1.7 Summary Product Characteristics (SPC)

NAME OF THE MEDICINAL PRODUCT:

Tetanus antitoxin 1500I.U.I.H.S. (1mL liquid vial).

COMPOSITION:

Each mL contains:

Enzyme refined, Equine Tetanus antitoxic immunoglobulin fragments not less than 1500 IU

Preservative : Cresol B.P.<0.25%v/v

Stabilizer : Glycine B.P.

Excipient : Sodium Chloride B.P.

PHARMACEUTICAL DOSAGE FORM:

Solution for injection.

THERAPEUTIC INDICATIONS:

General considerations

Tetanus (lockjaw) is a neurologic disease characterized by severe muscular spasms. It is caused by the neurotoxin produced by the anaerobic bacterium *Clostridium tetani* in a contaminated wound. Onset is gradual, occurring over 1 to 7 days, and progresses to severe generalized muscle spasms (severe enough to cause spinal fractures), which frequently are aggravated by any external stimulus. Severe spasms persist for 1 week or more and subside over a period of weeks in those who recover. Neonatal tetanus, a common cause of neonatal mortality in developing countries, is caused by contamination of the umbilical stump. Local tetanus is manifested by local muscle spasms in areas contiguous to a wound infected with *C. tetani.*

Wound cleaning, debridement when indicated, and proper immunization are important in the prevention and management of tetanus. The need for active immunization with tetanus toxoid, with or without tetanus antitoxin, depends on both the condition of the wound and the patient's vaccination history.

Determining whether the wound is clean or dirty is extremely important in categorizing patients. A wound is considered to be dirty if it is more than 6 hours old, if the wound is penetrating or

deep, if the instrument that caused the wound is contaminated, if the wound is infected, if the wound is caused by a deep partial- or full-thickness burn, or if it is a crush injury.

A thorough attempt must be made to determine whether a patient has completed primary vaccination. Patients with unknown or uncertain previous vaccination histories should be considered to have had no previous tetanus toxoid doses. Patients who have not completed a primary series may require tetanus toxoid and passive immunization with either tetanus antitoxin or tetanus immune globulin at the time of wound cleaning and debridement.

POSOLOGY AND METHOD OF ADMINISTRATION:

General Dosing Information

Anaphylaxis may occur following tetanus antitoxin administration, even in individuals with no prior history of hypersensitivity to tetanus antitoxin or horse serum. Prior to use of tetanus antitoxin, appropriate measures should be taken to detect the presence of dangerous sensitivity. The patient's history should be reviewed carefully, including any report of asthma, hay fever, urticaria, or other allergic manifestations; allergic reactions upon exposure to horses; and prior injections of horse serum. An intradermal skin test or conjunctival test for serum sensitivity using normal horse serum or the antitoxin and 0.9% sodium chloride injection should be performed under close medical supervision in every patient prior to administration of tetanus antitoxin, regardless of clinical history. Adrenaline injection (1:1000) should be on hand to treat an anaphylactic or other allergic reactions.

The skin test consists of an intradermal injection of 0.1 mL of a 1:100 dilution of 0.05 mL or a 1:1000 dilution (for persons with a history of allergy) of normal horse serum in 0.9% sodium chloride injection, and an equal volume of 0.9% sodium chloride injection at a separate site to serve as a control. A positive skin test result consists of an urticarial wheal surrounded by an erythematous zone.

The conjunctival test consists of instillation of one drop of a 1:10 dilution (for adults) or a 1:100 dilution (for children) of normal horse serum into the conjunctival sac. One drop of 0.9% sodium chloride injection is instilled into the other conjunctival sac to serve as a control. A positive conjunctival test result consists of itching of the eye and reddening of the conjunctiva.

Whenever there is a history of allergy, sensitivity to horse serum, or manifestations of sensitivity when in proximity to horses, or if the reaction to the skin or eye test is positive, great care must be exercised in the administration of tetanus antitoxin.

No single method can be advised for the administration of tetanus antitoxin for sensitive persons, as each presents an individual problem. Desensitization of the patient should be carried out by serial injections of diluted tetanus antitoxin as indicated below at intervals of 20 minutes, provided no reaction occurs.

Schedules for desensitization:

- 0.05 mL of 1:20 dilution subcutaneously.
- 0.1 mL of 1:10 dilution subcutaneously.
- 0.3 mL of 1:10 dilution subcutaneously.
- 0.1 mL of undiluted tetanus antitoxin subcutaneously.
- 0.2 mL of undiluted tetanus antitoxin subcutaneously.
- 0.5 mL of undiluted tetanus antitoxin subcutaneously

- The remaining therapeutic dose of tetanus antitoxin should be injected intramuscularly

After a patient can properly withstand these doses of tetanus antitoxin, it is usually safe to inject larger doses of tetanus antitoxin intramuscularly at intervals of 20 minutes. If a reaction occurs after a desensitizing dose, injections should be stopped for 1 hour and the schedule recommenced at intervals of 20 minutes, with the last dose that failed to cause a reaction repeated.

