Tetanus Immune Globulin (Human)

### HyperTET® S/D

#### Solvent/Detergent Treated

**250 Units**

**DESCRIPTION**

Tetanus Immune Globulin (Human) — HyperTET® S/D treated with solvent/detergent is a colorless to pale yellow or pink sterile solution of tetanus hyperimmune immune globulin for intramuscular administration; it is preservative-free, in a latex-free delivery system. HyperTET S/D is prepared from equine tetanus toxoid fractionation from the plasma of donors immunized with tetanus toxoid. The immune globulin is isolated from solubilized Cohn Fraction II. The Fraction II solution is adjusted to a final concentration of 0.3% tri-n-butyl phosphate (TBP) and 0.2% sodium cholate. After removal of solute (TBP and detergent) by precipitation with succinic acid, the solution is heated to 30°C and maintained at that temperature for not less than 6 hours. After the viral inactivation step, no viable agents capable of producing disease are detectable by precipitation, filtration and final ultracentrifugation and ultraviolet light. HyperTET S/D is formulated as a 15-18% protein solution at a pH of 6.4–7.2 in 0.21-0.32 M glycine. HyperTET S/D is then incubated in the final container for 21–28 days at 20–25°C. The product is standardized against the U.S. Standard Antitoxin and the U.S. Control Tetanus Toxin and contains not less than 250 tetanus antitoxin units per container.

The removal and inactivation of spiked model enveloped and non-enveloped viruses during the manufacturing process for HyperTET S/D has been validated in laboratory studies. Human Immunodeficiency Virus Type 1 (HIV-1), was chosen as the relevant virus for blood products; Bovine Viral Diarrhea Virus (BVDV) was chosen to model Hepatitis C Virus; Pseudorabies virus (PRV) was chosen to model Human Herpes viruses and other large enveloped DNA viruses; and Teno virus (BoV) and Influenza A virus was chosen to model the process of and its resistance to physical and chemical inactivation. Significant removal of model enveloped and non-enveloped viruses during the manufacturing process for HyperTET S/D, was achieved as evidenced by the results shown in Table I. Significant inactivation of enveloped viruses was much better achieved as shown in Table II.

The decline has resulted from widespread use of tetanus toxoid and improved wound management, including use of tetanus prophylaxis in emergency rooms.5

HyperTET S/D supplies passive immunity to those individuals who have low or no immunity to the toxoid produced by the tetanus organism, Clostridium tetani. The antibodies act to neutralize the free form of the powerful exotoxin produced by this bacterium. Historically, such passive protection was provided by antitoxin derived from equine or bovine serum; however, the foreign protein in these heterologous products often produced severe allergic manifestations, even in individuals who demonstrated negative skin and/or conjunctival tests prior to administration. The frequency of the results of these latter maneuvers was much lower than that of tetanus.5

Several studies suggest the value of human tetanus antitoxin in the treatment of active tetanus.7 In 1961 and 1962, Nation et al.6 using HyperTET treated 20 patients with tetanus using single doses of 3,000 antitoxin units in combination with other accepted clinical and nursing procedures. Six patients, all over 45 years of age, died of causes other than tetanus. The authors felt that the mortality rate (30%) compared favorably with their previous experience. All patients required vigorous wound care. In larger doses, better results were achieved than the 60% national death rate for tetanus reported from 1951 to 1954.7,8,9,10

The drug is prepared from equine tetanus toxoid (TIG) is the product of choice. It provides protection longer than antitoxin of animal origin, and is preserved by the addition of human serum globulin. The globulin is prepared from plasma collected during the 64th week of pregnancy and the 3rd trimester of pregnancy. The globulin is then mixed with freeze-dried tetanus toxoid and frozen. The product is sealed in clear glass ampules and sterilized by ethylene oxide gas. The finished product contains 1,000 antitoxin units per ampule.

### Guide to Tetanus Prophylaxis in Wound Management

#### Table: History of Tetanus Immunization

<table>
<thead>
<tr>
<th>Doses</th>
<th>Clean, Minor Wounds</th>
<th>All Other Wounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>TD</td>
<td>TIG†</td>
<td>Td TIG†</td>
</tr>
<tr>
<td>† Uncertain or less than 3 doses in 10 years or more than 5 doses if not a 10-year period.</td>
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<tr>
<td>§ If only three doses of fluid tetanus toxoid have been received, a fourth dose of toxoid, preferably an adsorbed toxoid, should be given.</td>
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#### CONTRAINDICATIONS

None known.

