
Keep the vial in the outer carton in order to protect from light.

Keep this medicine out of the sight and reach of children.

Do not use VariQuin after the expiry date, which is stated on the carton.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. They will then be destroyed in a responsible manner and will not end up in the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What VariQuin contains

- The active substance in this medicine is human varicella zoster immunoglobulin
- The other ingredients in thie medicine are glycine and water for injections

What VariQuin looks like and contents of the pack

VariQuin is a clear solution. The colour of the solution may vary from colourless or light yellow to light brown.

The retail packaging for VariQuin consists of a box containing:
* One VariQuin vial of 200 IU.
The product is supplied as a solution for injection for intramuscular use (for injection into a muscle).

Marketing Autorisation Holder and Manufacturer

Sanquin Plasma Products B.V., Plesmanlaan 125, 1066 CX Amsterdam, the Netherlands, tel. +31 (0)20 512 3355.

RVG 16948

This leaflet was last approved in September 2016.

The following information is intended for healthcare professionals only:

Composition

Human varicella immunoglobulin prepared from plasma of human donors.
The product contains 100 - 180 grams of protein per litre. The protein fraction consists of at least 90 % immunoglobulin G (IgG). The varicella antibody concentration is at least 100 IU/ml. The maximum IgA concentration is 6 g/l.
VariQuin is dispensed in a filling size of 200 IU.

Therapeutic indications

Prophylaxis against varicella zoster virus (VZV) infection in at risk patients exposed to varicella

(chickenpox) or herpes zoster:

- pregnant women with negative VZV immune status especially up to early in the third trimester
- neonates whose mothers develops varicella infection within 7 days before and 7 days after delivery
- neonates whose mothers have no history of varicella and/or a negative immune status
- premature infants <28 weeks of gestation or newborns with low birth weight
- adults and children with no history of varicella and/or a negative immune status, receiving immunosuppressive therapy including steroids, cytostatic agents, radiotherapy, recent stem cell transplantation, or who have congenital or acquired immunodeficiency disorders and are not receiving replacement therapy with immunoglobulin.

Posology

Newborns with body weight up to 2 kg: 1 ml
Persons with body weight of 2-10 kg: 1 vial of 2 ml
Persons with body weight of 10-30 kg: 2 vials of 2 ml
Persons with body weight of more than 30 kg: 3 vials of 2 ml

Administration to neonates where the mother has experienced varicella in the period from 7 days before to 7 days after delivery should be carried out as soon as possible.
In other cases administration should be carried out as soon as possible, preferably within 3 days, but at the latest within 10 days after the contact with a varicella patient.
It is recommended that the administration be repeated if re-exposure takes place more than three weeks after the first administration.

Method of administration

Human varicella immunoglobulin should be administered slowly and deep via the intramuscular route. It is recommended that the product is brought to body temperature before administration.

If a large volume (>2 ml for children or >5 ml for adults) is required, it is recommended to administer this in divided doses at two sites.

If intramuscular administration is contraindicated (haemorrhagic diathesis) the injection can be administered subcutaneously. However, it should be noted that there are no clinical efficacy data to support administration by the subcutaneous route.

Contra-indications

Hypersensitivity to any of the components.
Hypersensitivity to human immunoglobulins.

Special warnings and special precautions for use

Ensure that VariQuin is not administered into a blood vessel, because of the risk of shock.

True hypersensitivity reactions are rare.

It is not worthwhile to administer VariQuin in cases where varicella is clinically manifest.

VariQuin does not prevent herpes zoster in persons who have had varicella, or who exhibit antibodies against varicella zoster virus. Nor is the course of herpes zoster affected by the product.

VariQuin contains a small quantity of IgA. Individuals who are deficient in IgA have the potential for developing IgA antibodies and may have anaphylactic reactions after administration of blood components containing IgA. The physician must therefore weigh the benefit of treatment with VariQuin against the potential risks of hypersensitivity reactions.

Rarely, human varicella immunoglobulin can induce a fall in blood pressure with anaphylactic

reaction, even in patients who have tolerated previous treatment with human immunoglobulin.

Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the injection. In case of shock, standard medical treatment for shock should be implemented.

Patients should be observed at least 20 minutes after administration.

Thromboembolism
Arterial and venous thromboembolic events including myocardial infarction, stroke, deep venous thrombosis and pulmonary embolism have been associated with the use of immunoglobulins. Patients should be sufficiently hydrated before use of immunoglobulins. Caution should be exercised in patients with preexisting risk factors for thrombotic events (such as advanced age, hypertension, diabetes mellitus and a history of vascular disease or thrombotic episodes, patients with acquired or inherited thrombophilic disorders, patients with prolonged periods of immobilization, severely hypovolemic patients, patients with diseases which increase blood viscosity). Patients should be informed about first symptoms of thromboembolic events including shortness of breath, pain and swelling of a limb, focal neurological deficits and chest pain. Patients should be advised to contact their physician immediately upon onset of symptoms.

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation / removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV), and for the non-enveloped virus hepatitis A virus. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19.

There is reassuring clinical experience regarding the lack of hepatitis A or parvovirus B19 transmission with immunoglobulins. It is also assumed that the antibody content makes an important contribution to the viral safety.

It is strongly recommended that every time that VariQuin is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

Interactions with other medicinal products and other forms of interaction

Live attenuated virus vaccines
Immunoglobulin administration may interfere with the development of an immune response to live attenuated virus vaccines such as rubella, mumps and varicella for a period of up to 3 months. After administration of this product, an interval of at least 3 months should elapse before vaccination with live attenuated virus vaccines.
Interference with serological testing
After injection of immunoglobulin, the transitory rise of the various passively transferred antibodies in the patient’s blood may result in misleading positive results in serological tests.
Passive transmission of antibodies to erythrocyte antigens, e.g. A, B and D, may interfere with some serological tests for red cell allo-antibodies, for example the antiglobulin test (Coombs’ test).

List of excipients

Glycine, water for injections.

Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Shelf life

2 years.
The product should be used immediately after piercing the vial.

Special precautions for storage

Store in a refrigerator (2°C – 8°C). Do not freeze.
Keep the container in the outer carton in order to protect from light.

Nature and contents of container

VariQuin is supplied in a colourless glass vial (of glass type I) fitted with a bromobutyl rubber stopper and sealed with an aluminium cap. The filling size is 2 ml.

Special precautions for disposal and other handling

The product should preferably be brought to body temperature before use.

The colour can vary from colourless to pale-yellow up to light brown. During the storage period, a slight cloudiness or formation of a small amount of precipitation might occur. This is no impediment to clinical use.

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