



diphtheria antitoxin (equine)
immunoserum diphthericum (equinum)

composition

1 ml of preparation contains:

Active ingredient:

- immunoglobulin (equine) not more than 170 mg
- minimal antibody activity against *C. diphtheriae* 1000 I.U.

Excipients:

- m-Cresol (preservative) 0.027 mmol
- Sodium chloride 0.150 mmol
- Sterile water for injection up to 1 ml

pharmaceutical form and packaging

Sterile preparation for parenteral administration.
Vial containing 10000 I.U.: box containing 1 vial
box containing 50 vials

pharmacotherapeutic group (ATC code):

J 06 A A01

name and address of manufacturer and marketing authorisation holder

Institute of Immunology, Inc., Rockefellerova 2, HR-10000 Zagreb, Croatia

legal category

Subject to medical prescription, supply through medical institutions only.

therapeutic indications

Diphtheria antitoxin (equine) is used for treatment of diphtheria, and very rarely, for prevention of diphtheria in cases of asymptomatic unimmunized persons who were exposed to diphtheria. The diphtheria toxin antibodies present in antitoxin bind to a toxin and neutralize toxin that is produced by a toxogenic species *Corynebacterium diphtheriae*. Before administration of antitoxin, the patient should be tested for allergy (i.e. skin-prick test). In the treatment of diphtheria, diphtheria antitoxin should be administered as soon as clinical evidence of diphtheria appears (clinical diagnosis); one should not wait for bacterial proof of diagnosis to administer antitoxin since the patient's condition with diphtheria can deteriorate rapidly. Antitoxin doses used for treatment of diphtheria are empiric and related to the site and size of the membrane formation, degree of toxicity and duration of the disease. The presence of soft, diffuse cervical lymphadenitis indicates medium to intensive toxin absorption. Anti-infective therapy (i.e. erythromycin, penicillin G) can eliminate bacteria from the infected sites; prevent spreading of bacteria and further toxin production as well as prevent or stop bacteria transmission. However, anti-infective agents cannot neutralize diphtheria toxin and should not replace antitoxin therapy. Though efficacy of the treatment with antitoxin for cutaneous diphtheria is not determined (in most cases a skin form of diphtheria is caused by the nontoxic species of *C. diphtheriae*), some physicians recommend the use of antitoxin for this form also, because the toxic sequel can also be seen in these patients. For prophylaxis in asymptomatic, unimmunized persons exposed to diphtheria administration of diphtheria antitoxin (equine) should be considered because of the risk of side effects (hypersensitivity, serum disease). Chemoprophylaxis with an anti-infective agent (i.e. erythromycin orally for 7 to 10 days or 1 intramuscular injection of penicillin G) and active immunization with diphtheria toxoid is recommended for prevention of respiratory or cutaneous diphtheria in asymptomatic, unimmunized patients who were in close contact with the patient.

contraindications

Injection of the antitoxin to persons with a history of allergic reactions to equine protein and to allergic individuals is contraindicated. Epinephrine and other supportive measures should be available in case of an anaphylactic reaction.

special warnings and precautions for use

Prior to administering the antiserum, a detailed anamnesis should be taken and an inquiry should be made concerning previous application of horse proteins; as well as an inquiry concerning any allergic manifestations (asthma, eczema, etc.).

If the patient did not previously receive horse proteins, a complete dose can be administered at once, except in patients with allergic diseases in their personal or family anamnesis.

In patients who have previously received horse proteins without allergic reaction, a 0.2 ml dose is administered subcutaneously. If after at least 30 minutes no allergic reaction occurs, the remainder of the dose can be administered intramuscularly (IM). In patients who have previously received horse antiserum with local or general reactions (as in individuals with allergy), an antiserum of another animal should be administered. Only if it is unavoidable (there is no antiserum available of another animal), desensitization should be tried with 0.2 ml of a 1:10 dilution subcutaneously, and after 30 minutes with 0.2 ml undiluted antiserum. If in the next 30 minutes there is no reaction, the remaining quantity of antiserum can be administered intramuscularly.

interaction with other medicinal products

None known.

pregnancy and lactation

Diphtheria antitoxin (equine) must not be administered during pregnancy.

posology and methods of administration

It is administered intramuscularly (*im*).

