Summary of Product Characteristics

1. Trade name of the medicinal product

VariQuin®.

2. Qualitative and quantitative composition

2.1 Active ingredient

VariQuin® consists of a protein fraction prepared from human plasma with a high titre of varicella zoster antibodies. The product contains 100 - 180 grams of protein per litre. The protein fraction consists of at least 90% immunoglobulin G (IgG), small quantities of immunoglobulin A (IgA) and immunoglobulin M (IgM), and traces of other plasma proteins. The content of varicella antibodies is at least 100 IU/ml. VariQuin® is supplied in quantities of 2 ml. The product is supplied sterile and pyrogen-free.

2.2 Viral safety

VariQuin® is prepared from venous plasma by ethanol fractionation. The plasma has to be derived from voluntary, nonremunerated donors, who satisfy the requirements of the Blood Transfusion Council of the Netherlands Red Cross. This means, among other things, that each individual donation has been tested and found negative for hepatitis B surface antigen (HBsAg), for antibodies against human immunodeficiency virus 1 and 2 (HIV-1 and HIV-2, the inducers of AIDS), and for antibodies against hepatitis C virus. The manufacturing by means of ethanol fractionation and treatment at pH 4 ensure that the risk of transmission of viral diseases, in particular AIDS, hepatitis B and hepatitis non-A, non-B (including hepatitis C), is extremely small.

3. Pharmaceutical form

Solution for injection for intramuscular administration.

4. Clinical particulars

4.1 Therapeutic indications

Prophylaxis of varicella (chickenpox) in:

1. Neonates of mothers who develop varicella (chickenpox) within 5 days before and 2 days after delivery.
2. Persons who must be regarded as immune deficient and who have not had chickenpox, or who exhibit no antibodies against the varicella zoster virus and have had contact with a patient with varicella. This applies in particular to patients with leukaemia, Hodgkin’s disease or other malignant disorders, who have impaired immune response as the result of treatment with cytostatics, corticosteroids, radiotherapy, etc. Patients with congenital or acquired immune deficiency also come within this category.
3. Premature infants born before 28 weeks of gestation, or those with a birth weight of 1000 g or less, who have had contact with a patient with varicella, regardless of the presence or absence of antibodies against varicella zoster virus in the mother. Other premature infants who have had contact with a patient with varicella, where the mother exhibits no clinical or immunological indications of having had varicella, for the period of admission to hospital.
4. Indications to be considered:
   * pregnant women with no varicella in the case history, who have had contact with a patient with varicella;
   * adults and elderly persons in poor health, with no varicella in the case history, who have had contact with a patient with varicella.
4.2 Posology and method of administration

**Posology:**
Persons with body weight up to and including 20 kg: 1 dose (1 vial).
Persons with body weight of more than 20 kg: 2 doses (2 vials).

Administration should be carried out as soon as possible to neonates where the mother has varicella (chickenpox) in the period from 5 days before to 2 days after delivery (see Indication 1). In other cases (see Indications 2, 3 and 4) administration should be carried out as soon as possible, but at the latest within 72 hours 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:**
The product should be administered slowly as a deep intramuscular injection. It is recommended that the product be warmed to body temperature before administration.

4.3 Contra-indications

Known intolerance of the product, or of other products with similar composition of homologous immunoglobulins. This applies also to patients with selective IgA deficiency in whom anti-IgA antibodies have been detected. See below under ‘Special warnings and special precautions for use’.

Hypersensitivity to other ingredients of the product.

4.4 Special warnings and special precautions for use

**The preparation is not suitable for intravenous administration.**
In order to ensure that the tip of the needle is not in a blood vessel, the plunger of the injection syringe should be retracted a little before administration.

Subcutaneous administration of the preparation can be considered in patients with haemorrhagic diathesis. It should be noted that no studies have been performed to ascertain whether the efficacy of the product in preventing varicella is guaranteed by this route of administration.

Patients with selective IgA deficiency in whom anti-IgA antibodies have been detected, a very rare disorder, may suffer an anaphylactic reaction. These patients should preferably not be treated with the preparation, nor with other blood products which contain IgA. If, for some urgent reason, this rule must be departed from, administration should take place under strict clinical control.

An anaphylactic reaction may occur in patients who have exhibited an atypical reaction during earlier use of blood or blood products. These patients should preferably not be treated with the preparation, nor with other blood products. If for some urgent reason this rule must be departed from, administration should take place under strict clinical control.

Allergic reactions to VariQuin® that has been administered in the prescribed way by intramuscular injection, are rare.

Mild reactions, such as urticaria, should they arise, can be treated with antihistamines or corticosteroids. In case of serious reactions (e.g. anaphylactic shock) the reaction should be treated with intravenously administered corticosteroids and adrenaline (not intramuscularly).

Patients should be observed at least 20 minutes after administration.