#### WARNINGS

HyperTET S/D is made from human plasma. Products made from human plasma may contain viruses, such as viruses, that are not yet known or are newly emerging that can cause disease. The risk of such products causing disease cannot be completely eliminated even with measures to reduce and inactivate such viruses. The risk may be greater for products made before the mid-1960s because effective screening techniques were not available to identify donors who were infected with such viruses.

HyperTET S/D should be given with caution to patients with a history of prior systemic allergic reactions following the administration of human immunoglobulin preparations. Patients who have severe acute allergic reactions to immune globulin or another blood product in the same manufacturing process for HyperTET S/D may be at increased risk of adverse reactions to HyperTET S/D. Such patients should receive the product only if there is a likely medical benefit for the patient that is expected to outweigh the risks of anaphylaxis.

#### PRECAUTIONS

**Genetic Considerations**

HyperTET S/D should not be given intravenously. Intravenous injection of immunoglobulin intended for intramuscular use can, on occasion, cause a precipitous fall in blood pressure, and a picture not unlike anaphylaxis. Injections should only be made intramuscularly and care should be taken to draw back on the plunger of the syringe before injection in order to be certain that the needle is not in a blood vessel. Intramuscular injections are preferably administered in the deltoid muscle of the upper arm or lateral thigh muscle. The gluteal region should not be used as an injection site because of the risk of injury to the sciatic nerve.

Chromopexyaphagomyxis tetanus is neither practical nor useful in managing wounds. Wound cleaning, debridement when indicated, and proper immunization are important. The need for tetanus toxoid (active immunization), with or without TIG (passive immunization), depends on both the condition of the wound and the patient’s vaccination history. Rarely has tetanus occurred in a person who has received a primary series of toxoid injections.2 See table under INDICATIONS AND USAGE.

Skin tests should not be done. The intradermal injection of concentrated IgG solutions often cause cutaneous reactions which may be misinterpreted as a positive allergy reaction. In actuality, this does not represent an allergy; rather, it is localized tissue irritation. Misinterpretation of the results of such tests can lead the physician to withhold needed human antitoxin from a patient who is not actually allergic to this material. True allergic responses to human IgG given in the prescribed intramuscular manner are rare.

Although systemic reactions to human immunoglobulin preparations are rare, epinephrine should be available for treatment of acute anaphylactic reactions.

#### Drug Interactions

Interactions in immunoglobulin preparations may interfere with the response to live viral vaccines such as measles, mumps, polio, and rubella. Therefore, use of such vaccines should be deferred until approximately 3 months after Tetanus Immune Globulin (Human) — HyperTET® S/D administration.

No interactions with other products are known.

#### Pregnancy Category C

Animal reproduction studies have not been conducted with HyperTET S/D. It is also not known whether HyperTET S/D can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. HyperTET S/D should be given to a pregnant woman only if clearly needed.

#### Pediatric Use

Safety and effectiveness in the pediatric population have not been established.

#### ADVERSE REACTIONS

Slight soreness at the site of injection and slight temperature elevation may be noted at times. Sensitization to tetanus toxoid in human immunoglobulin is extremely rare. In the course of routine injections of large numbers of persons with immunoglobulin there have been a few isolated occurrences of angioneurotic edema, nephrotic syndrome, and anaphylactic shock after injection.

#### OVERDOSAGE

Although no data are available, clinical experience with other immunoglobulin preparations suggests that the only manifestations would be pain and tenderness at the injection site.
DOSE AND ADMINISTRATION

Routine prophylactic dosage schedule:

- Adults and children 7 years and older: HyperTET S/D, 250 units should be given by deep intramuscular injection (see PRECAUTIONS). At the same time, but in a different extremity and with a separate syringe, Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use) (Td) should be administered according to the manufacturer’s package insert. Adults with uncertain histories of a complete primary vaccination series should receive a primary series using the combined Td toxoid. To ensure continued protection, booster doses of Td should be given every 10 years.3

- Children less than 7 years old: In small children the routine prophylactic dose of HyperTET S/D may be calculated by the body weight (4.0 units/kg). However, it may be advisable to administer the entire contents of the syringe of HyperTET S/D (250 units) regardless of the child’s size, since theoretically the same amount of toxin will be produced in the child’s body by the infecting tetanus organism as it will in an adult’s body. At the same time but in a different extremity and with a different syringe, Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (DTP) or Diphtheria and Tetanus Toxoids Adsorbed (For Pediatric Use) (DT), if pertussis vaccine is contraindicated, should be administered per the manufacturer’s package insert.