For treatment of adverse effects:

Recommended treatment consists of the following:

• For a mild hypersensitivity reaction—Administering antihistamines and, if necessary, corticosteroids. In mild anaphylaxis, antihistamines or subcutaneous adrenaline may be all that is necessary if the condition is progressing slowly and is not life-threatening, regardless of the organ or system affected. Under these circumstances the risks associated with intravenous adrinaline administration outweigh the benefits.

- For a severe hypersensitivity or anaphylactic reaction—administering adrenaline.

Antihistamines or corticosteroids may also be administered as required. Adrenaline is the treatment of choice for a severe hypersensitivity or anaphylactic reaction. If the patient's condition is not stable, adrenaline should be infused. Noradrenaline may be preferable if there is no bronchospasm. For bronchospasm, adrenaline should be given with corticosteroids. Other bronchodilators, such as intravenous aminophylline or albuterol by nebulization, also should be considered.

Usual adult and adolescent dose

[*Clostridium tetani* infection (prophylaxis)]

Patients weighing up to 65 pounds (29.5 kgs): Intramuscular, 1500 Units as a single dose. Patients weighing 65 pounds (29.5 kgs) or more: Intramuscular, 3000 to 5000 Units as a single dose.

Usual pediatric dose

[*C. tetani* infection (prophylaxis)]

Intramuscular, 1500 Units as a single dose.

CONTRAINDICATIONS:

There are no contraindications.

Risk-benefit should be considered when the following medical problem exists

» Hypersensitivity to tetanus antitoxin or horse serum.

WARNINGS ANDPRECAUTIONS:

Serum Reaction

In case of patients receiving Tetanus antitoxin, it should be essential to test for hypersensitivity of the individual with a test dose. Serum sensitivity test is carried out by injecting 0.1 mL Tetanus Antitoxin serum in 1:10 dilution either subcutaneously or intradermally and observing for half an hour for any reaction of local or general. In case of hypersensitive reaction, serum should be given with great caution in small divided dose subcutaneously at regular intervals of half an hour. Adrenaline injection (1:1000) must be had for immediate

treatment of shock if it develops. Intravenous administration of serum is not recommended in hypersensitive cases.

Interactions with other medicaments:

Immunoglobulins may interfere with the ability of live vaccines to induce an immune response.

Pregnancy

Pregnancy is not a contraindication to the use of Tetanus antitoxin, unless clearly indicated.

Lactation

Breastfeeding is not a contraindication to Tetanus antitoxin, unless clearly indicated. It is not known if antitoxin antibodies are excreted into breast milk.

Pediatrics

Appropriate studies on the relationship of age to the effects of tetanus antitoxin have not been performed in the pediatric population. However, pediatrics-specific problems that would limit the usefulness of this medication in children are not expected.

Geriatrics

No information is available on the relationship of age to the effects of tetanus antitoxin in geriatric patients.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:

Not installed.

PREGNANCY AND LACTATION:

Pregnancy

Pregnancy is not a contraindication to the use of Tetanus antitoxin, unless clearly indicated.

Lactation

Breast feeding is not a contraindication to Tetanus antitoxin, unless clearly indicated. It is not known if antitoxin antibodies are excreted into breast milk.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

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

SIDE/ADVERSE/UNDESIRABLE EFFECTS:

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)—not necessarily inclusive:

Anaphylactic reaction (difficulty in breathing and swallowing; hives; itching; reddening of skin, especially around ears; swelling of eyes, face, or inside of nose; unusual tiredness or weakness, sudden and severe).

Serum sickness (feeling of discomfort; fever; inflammation of joints; itching; muscle aches; rash; swollen lymph glands).

OVERDOSE:

The dose is usually dependent on the severity of the infection, a symptomatic treatment should be given in case of overdose and supportive therapies are recommended

PHARMACOLOGICAL PROPERTIES:

Pharmacology/Pharmacokinetics

Physicochemical characteristics:

Source—

Tetanus antitoxin is a sterile, non pyrogenic solution of the refined and concentrated proteins, chiefly globulins, containing antitoxic antibodies obtained from the blood serum or plasma of healthy horses that have been immunized against tetanus toxin or toxoid.

Mechanism of action/Effect:

Tetanus antitoxin neutralizes the toxin produced by *Clostridium tetani.*

Precautions to Consider

Cross-sensitivity and/or related problems

Patients allergic to any product prepared from horse serum may also be allergic to tetanus antitoxin.

SHELF-LIFE:

2-Years (Stored at 2-8°C)

STORAGE CONDITION

The liquid Tetanus antitoxin should be stored at 2°C to 8°C.It should not be allowed to freeze.

PRESENTATION

Tetanus antitoxin 1500 I.U/mL is supplied as 1 mLliquid in glass vial.

DISPOSABLE

Left over antiserum and used vials should be discarded as Biomedical waste.