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SCORPIFAV

ANTI-NORTH AFRICAN AND MIDDLE EASTERN SCORPION SPECIES VENOM (*ANDROCTONUS AUSTRALIS, BUTHUS OCCITANUS, LEIURUS QUINQUESTRIATUS*) EQUINE IMMUNOGLOBULIN $F(ab')_2$ FRAGMENTS

COMPOSITION

– The active ingredients consist of a sufficient quantity of equine immune globulin G_T (IgG_T) containing anti-venom immunoglobulin $F(ab')_2$ fragments in 1 ml to neutralize:

- *Androctonus australis hector* venom ..... ≥ 50 LD_{50} in mice
- *Leiurus quinquestriatus quinquestriatus* venom ..... ≥ 50 LD_{50} in mice
- *Buthus occitanus mardochei* venom ..... ≥ 50 LD_{50} in mice

– The other ingredients are sodium chloride, polysorbate 80, and water for injections.

Sodium hydroxide base and/or hydrochloric acid may be added during manufacture to adjust the pH. These substances are present as sodium and chloride ions, sodium salts and chlorides and are not identifiable as an acid or a base.

NAME AND ADDRESS OF MARKETING AUTHORIZATION HOLDER

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1. WHAT IS SCORPIFAV AND WHEN IS IT USED?

SCORPIFAV is a solution, to be diluted for intravenous infusion, available in the form of 1 ml ampoules.

SCORPIFAV is a clear, or slightly opalescent, colourless to slightly coloured solution.

SCORPIFAV is indicated for the treatment of envenomations caused by venomous scorpion species found in North Africa and the Middle East (i.e., *Androctonus australis, Leiurus quinquestriatus, Buthus occitanus*).

The use of SCORPIFAV is recommended in all subjects suffering from scorpion stings and envenomations, particularly for at-risk subjects such as:

– children, due to unfavourable venom to body weight ratio;
– pregnant women, since certain constituents of the venom can cross the placenta, resulting in foetal death;
– elderly subjects; and
– subjects suffering from a cardiomyopathy.

2. INFORMATION NEEDED BEFORE USING SCORPIFAV

Do not use SCORPIFAV:

If the patient has a history of sensitivity to heterologous proteins of equine origin or to any of the other ingredients contained in SCORPIFAV.

This is a relative contra-indication if the envenomation presents a mortal risk, provided that treatment for possible anaphylactic shock can be implemented immediately.

Take special precautions with SCORPIFAV:

Given the heterologous (non-human) nature of SCORPIFAV, the risk of anaphylaxis should always be assessed in relation to the severity of the envenomation. The risk of anaphylaxis should be considered to be rare given the high purity of SCORPIFAV.

In order to determine if they have been pre-sensitized to proteins of animal origin, subjects must be questioned in detail on their history of allergies, paying particular attention to previous injections of heterologous sera and possible reactions, to any reactions to other $F(ab')_2$ fragments of equine origin, and to animal contact allergies (particularly to horses) or food allergies.

The infusion should always be started under strict medical supervision at a slow rate of 50 ml/hour (i.e., 17 drops/minute). In the event of signs of intolerance, slow down or even stop the infusion, as required. A syringe containing adrenaline and suitable intensive care facilities should be immediately available.

Pregnancy and Lactation:

The fetus represents an at-risk population since the venom can cross the placenta. The administration of SCORPIFAV has not been the subject of specific studies on pregnant or lactating women.

Ability to drive and use machinery:

No data concerning the effects of SCORPIFAV administration on the ability to drive and use machinery is available.

Use of other medicinal products:

No known interaction.

3. HOW TO USE SCORPIFAV

Clinical grading of envenomation:

Four stages, in increasing order of severity, have been described in subjects stung by *Androctonus australis* scorpions. These clinical stages do not necessarily correspond to progression of the envenomation, which may be severe from the outset.

Stage 1: the local symptoms at the site of the sting are intense pain and burning, but without swelling or inflammation, confirming inoculation of venom and therefore envenomation.

Stage 2: the local symptoms are accompanied by moderate systemic signs (e.g., sweating, agitation, excessive salivation, nausea, and muscarinic syndrome characteristics), high blood pressure, and tachycardia that may be associated with fever.

Stage 3: the local symptoms are accompanied by severe systemic signs (e.g., vomiting and diarrhoea, bronchial obstruction and/or pulmonary oedema with cyanosis, and tendency towards cardiovascular collapse with significant ECG disturbances); consciousness is retained.

Stage 4: concerns 10 to 20% of aggravated cases of stage 3, indicate significant neurotoxicity. Progression is characterised by shock with cardiovascular collapse, pulmonary and respiratory failure, hyperthermia, and finally coma. This final stage is a manifestation of severe envenomation, with mortality on the order of 50%.

