SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TetaQuin 250 IU solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Human tetanus 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 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.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection for intramuscular use.

4. CLINICAL PARTICULARS

4.1 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 confirmation of adequate vaccination.

4.2 Posology and method of administration

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 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.

4.3 Contraindications

Hypersensitivity to any of the components.

Hypersensitivity to human immunoglobulins.

4.4 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 had 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.

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 and 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.

4.5 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).

4.6 Pregnancy and lactation

The safety of this medicinal product for use in human pregnancy has not been established in controlled clinical trials. Clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy, or on the foetus and the neonate are to be expected.

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

There are no robust data on the frequency of undesirable effects from clinical trials. The following undesirable effects have been reported:

MedDRA Standard System Organ Class	**Undesirable effect**	**Frequency**
Immune system disorders	Hypersensitivity, anaphylactic shock*	Rare
Nervous system disorders	Headache	Rare
Cardiac disorders	Tachycardia	Rare
Vascular disorders	Hypotension	Rare
Gastrointestinal disorders	Nausea, vomiting	Rare
Skin and subcutaneous tissue disorders	Skin reaction, erythema, pruritis	Rare
Musculoskeletal and connective tissue disorders	Arthralgia	Rare
General disorders and administration site conditions	Fever, malaise, chills At the injection site: pain and sensitivity**, swelling, erythema, induration, warmth, pruritis, rash	Rare Not known***

* Please refer to section 4.4 “Special warnings and precautions for use” for an explanation.
** This can be reduced by dividing larger doses over several injection sites.
*** Not known: cannot be estimated from the available data.

See section 4.4 for safety with regards to transmissible agents.

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Netherlands Pharmacovigilance Centre Lareb, website: www.lareb.nl.

4.9 Overdose

Consequences of an overdose are not known.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins

– Human tetanus immunoglobulin ATC code: J06BB02

Human tetanus immunoglobulin contains mainly immunoglobulin G (IgG) with a specifically high content of antibodies against the toxins produced by the bacteria clostridium tetanus.

5.2 Pharmacokinetic properties

Following intramuscular administration, the immunoglobulin administered to the patient is gradually released into the circulation from the intramuscular depot. The maximum concentration is achieved after two to three days.

Human tetanus immunoglobulin has a half-life of about 3-4 weeks. This half-life may vary from patient to patient.

IgG and IgG complexes are broken down in cells of the reticuloendothelial system.

5.3 Preclinical safety data

Immunoglobulins are normal components of the human body. Animal studies of the toxicity following a single administration are not relevant, as higher doses will result in an overdose. Research into the toxicity of repeated administration and the toxicity for the embryo/foetus cannot be performed due to the induction of and the disruption by antibodies. No research has been performed into the effects of the product on the immune system of neonates.
As clinical research has not revealed any indications for oncogenic or mutagenic effects of immunoglobulins, experimental studies – particularly in heterologous species – is not deemed necessary.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine, water for injections.

6.2 Incompatibilities

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

6.3 Shelf life

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

6.4 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.

6.5 Nature and contents of container

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.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTORISATION HOLDER

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8. MARKETING AUTORISATION NUMBER(S)

RVG 17058

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

5 September 1996

10. DATE OF REVISION OF THE TEXT

Last partial revision involving section 4.4: 14 September 2016