SUMMARY OF PRODUCT CHARACTERISTICS
(CPMP/BPWG/3730/02)

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.

Human protein 100 – 180 g/l of which at least 90% is immunoglobulin G (IgG) with antibodies against the tetanus toxin 125 – 250 IU/ml (250 – 500 IU/container).

Maximum content of IgA 0.3 mg/ml.

For 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:

- 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 the value of human tetanus immunoglobulin in the treatment of clinically manifest tetanus using single doses of 3000 to 6000 IU in combination with other appropriate clinical procedures.

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

4.4 Special warnings and special precautions for use
Ensure that TETANUS GAMMA is not administered into a blood vessel, because of the risk of shock.
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.
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 HIV, HBV and HCV and for the non-enveloped viruses such as 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.

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 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

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

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 effects
Immune system disorders	Hypersensitivity, anaphylactic shock
Nervous system disorders	Headache
Cardiac disorders	Tachycardia
Vascular disorders	Hypotension
Gastrointestinal disorders	Nausea, vomiting
Skin and subcutaneous disorders	Skin reaction, erythema, itching, pruritus
Musculoskeletal and connective tissue disorders	Arthralgia

General disorders and administration site conditions	Fever, malaise, chill At injection site: swelling, pain, erythema, induration, warmth, pruritus, rash, itching

For safety with respect to transmissible agents, see 4.4.

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
Human tetanus immunoglobulin for intramuscular administration is bioavailable in the recipient's circulation after a delay of 2-3 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
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 product 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
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 Instructions for use and handling and 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 product 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

Renewal: June 2010

10 DATE OF REVISION OF THE TEXT

October 2011

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.