INSTRUCTIONS FOR USE

Alacramyn®

Antivenin Centruroides (scorpion) Polyvalent (Fab therapy)

Solution for injection

THERAPEUTIC INDICATIONS:

For the treatment of scorpion sting evenomation.

CONSIDERATIONS REGARDING THE VENOM OF *Centruroides spp:*

There are over 1,500 species of scorpion described worldwide, 9 of which are medically important. In Mexico all scorpions of medical significance belong to the genus *Centruroides*. Over 200 biologically active peptides have been isolated from the venom of various scorpion species worldwide. The majority of these peptides, which explain the toxic effect exerted by the scorpion venom, are ion channel modulators of the cell membrane (sodium, potassium, calcium and chlorine) of insects, molluscs and vertebrates. Scorpion venom that can cause systemic evenomation in humans contains a toxin that affects the sodium channels of the peripheral (somatic) and autonomic nerves, so that spontaneous action potentials occur.

From the clinical point of view, the potential degree of evenomation varies from minimal, with pain and paraesthesias at the sting site, to severe evenomation characterised by life-threatening respiratory failure. This last symptom is more common in children under 5 years of age, although adults can also be affected. Respiratory failure is multifactorial and includes respiratory muscle incoordination, hypersalivation, difficulty in swallowing and noncardiogenic pulmonary oedema.

Generalised activation of the peripheral nerves brings about a very characteristic set of symptoms. Activation of the peripheral nervous system causes pain and paraesthesias at the sting site, nasal pruritus, the sensation of a foreign body in the pharynx, hypersalivation, inability to swallow, abnormal eye movements, involuntary movements of the limbs, motor incoordination, fasciculations, abdominal distention and scotoma. Activation of the autonomous nervous system causes diaphoresis, hypertension, priapism, noncardiogenic pulmonary oedema and cardiac arrhythmia.

GENERAL PRECAUTIONS AND RECOMMENDATIONS:

- In areas where scorpions are prevalent, **Alacramyn®** should be administered in case of suspected envenomation based on the clinical symptoms, even when no scorpion has been observed.

- The ideal route of administration is intravenous. The intramuscular administration of **Alacramyn®** diminishes its efficacy.

- The dose tends to be higher in children than in adults: venom concentration is more elevated in paediatric patients as they are smaller and weigh less than adults.

- Scorpion sting envenomation is an emergency, and the patient should therefore be assessed by a doctor.

- No fluid or food should be administered orally to the envenomated patient.

- **Alacramyn®** is the specific treatment. The doctor should assess the need to use support therapy, including among others oxygen, intravenous hydration and analgesics.

- As a maximum dosage has not been established, the doses required to neutralise the venom should be used.

METHOD OF ADMINISTRATION:

- The ideal route of administration is intravenous. The intramuscular administration of Alacramyn® diminishes its efficacy.

  - **<u>Reconstitution of Alacramyn® for use</u>**

    Prepare the **Alacramyn®** vials required by the patient as follows:

    1. Remove the flip-off cap from the vial of **Alacramyn®.**

    2. With a piece of cotton wool moistened with alcohol, clean the exposed rubber diaphragm.

    3. Open the ampoule with the diluent and using a syringe and sterile needle (a 10 mL syringe is recommended), withdraw the fluid contained and inject it into the vial through the rubber diaphragm.

    4. Withdraw the syringe from the vial.

    5. Shake gently, continuously swirling, until the tablet is dissolved completely. Avoid vigorous or prolonged shaking. Because of the protein content of the antivenin, foaming may occur during the reconstitution process. The solution should be translucent or slightly opalescent.

    6. Reintroduce the syringe and needle into the rubber diaphragm of the vial and withdraw all the solution contained in the vial.

    7. Once the solution is extracted from the vial, remove the syringe and needle from the vial.

8. Repeat the above steps to open and prepare the vials of Alacramyn® that are required.

9. Assess the Alacramyn® reconstituted to 50 mL of physiological saline solution and administer it in approximately 30 minutes.

10. Repeat the procedure for administration of the maintenance doses.

DOSAGE:

Based on the degree of envenomation, the following dosage scheme is suggested:

ENVENOMATION CATEGORY	SIGNS AND SYMPTOMS	AGE GROUP	DOSE OF Alacramyn®
MINIMAL OR GRADE 1	Local pain, local and remote paraesthesias, nasal and pharyngeal pruritus.	Any age	1 Vial IV
MODERATE OR GRADE 2	Signs and symptoms of category 1 plus: sensation of foreign body or obstruction in oropharynx, hypersalivation, diaphoresis, nystagmus, lingual fasciculations, dyspnoea, abdominal distention, priapism and muscle spasms.	Less than 15 years of age Older than 15 years of age	2 Vials IV 1 Vial IV
SEVERE OR GRADE 3	Signs and symptoms of category 2 plus: tachycardia, hypertension, visual disturbances, transient blindness, vomiting, nystagmus, retrosternal pain, acute pulmonary oedema and respiratory failure.	Less than 15 years of age Older than 15 years of age	3 Vials IV 2 Vials IV

CONTRAINDICATIONS

Known cases of allergy to proteins of heterologous origin (horse).

SIDE EFFECTS AND ADVERSE REACTIONS.

IgE-mediated type I hypersensitivity reactions can occur, characterised by rash, urticaria, pruritus and bronchospasm, among others. Non-immunoglobulin-mediated anaphylactoid reactions can also occur.

Type III hypersensitivity reactions may also present. These are immune-complex-mediated reactions and are characterised by urticaria and arthralgia 5 to 15 days after administration of the product.

USE DURING PREGNANCY AND LACTATION.

No preclinical safety studies have been conducted during pregnancy or lactation. The use of Alacramyn® during pregnancy will depend on the degree of envenomation and should be assessed in relation to the risk/benefit and individual condition.

Use of the product in these conditions is subject to medical indication and criterion.

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