Although precautions have been taken to eliminate blood-borne infectious agents both from the
starting material (plasma) and the final product, the risk of infection by blood-borne infectious agents cannot be entirely excluded.

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.

During the period of storage, slight turbidity or a small amount of precipitation may occur. This is not an impediment to clinical use.

4.5 Interaction with other medicinal products and other forms of interaction

1. Live attenuated vaccines
   The immune response to certain live attenuated vaccines - especially measles, mumps, varicella and rubella vaccine - can be impaired by immunoglobulin. After administration of such a vaccine, immunoglobulin should not be administered for three to four weeks; if administration is unavoidable, revaccination must take place three months after the administration of the immunoglobulin.
   After administration of VariQuin®, vaccination with live attenuated vaccine should be postponed for at least three months.

2. Interference with serological testing
   After an injection with immunoglobulins, the transitory rise of the various passively transferred antibodies in the patient’s blood can lead to misleading positive results in serological testing.

4.6 Pregnancy and lactation
   The safety of the use of VariQuin® during pregnancy has not been established in controlled clinical trials, and care must therefore be exercised in administering it to pregnant women and breast-feeding mothers. Long lasting clinical experience with immunoglobulin has revealed that no harmful effects on the course of the pregnancy, on the foetus or on the neonate are to be expected.

   Immunoglobulins are excreted into the milk and contribute to the transfer of protective antibodies to the neonate.

4.7 Effects on ability to drive and use machines
   There are no indications that immunoglobulins may impair the ability to drive or use machines.

4.8 Undesirable effects
   Pain and sensitivity at the injection site may be observed; this can be reduced by dividing larger doses over several injection sites.
   Occasionally fever and/or exanthema may occur. In rare cases nausea, vomiting, hypotension, tachycardia and hypersensitivity reactions or anaphylactic reactions, including shock, have been reported.

   When medicinal products prepared from human blood or plasma are administered, infectious diseases resulting from the transfer of pathogens cannot be completely ruled out. This also applies to pathogens, the nature of which is as yet unknown.

4.9 Overdose
   With respect to the occurrence and symptoms of possible overdose, no data is yet available.
5. Pharmacological properties

5.1 Pharmacodynamic properties

The action of VariQuin® in the prevention of varicella (chickenpox) is based on passive immunisation. The antibodies in the product will neutralise the varicella zoster virus, so that the virus can no longer bind to the target cell. Then further elimination takes place. In this way varicella is prevented, or any infection which does occur is weakened. The period of action of the product is about 2 weeks, possibly longer. Outbreaks of herpes zoster (shingles) in patients who have had varicella, or who exhibit antibodies against the varicella zoster virus, are not prevented by administration of VariQuin®. The course of herpes zoster is also unaffected by VariQuin®.

5.2 Pharmacokinetic properties

Absorption: after i.m. administration the immunoglobulin administered to the patient is gradually released from the intramuscular depot into the circulation. The maximum level of IgG is achieved after two to four days.

Metabolism/elimination:
The half-life of IgG is approximately 21 days. IgG itself or IgG-complexes are broken down in the cells of the reticulo-endothelial system (mononuclear phagocytes).

5.3 Preclinical safety data

Immunoglobulins are normal constituents of the human body. Animal experiments into the toxicity of a single administration are not relevant, since overdosage occurs at higher doses. Research into toxicity following repeated administration and into toxicity for the embryo or foetus is not feasible due to induction of and disturbance by antibodies. No research has been done into the effects of the product on the immune system of the neonate.

Given that clinical trials have not shown any evidence of oncogenic and mutagenic effects of immunoglobulins, experimental research, especially into heterologous species, is considered unnecessary.

6. Pharmaceutical particulars

6.1 List of excipients

VariQuin® contains 100 - 180 g/l of protein. The protein fraction consists of at least 90% IgG, small amounts of IgA and IgM and traces of other plasma proteins. The content of varicella antibodies is at least 100 IU/ml. The product contains 0.3 mol/l of glycine. VariQuin® is supplied sterile and pyrogen-free in quantities of 2 ml.

6.2 Incompatibilities

No medication may be added to VariQuin® because of the possibility of incompatibilities.

6.3 Shelf life

VariQuin® has a shelf life of two years. If stored according to the instructions, the product can be kept until the date stated on the package. After this date it should no longer be used.
The product should be used immediately after piercing the vial. Any remainder should be destroyed.

6.4 Special precautions for storage

VariQuin® should be stored between 2-8 °C protected from light.
6.5 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.

6.6 Instructions for use/handling

It is recommended that the product be warmed to body temperature before administration.

7. Holder of the marketing authorisation

Sanquin, Amsterdam, the Netherlands, tel: +31 20 512 3355

8. Marketing authorisation number

Registered in the Netherlands under RVG 16948.

9. Date of first authorisation/renewal of the authorisation

7 February 1997

10. Date of revision of the text

February 2003
Latest partial revision: 2 September 2003, concerning 1, 7