Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tetabulin S/D 250 IU/ml Solution for Injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Human Tetanus Immunoglobulin

One pre-filled syringe of Tetabulin S/D 250 IU (1ml) contains:

Human tetanus immunoglobulin 250 IU
human protein 100-170g/l
(of which at least 90% are immunoglobulin G)
Max. 1gA content: 4.8mg/ml

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
The product is a clear or slightly opalescent, colourless to pale yellow solution.

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 immunization 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 of tetanus 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:
- Available data suggest the value of human tetanus immunoglobulin in the treatment of clinically manifest tetanus using single doses of 3,000 to 6,000 IU intramuscularly in combination with other appropriate clinical procedures.

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

for intramuscular use.

Method of Administration
Human tetanus immunoglobulin should be administered via the intramuscular route.
If large volume (≥ 2ml for children or >5ml 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 (coagulation bleeding disorders), the injection can be done 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 precautions for use

Ensure that TETABULIN S/D is not administered into a blood vessel, because the risk of shock.

True hypersensitivity reactions are rare.

TETABULIN S/D 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 TETABULIN S/D against the potential risk of hypersensitivity reactions.

Rarely, human tetanus immunoglobulin can induce a fall in blood pressure with anaphylactic reactions, even in patients who had tolerated previous treatments with human immunoglobulin.
Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the injection. In case of shock, standard medical treatment should be implemented. The current medical standards for shock treatment should be observed.

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.

The measures taken may be of limited value against non-enveloped viruses such as HAV and 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 TETABULIN S/D 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 Interaction 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 at least 6 weeks and 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 and D, may interfere with some serological tests for red cell antibodies, for example the antiglobulin test (Coombs test postivity).

4.6 Fertility, 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 effect 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 the ability to drive and use machines have been observed.

4.8 Undesirable effects

The most commonly reported ADRs are dizziness, fever, hyperthermia, fatigue, erythema, and injection site reactions, all occurring in very rare cases (≤1/10,000 patients).

ADRs have been reported from clinical studies and from post-marketing experience and may be experienced as given in the following table:

MedDRA Standard System Organ Class	**Undesirable effects Preferred Term (PT)**	**Frequency**
Immune system disorders	Hypersensitivity Anaphylactic shock	Very rare (<1/10,000) Very rare (<1/10,000)
Nervous system disorders	Headache Dizziness,vertigo Syncope Tachycardia	Very rare (<1/10,000) Very rare (<1/10,000) Very rare (<1/10,000) Very rare (<1/10,000)
Vascular disorders	Hypotension Pallor	Very rare (<1/10,000) Very rare (<1/10,000)
Gastrointestinal disorders	Nausea, vomiting	Very rare (<1/10,000)
Skin and subcutaneous disorders	Erythema Hyperhidrosis Pruritus, itching Rash	Very rare (<1/10,000)
Muskuloskeletal and connective tissue disorders	Arthralgia	Very rare (<1/10,000)
General disorders and administration site conditions	Fever, malaise, chill Fatigues Hyperthermia At injection site: erythema, induration, warmth, pruritus, rash, itching, swelling. Oedema, pain	Very rare (<1/10,000) Very rare (<1/10,000)

For safety with respect to transmissible agents, *see section 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 human antibodies against the toxin produced by the bacteria Clostridium tetani.

5.2 Pharmacokinetic properties

Human tetanus immunoglobulin for intramuscular administration is bioavailable in the recipient's circulation after a delay of 2 to 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 reticulo-endothelial system.

5.3 Preclinical safety data

Because the effects observed in animals after application of heterologous proteins are not comparable to those observed in humans, only a limited number of pharmacodynamic studies in animals were performed with TETABULIN S/D.

Single dose toxicity studies demonstrate that doses several times higher than the maximum recommended dose had no toxic effects on laboratory animals.

Repeated dose toxicity testing in animals is impracticable due to interference with developing antibodies to heterologous protein.
Since human proteins are not known to cause tumorigenic and mutagenic effects, experimental studies, particularly in heterologous species, are not considered necessary.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine
Sodium chloride
Polyethylene Glycol
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Three years.

6.4 Special precautions for storage

Store in a refrigerator(2°C to 8°C)
Store in the original package to protect from light.
Do not freeze.

6.5 Nature and contents of container

This product is supplied in prefilled syringes containing single doses of 1 ml (250 IU) solution for injection. The syringe consist of hydrolytic type I glass, and the syringe plungers of halogenobutyl rubber.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

The product should be brought to room or body temperature before use.

The colour can vary from colourless to pale yellow. The solution should be clear or slightly opalescent. During storage it may show formation of slight turbidity or a small amount of particulate matter. Do not use solutions that are more than just slightly turbid, i.e. are cloudy or have deposits.
TETABULIN S/D is for single use only.
Any unused product or waste material should be disposed of a in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Baxter Healthcare Ltd
Caxton Way
Thetford
Norfolk, IP24 3SE
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 0167/126/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 April 1978

Date of last renewal: 26 October 2008

10 DATE OF REVISION OF THE TEXT

October 2012