Treatment of scorpion envenomation is based on two separate but complementary therapeutic strategies. It consists of combining a specific action against the diffusion of the toxin and of fixation of the toxins with establishment of symptomatic treatment against their toxic effects.

Specific severity factors of envenomation:
The presence of a state of shock, of digestive disorders (vomiting and diarrhoea), respiratory failure and deterioration of consciousness, are signs of severe envenomation.

First aid treatment:
The purpose of first aid is to support the patient effectively and to facilitate subsequent hospital treatment.
It is recommended to restrict first aid to the following acts:
- making the victim rest and providing reassurance;
- immobilizing the stung limb;
- cleaning of the wound (alcohol, antiseptics or soap);
- compressing moderately the stung limb with a gauze bandage to limit the lymphatic diffusion of the venom, while monitoring the peripheral pulse. Tourniquets are strictly forbidden. The bandage should only be removed in a medical environment;
- administering mild analgesic and sedative treatment; and
- evacuating to a health centre/specialised hospital (emergency) department.

It is strongly recommended not to perform first aid acts such as cauterization, debridement, sucking of the wound, or application of tourniquets.

Hospital treatment:
In all cases of envenomation, the subject must be brought to a health centre/specialised hospital (emergency) department as soon as possible.
The victim must be immobilized, reassured, and analgesics given to provide relief. Local disinfection must be performed or completed. In the event of superinfection, a general antibiotic treatment covering anaerobic organisms must be planned. Vaccination and passive immunoprophylaxis against tetanus must be performed systematically as indicated.

POSOLOGY AND ADMINISTRATION METHOD

SCORPIFAV must be administered as soon as possible after envenomation; the earlier the stage at which administration is performed, the more effective the treatment will be.
The recommended dose is 10 ml (10 × 1 ml ampoules) diluted in 50 ml of 0.9% sodium chloride solution.
However, the standard 1/5 dilution (10 ml in 50 ml) may be adapted (1/4 to 1/10 dilution) according to the overall volume that the patient can receive and tolerate.
In children, the same dose is used as for adults, irrespective of age or weight.
Take up the product in a sterile syringe fitted with a sterile needle and inject into the appropriate volume of 0.9% sodium chloride solution.
The product should be administered to the patient by slow intravenous infusion, started at a slow rate (17 drops/minute or 50 ml/hour) under medical supervision in a medical structure equipped to be able to control any immediate hypersensitivity reaction. The infusion rate should be increased progressively to 250 ml/h.
In the event of signs of intolerance, slow down the infusion rate or stop the infusion if required. A syringe containing adrenaline, and suitable intensive care facilities, should be immediately available.
The initial dose may be readministered every 4 hours during the 12 hours following the first administration, while signs of envenomation persist.

4. WHAT ARE THE POSSIBLE UNDESIRABLE EFFECTS?

Like all medicinal products, SCORPIFAV is liable to have undesirable effects: the undesirable reactions that may occur after the use of equine immunoglobulin $F(ab')_2$ fragments (e.g., anti-rabies, anti-tetanus, anti-venom) are primarily immediate or delayed-type allergic reactions.
- Immediate reactions: the reactions liable to be observed are anaphylactoid (allergic type) reactions with hypotension, dyspnoea, and urticaria. More serious reactions such as Quincke's oedema or anaphylactic shock may occur. Nevertheless, true anaphylactic shock remains exceptional.
- Delayed reactions: Serum sickness-like reactions reported after the administration of proteins of animal origin may occur about six days after the beginning of treatment. They consist of an inflammatory reaction due to complement activation and of the formation of immune complexes (type III hypersensitivity reaction). Clinical symptoms are fever, pruritus, rash or urticaria, adenopathy, and arthralgia.

Undesirable effects must be treated as follows:
- In the event of signs of intolerance, slow down the infusion rate or stop the infusion if required.
- In the event of an anaphylactic reaction during the administration of SCORPIFAV, the infusion must be stopped immediately.
- If the effect worsens despite the discontinuation of the infusion, treatment must be established. The treatment of anaphylactic shock essentially consists of:
  - injection of intravenous fluids to maintain blood pressure;
  - administration of oxygen by face mask and, if necessary, intubation and placing under artificial respiration; and
  - administration 0.5 ml of a 1/1000 adrenaline solution by the subcutaneous route until a satisfactory haemodynamic condition is obtained; and
  - antihistamines can be administered as a complementary treatment, associated with corticosteroids if necessary.

Serum sickness is treated by administering corticosteroids (e.g., 1 mg/kg of methylprednisolone followed by decreasing doses) and antihistamines.

5. HOW TO STORE SCORPIFAV

Store SCORPIFAV at a temperature between + 2°C and + 8°C (in a refrigerator).
Do not freeze.
Keep out of the reach and sight of children.
Do not use after the expiry date marked on the box.

The last date on which this package insert was approved is: 11/2000