Note: The single injection of tetanus toxoid only initiates the series for producing active immunity in the recipient. The physician must impress upon the patient the need for further toxoid injections in 1 month and 1 year. Without such treatment, the active immunization is incomplete. If a contraindication to using tetanus toxoid-containing preparations exists for a person who has not completed a primary series of tetanus toxoid immunization and that person has a wound that is neither clean nor minor, only passive immunization should be given using tetanus immune globulin.2 See table under INDICATIONS AND USAGE.

Available evidence indicates that complete primary vaccination with tetanus toxoid provides long lasting protection ≥10 years for most recipients. Consequently, after complete primary tetanus vaccination, boosters—even for wound management—need be given only every 10 years when wounds are minor and uncontaminated. For other wounds, a booster is appropriate if the patient has not received tetanus toxoid within the preceding 5 years. Persons who have received at least two doses of tetanus toxoid rapidly develop antibodies.2 The prophylactic dosage schedule for these patients and for those with incomplete or uncertain immunity is shown on the table in INDICATIONS AND USAGE.

Since tetanus is actually a local infection, proper initial wound care is of paramount importance. The use of antitoxin is adjunctive to this procedure. However, in approximately 10% of recent tetanus cases, no wound or other breach in skin or mucous membrane could be implicated.17

Treatment of active cases of tetanus:

Standard therapy for the treatment of active tetanus including the use of HyperTET S/D must be implemented immediately. The dosage should be adjusted according to the severity of the infection.14

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. They should not be used if particulate matter and/or discoloration are present.

HyperTET S/D is supplied with a syringe and an attached UltraSafe® Needle Guard for your protection and convenience. Please follow instructions below for proper use of syringe and UltraSafe® Needle Guard.

Directions for Syringe Usage

1. Remove the prefilled syringe from the package. Lift syringe by barrel, not by plunger.
2. Twist the plunger rod clockwise until the threads are seated.
3. With the rubber needle shield secured on the syringe tip, push the plunger rod forward a few millimeters to break any friction seal between the rubber stopper and the glass syringe barrel.
4. Remove the needle shield and expel air bubbles. [Do not remove the rubber needle shield to prepare the product for administration until immediately prior to the anticipated injection time.]
5. Proceed with hypodermic needle puncture.
6. Aspirate prior to injection to confirm that the needle is not in a vein or artery.
7. Inject the medication.
8. Keeping your hands behind the needle, grasp the guard with free hand and slide forward toward needle until it is completely covered and guard clicks into place. If audible click is not heard, guard may not be completely activated. (See Diagram A and B)
9. Place entire prefilled glass syringe with guard activated into an approved sharps container for proper disposal. (See Diagram C)

A number of factors could reduce the efficacy of this product or even result in an ill effect following its use. These include improper storage and handling of the product after it leaves our hands, diagnosis, dosage, method of administration, and biological differences in individual patients. Because of these factors it is important that this product be stored properly and that the directions be followed carefully during use.

HOW SUPPLIED

HyperTET S/D is supplied in 250 unit prefilled disposable syringes with attached needles. HyperTET S/D is preservative-free, in a latex-free delivery system.

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<thead>
<tr>
<th>NDC Number</th>
<th>Size</th>
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<tbody>
<tr>
<td>125334-634-02</td>
<td>250 unit syringe</td>
</tr>
</tbody>
</table>

STORAGE

Store at 2–8°C (36–46°F). Solution that has been frozen should not be used.

CAUTION

B only

U.S. federal law prohibits dispensing without prescription.

REFERENCES


GRIFOLS
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U.S. License No. 1871
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