SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

TETANUS GAMMA 250 IU/1 ml Solution for injection for intramuscular use
TETANUS GAMMA 250 IU/2 ml Solution for injection for intramuscular use
TETANUS GAMMA 500 IU/2 ml Solution for injection for intramuscular use

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Human tetanus immunoglobulin.

	TETANUS GAMMA 250 IU/1 ml	TETANUS GAMMA 250 IU/2 ml	TETANUS GAMMA 500 IU/2 ml
Human protein	100 – 180 g/l	100 – 180 g/l	100 – 180 g/l
of which immunoglobulin G (IgG) at least	90%	90%	90%
antibodies against the tetanus toxin	250 IU/ml (250 IU/ pre-filled syringe)	125 IU/ml (250 IU/ pre-filled syringe)	250 IU/ml (500 IU/ pre-filled syringe)

Distribution of IgG subclasses:
IgG_1 65.1 %
IgG_2 30.3 %
IgG_3 3.2 %
IgG_4 1.4 %

Maximum content of IgA: 300 micrograms/ml.

Excipient(s) with known effect: this medicinal product contains 0.39 mmol (or 9 mg) sodium per ml, i.e. essentially "sodium-free".
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.

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, unless the risk is thought to be extremely high.
- the dose may be increased to 500 IU in the case of:
    - 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)

Therapy of clinically manifest tetanus
Several studies suggest a value of human tetanus immunoglobulin in the treatment of clinically manifest tetanus equal to single doses of 3000 to 6000 IU in combination with other appropriate clinical procedures.

Paediatric population
The posology in children and adolescents (0-18 years) is not different to that of adults.

Method of administration
Human tetanus immunoglobulin should be administered via the intramuscular route.

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

When simultaneous vaccination is necessary, the immunoglobulin and the vaccine should be administered at two different sites.

For prophylaxis, if intramuscular administration is contra-indicated (bleeding disorders), 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.

For acute therapy, if intramuscular administration is not clinically appropriate, an alternative intravenous product may be used if available.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Hypersensitivity to human immunoglobulins.

Don’t administer TETANUS GAMMA into a blood vessel, because of the risk of shock (see section 4.4).

Don’t administer TETANUS GAMMA in individuals that have antibodies against IgA. The presence of antibodies against IgA is a rare condition showed in individuals without IgA in the blood (see section 4.3).

4.4 Special warnings and precautions for use

Ensure that TETANUS GAMMA is not administered into a blood vessel, because of the risk of shock (see section 4.3).
True hypersensitivity reactions are rare.

TETANUS GAMMA 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 TETANUS GAMMA against the potential risk of hypersensitivity reactions (see section 4.4).

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

Viral safety
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 viruses such as hepatitis A 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 TETANUS GAMMA 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.

Paediatric population
No specific data are available for paediatric population. The special warnings and precautions for use mentioned above apply also in children and adolescents (0-18 years).

4.5 Interactions with other medicinal products and other forms of interactions

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.

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, D may interfere with some serological tests for red cell antibodies, for example the antiglobulin test (Coombs' test).

4.6 Fertility, pregnancy and lactation

Pregnancy and breast feading
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 lactation, or on the foetus and the neonate are to be expected.

Fertility
The impact of treatment with TETANUS GAMMA on fertility has not been evaluated in controlled clinical trials. However, clinical experience with immunoglobulins suggests that no harmful effects on fertility are to be expected.

4.7 Effects on ability to drive and use machines

TETANUS GAMMA has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Clinically significant undesirable effects with products containing human tetanus immunoglobulin for intramuscular use may include hypersensitivity and anaphylactic shock.

Other undesirable effects, which may occur with the use of products containing human tetanus immunoglobulin, are tachycardia, hypotension, headache, nausea, vomiting, skin reaction, erythema, pruritus, arthralgia, fever, malaise and chills.

At the injection site may occur the undesirable effects as: swelling, pain, erythema, induration, warmth, rash and itching.
For safety with respect to transmissible agents, see 4.4.

Tabulated list of adverse reactions

The table presented below is according to the MedDRA system organ classification (SOC and Preferred Term Level) and it includes possible undesirable effects with products containing human tetanus immunoglobulin for intramuscular use.

Frequencies have been evaluated according to the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

MedDRA System Organ Class (SOC)	Adverse reactions (MedDRA Preferred Term*)	Frequency
Immune system disorders	Hypersensitivity, anaphylactic shock	Not known
Nervous system disorders	Headache	Not known
Cardiac disorders	Tachycardia	Not known
Vascular disorders	Hypotension	Not known
Gastrointestinal disorders	Nausea, vomiting	Not known
Skin and subcutaneous tissue disorders	Skin reaction, erythema, itching, pruritus	Not known
Musculoskeletal and connective tissue disorders	Arthralgia	Not known
General disorders and administration site conditions	Fever, malaise, chills At injection site: swelling, pain, erythema, induration, warmth, pruritus, rash, itching	Not known

During a clinical trial conducted with Tetanus Gamma, 30 patients were treated, none of the adverse events occurred was related with the administration of Tetanus Gamma.

Paediatric population
No specific data are available for paediatric population.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 the national reporting system.

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 toxin produced by the bacteria *Clostridium tetanus*.

5.2 Pharmacokinetic properties

Absorption
Human tetanus immunoglobulin for intramuscular administration is bioavailable in the recipient's circulation after a delay of 2-3 days.

Elimination
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

Immunoglobulin is normal constituent of the human body.

In animals, single dose toxicity testing is of no relevance since higher doses result in overloading. Repeated dose toxicity testing and embryo-foetal toxicity studies are not practicable due to induction of, and interference with antibodies. Effects of the immunoglobulins on the immune system of the newborn have not been studied.

Since clinical experience provides no hint for tumorigenic and mutagenic effects of immunoglobulin, experimental studies, particularly in heterologous species, are not considered necessary.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine
Sodium chloride
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

3 years.

6.4 Special precautions for storage

TETANUS GAMMA should be stored in a refrigerator (2°C - 8°C).
Do not freeze.
Store in the original package in order to protect from light.

6.5 Nature and contents of container

Pre-filled syringe with solution for injection with 250 IU and 500 IU
Box containing one pre-filled syringe of neutral transparent glass containing 250 IU or 500 IU of human tetanus immunoglobulin.

6.6 Special precautions for disposal

TETANUS GAMMA solution for injection, pre-filled syringe.
Screw in the plunger shaft and inject.

The product should be brought to room or body temperature before use. The colour can vary from colourless to pale-yellow up to light brown. Do not use solutions that are cloudy or have deposits.

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

7 MARKETING AUTHORISATION HOLDER

Kedrion S.p.A.
Loc. Ai Conti,
Castelvecchio Pascoli, 55051
Barga (Lucca) - Italy.

8 MARKETING AUTHORISATION NUMBERS

TETANUS GAMMA 250 IU Solution for injection, one 2 ml pre-filled syringe n. 022488047
TETANUS GAMMA 250 IU Solution for injection, one 1 ml pre-filled syringe n. 022488062
TETANUS GAMMA 500 IU Solution for injection, one 2 ml pre-filled syringe n. 022488050

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 12/08/1976
Date of latest renewal: June 2010

10 DATE OF REVISION OF THE TEXT

25 June 2015

This is a translation of the Italian Summary of Product Characteristics (SPC).
As not all the information given applies to your country, please refer to your local SPC.