Prophylaxis

Diphtheria antitoxin is rarely used for prophylaxis of diphtheria. When prophylactic therapy with diphtheria antitoxin is considered necessary in an asymptomatic, nonimmunized contact of a patient with respiratory or cutaneous diphtheria, the contact should receive chemoprophylaxis with an appropriate anti-infective agent (i.e. a 7 to 10-day course of oral erythromycin or a single intramuscular dose of penicillin G), active immunization with a diphtheria toxoid preparation and a single dose of antitoxin. The dose of diphtheria antitoxin (equine) for prophylaxis depends on the time since exposure, the extent of exposure, and the medical condition of the individual, but is usually 5 000 to 10 000 I.U. administered intramuscularly as a single dose to adults or children. Diphtheria antitoxin (equine) and diphtheria toxoid (diphtheria and tetanus vaccine) should not be injected simultaneously or in the same place due to possible diphtheria toxoid neutralization in the composition of the vaccine.

Treatment

The therapeutic dose of diphtheria antitoxin is determined by the severity and duration of the disease, age and body weight of the patient. The entire dose should be administered at one time. Any delay in administration of the antitoxin may result in an increased dose requirement and decreased effectiveness. The usual dose of diphtheria antitoxin in adults and children is 250 I.U./kg for laryngeal or pharyngeal disease of 48 hours duration. In advanced diphtheria (nasopharyngeal lesions), the dose is 500 I.U./kg. In cases of pretoxic diphtheria the dose is 750 to 1000 I.U./kg. Toxic diphtheria requires a dose of 1000 to 2000 I.U./kg, and diphtheria croup requires 100 000 I.U. in a single dose. If administration of diphtheria antitoxin started three days after the duration of the disease, the dose should be doubled. In very severe cases, half of the first dose can be administered diluted with saline solution by slow intravenous infusion. In the therapeutic protocol for diphtheria antitoxin anti-infective therapy should be included (e.g. erythromycin, penicillin G).

side effects

In administering diphtheria antitoxin (equine), a foreign protein enters the body and this may cause hypersensitivity reactions. Reactions occur in individuals sensitized to horse proteins or proteins of other animals either by previous administration of the antiserum or in some other way. Reactions to a foreign protein may be manifested as an anaphylactic reaction and serum sickness.

An anaphylactic reaction to horse antiserum is immediate and includes urticaria, dyspnoea, and vascular collapse due to disorder in the blood system and sudden drop in blood pressure accompanied by paleness, cyanosis and an accelerated pulse.

Serum sickness (7-12 days after the first injection of antiserum, or 3-5 days after the second injection, which follows 4-5 months after the first), is evident in a small percentage of patients with more or less generalised erythema, urticaria, itching, occasionally fever, pain and oedema of the joints and lymph nodes.

The incidence of anaphylactic reaction and serum sickness depends on the quantity of the horse proteins administered for treatment. During manufacture of diphtheria antitoxin (equine), non-specific proteins, other than immunoglobulins, are removed by purification, so that in the preparation less than 50% of the total proteins present in the hyperimmune horse plasma remain. Purification increases the specific activity of the preparation considerably.

storage

Store at 2 °C to 8 °C. Once the vial is opened, the preparation must be used immediately.

shelf-life

The expiration date is indicated on the outer carton.

number and date of marketing authorisation number in the Republic of Croatia

Diphtheria antitoxin (equine) (box: 1 vial/ 10000 I.U.): UP/I-530-09/03-02/24 (19.11.2003)

Diphtheria antitoxin (equine) (box: 50 vials/ 10000 I.U.): UP/I-530-09/03-02/25 (19.11.2003)