(English translation of official Dutch version)

PACKAGE LEAFLET

Package leaflet: Information for the user

TetaQuin 250 IU solution for injection

Human tetanus 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 TETAQUIN AND WHAT IT IS USED FOR

TetaQuin is a solution for injection. The solution contains the protein “human tetanus immunoglobulin” (human tetanus 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 toxins (poisonous substances) that are produced by the bacteria clostridium tetanus. These toxins cause the disease tetanus. The maximum IgA concentration is 6 g/l.

Tetanus immunoglobulin is an antibody that is effective against toxins (poisonous substances) produced by the tetanus bacterium. The so-called “tetanus toxin” can cause severe acute muscle cramps in humans following the infection of a wound (this severe disease is called tetanus). The antibodies against tetanus toxin that are present in this product nullify the harmful effect of the toxin. This neutralises the toxin and prevents or combats tetanus (so-called passive immunisation).

2. WHAT YOU NEED TO KNOW BEFORE YOU USE TETAQUIN

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

The administration of TetaQuin 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 TetaQuin.

TetaQuin contains a small quantity of IgA. TetaQuin 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, TetaQuin 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 TetaQuin
TetaQuin 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 TetaQuin). TetaQuin 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 TetaQuin before you can be vaccinated with any of these vaccines. In the case of measles, this reduced efficacy can last a maximum of 5 months.

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

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

Pregnancy and breast-feeding
The use of TetaQuin during pregnancy or whilst breast-feeding has not been studied. The use of immunoglobulins – such as TetaQuin – 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
- including 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 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 TetaQuin 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 TETAQUIN

Administration
Administration of TetaQuin should be performed by a doctor. TetaQuin 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 is divided over several injection sites.

TetaQuin provides short-term protection against tetanus. This is an injection with antibodies against the toxin produced by the tetanus bacteria (passive immunisation).

Long-term protection against tetanus can only be achieved by administration of a tetanus vaccine. The human body then forms its own antibodies after vaccination with deactivated tetanus toxin (active immunisation). TetaQuin and tetanus vaccine can be administered simultaneously. In this case, TetaQuin offers protection (immunity) against the disease tetanus, whilst the body simultaneously starts building up long-term protection against this disease as a result of administration of the tetanus vaccine. The tetanus vaccine contains deactivated tetanus toxin, which encourages the body to form antibodies against this toxin through so-called active immunisation.

Whether you receive a tetanus vaccine (active immunisation) and/or TetaQuin (passive immunisation) depends on the extent to which you have already been vaccinated against tetanus (vaccination status).
If active and passive immunisations are required simultaneously, then the immunoglobulin and the vaccine must be administered at different injection sites.

In the case of children: if your child is still taking part in the vaccinations offered by the National Vaccination Programme, he/she will never receive a separate tetanus vaccine after an injury, but he/she will instead receive the next vaccination including tetanus toxoid that he/she is eligible for under the National Vaccination Programme.
Following recovery from tetanus, you will require complete vaccination as an episode of tetanus does not offer protection (immunity) against a further occurrence of the disease.

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
Prophylaxis of tetanus prone wounds:

- 250 IU (1 TetaQuin vial), unless the risk is thought to be extremely high
- the dose may be doubled to 500 IU in:
    - infected wounds where surgically appropriate treatment cannot be achieved within 24 hours
    - deep or contaminated wounds with tissue damage and reduced oxygen supply, as well as

foreign body injury (e.g. bites, stings and shots)

Administration is useful up to three weeks after the injury.

Therapy of clinically manifest tetanus: as soon as the diagnosis is made, 3000 IU (12 vials of TetaQuin) should be administered. The administration of a dose of 3000 IU is repeated the following day.

Consideration should also be given to dose and dose schedules for human tetanus immunoglobulin for intramuscular use recommended in other official guidance.

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.

Reporting of side effects
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 TETAQUIN

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 this medicine 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 way and will not end up in the environment.

6. Contents of the pack and other information

What TetaQuin contains

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

What TetaQuin looks like and contents of the pack

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

The retail packaging for TetaQuin consists of a box containing:
* One TetaQuin vial of 250 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 17058

This leaflet was last approved in September 2016.

The following information is intended for healthcare professionals only:

Composition

Human tetanus immunoglobulin is prepared from plasma obtained from human donors.
The product contains 100 – 180 grams of protein per litre. The protein fraction consists of at least 90% immunoglobulin G (IgG). The tetanus antibody concentration is at least 100 IU/ml. The maximum IgA concentration is 6 g/l.
TetaQuin is dispensed in a filling size of 250 IU.

Therapeutic indications

1. Post-exposure prophylaxis
Immediate prophylaxis after tetanus prone injuries, in patients not adequately vaccinated, in patients whose immunisation status is not known with certainty, and in patients with severe deficiency in antibody production.

Consideration should also be given to other official guidance on the appropriate use of human tetanus immunoglobulin for intramuscular use.

2. Therapy of clinically manifest tetanus
Active tetanus vaccination should always be administered in conjunction with tetanus immunoglobulin, unless there are contraindications or there is confirmation of adequate vaccination.

Posology

Prophylaxis of tetanus prone wounds:

- 250 IU (1 vial TetaQuin), unless the risk is thought to be extremely high
- the dose may be increased to 500 IU in:
    - infected wounds where surgically appropriate treatment cannot be achieved within 24 hours
    - deep or contaminated wounds with tissue damage and reduced oxygen supply, as well as foreign body injury (e.g. bites, stings or shots)

Administration is useful up to three weeks after the injury.

Therapy of clinically manifest tetanus: as soon as the diagnosis is made, 3000 IU (12 vials of TetaQuin) should be administered. The administration of a dose of 3000 IU is repeated the following day. Consideration should also be given to dose and dose schedules for human tetanus immunoglobulin for intramuscular use recommended in other official guidance.

Method of administration

The product 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 different sites.

When simultaneous vaccination is necessary, the immunoglobulin and the vaccine should be administered at two different injection sites. The tetanus toxoid should then be injected via the intramuscular route using a separate injection syringe on the contralateral side of the body.

For prophylaxis, 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.

Contraindications

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

Special warnings and precautions for use

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

True hypersensitivity reactions are rare.

TetaQuin 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 TetaQuin against the potential risk of hypersensitivity reactions.

Rarely, human tetanus immunoglobulin can induce a fall in blood pressure with an 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.

The patient must be monitored for at least 20 minutes after administration.

<u>Thromboembolism</u>
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 HIV, HBV and HCV, and for the non-enveloped virus HAV. 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 and it is also assumed that the antibody content makes an important contribution to the viral safety.

It is strongly recommended that every time that TetaQuin 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.

Children who take part in the National Vaccination Programme should never receive separate tetanus toxoid, but should always receive the next scheduled vaccination that contains tetanus toxoid as set out in the National Vaccination Programme.

As a case of tetanus does not result in immunity to the disease, all patients should receive active vaccination against tetanus once they have made a complete recovery.

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. In the case of measles, this impairment may persist for up to 5 months.

N.B.: Simultaneous administration of tetanus toxoid and TetaQuin can take place without problems: TetaQuin provides immunity during the period that the active immunity is being acquired.

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 testing.

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

4 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 the package

250 IU in a glass, colourless vial (glass type I), closed with a bromobutyl rubber stopper and sealed by an aluminium cap. TetaQuin is supplied in a single-vial package and in boxes containing 10 or 50 vials.

Special precautions for disposal and other instructions

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

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