

## ANTIBOTHROPS-CROTALUS SERUM

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### DESCRIPTION

ANTIBOTHROPS-CROTALUS SERUM is supplied in 10 ml ampoules containing an injectable solution of F(ab')<sub>2</sub> fraction of specific and purified immunoglobulins obtained from the plasma of horses hyperimmunized with the mixture of snake venoms of genus *Bothrops* and *Crotalus*.

### PEDIATRIC AND ADULT USE

### COMPOSITION

Each 10 ml ampoule contains:

- F(ab')<sub>2</sub> fraction of immunoglobulins able to neutralize at least 50 mg of reference venom of *Bothrops jararaca* and 15 mg of reference venom of *Crotalus durissus terrificus* (serum neutralization in mice).
- Phenol..... 35 mg (maximum)
- 0.85% Physiological Solution qsf.....10 mL

### INFORMATION FOR PATIENTS

THE ANTIBOTHROPS-CROTALUS SERUM SHOULD BE KEPT OUT OF THE REACH OF CHILDREN.

Store the ANTIBOTHROPS-CROTALUS SERUM in a refrigerator at 2 - 8°C. **Do not freeze.**

The ampoule contents should be clear and transparent. Do not use in case of turbidity or presence of precipitates.

THE EXPIRATION DATE AND LOT NUMBER are indicated on the packaging and ampoule. Once the ampoule is opened, the serum should be used immediately. Do not use after the expiration date.

The serum takes effect immediately after administration, neutralizing the toxin of snake venom of *Bothrops* and *Crotalus* in blood. It is possible the neutralization of venom in tissue, later. There is no contraindication to the use of ANTIBOTHROPS-CROTALUS SERUM during pregnancy, but the physician should be informed about the patient's pregnant state.

The ANTIBOTHROPS-CROTALUS SERUM should be administered under medical supervision, preferably intravenously in the recommended doses (See DOSAGE AND ADMINISTRATION).

The administration of hyperimmune sera may trigger allergic reactions of various degrees. The most commonly noted were: cutaneous pruritus/rubor; urticaria; dry cough/hoarseness; nausea/vomits; asthmatic crisis. Severe reactions are uncommon and fatal anaphylactic shock was reported in 1:50,000 patients that used the equine serum.

Once prescribed, the ANTIBOTHROPS-CROTALUS SERUM should be administered as soon as possible. There is no contraindication to the administration of the serum after the ingestion of food and/or drinks, but the patient should be under closer supervision due to risk of complications related to vomits (aspiration).

There are practically no contraindications. The serum should preferably be used in hospitals since it may trigger allergic reactions, some potentially serious.

## RECOMMENDATIONS

- **DO NOT** USE GARROTES OR TORNIQUETS
- **DO NOT** MAKE INCISIONS AT THE BITE SITE
- **DO NOT** USE AMMONIA, CAUSTICS, IRRITATING OR CONTAMINATED SUBSTANCES ON THE BITE SITE
- **DO NOT** INGEST TOXIC LIQUIDS OR ALCOHOLIC BEVERAGES
- KEEP THE PATIENT AT REST, AVOID WALKS
- KEEP THE PATIENT WELL HIDRATED

## TECHNICAL INFORMATION

### INDICATION

ANTIBOTHROPS-CROTALUS SERUM is the most effective medicine for treating poisoning caused by the bite of snakes of the genus *Bothrops* ("jararaca", "jararacuçu", "urutu", "cotiara", "caçaca", among others) and *rattlesnakes* (*Crotalus*). Not indicated for treating poisoning caused by coral snakes (*Micrurus*) and *Lachesis* snakes. The sooner the serum is administered, the better the serum therapeutic potential. Hence the need of starting the treatment as soon as possible.

### CHARACTERISTICS OF BOTHROPS POISONING

Approximately 90% of all cases of snake-bite poisoning in Brazil are caused by snakes of the genus *Bothrops*.

The clinical manifestatios are evident and characterized by:

#### Local manifestations:

- Firm, cold and painful edema of a progressive nature in the first hours, together with lymph node enlargement. The occurrence of ecchymosis at the bite site is frequent;
- Blisters and signs of infection/ abscess may occur in the following days;
- The clinical picture may develop into late necrosis.

#### Systemic manifestations:

- spontaneous bleeding (gums, skin, urine, recent injuries);
- in severe cases, shock and renal insufficiency;
- in lachesis poisoning, the following were also observed: nausea, vomiting, diarrhea, dizziness, perspiration, bradycardia and hypotension.

The Coagulation Time (CT) can be used to identify alterations in coagulation.

The snake should be identified.

### CHARACTERISTICS OF CROTALUS POISONING

Approximately 8% of snake poisoning cases in Brazil are caused by snakes of genus *Crotalus*.

**Clinical symptoms**, if they appear, are mild and include mild edema and paresthesia.

**Poisoning systemic symptoms** are:

- Dropping of eyelids (ptosis) and facial muscle paralysis (neurotoxic or myasthenic facies);
- Ocular problems such as visual disturbance, double vision (diplopia), alteration of pupil diameter (mydriasis or miosis), photophobia and ocular movement disorders (ophthalmoplegia);
- Paralysis of respiratory muscles that may evolve into respiratory insufficiency;

- Diffuse muscle pain (myalgia);
- Dark urine (myoglobinuria). It may lead to acute renal insufficiency (ARI) which, in most cases, occurs within the first 48 hours;
- Inability to clot blood due to hypofibrinogenemia may occur in approximately 40% of the patients. Spontaneous bleeding, particularly from the gums, occurs sporadically.

It is important to identify the snake. Thus, whenever possible, the snake should be captured in a careful and safe manner so that it can be properly identified and the appropriate serum can be administered.

### **CONTRAINDICATIONS**

There are practically no contraindications. In patients with a history of allergy or sensitivity to serum of equine origin, the administration of the ANTIBOTHROPS-CROTALUS SERUM, especially via intravenous route, should be conducted under close medical supervision.

### **DRUG INTERACTIONS**

Concomitant medication is not contraindicated during ANTIBOTHROPS-CROTALUS SERUM therapies, but the patient's physician should be informed of all medications the patient is taking.

### **ADVERSE REACTIONS TO ANTIBOTHROPS-CROTALUS SERUM THERAPY**

Since it is a heterologous serum, the following reactions may occur:

#### **a) Early reactions**

The frequency varies and the reactions occur within the first 24 hours after the serum administration. These reactions, of anaphylaxis and anaphylactoid nature, may be serious and do require medical care.

Patients previously treated with serum of equine origin may present a higher incidence of reaction.

#### **Prevention of reactions:**

1. Ask information about the patient's history related to the previous use of heterologous serum (anti-tetanus, anti-rabies, anti-venom) and allergic events. Should that be the case, consider the potential for adverse reactions and the administration of antihistamines (H<sub>1</sub> and H<sub>2</sub> antagonists) and corticosteroids 15 minutes before administering the recommended dose of serum.
1. The sensitivity test has not been conducted in heterologous serum treatments because it has shown ineffective to evaluate the patient's sensitivity, apart from the fact it may trigger reactions. The time spent on the test delays the serum therapy.

#### **Treatment of early reactions**

Once the reaction is established, discontinue the serum therapy and start treatment for these reactions. In the event of generalized urticaria, asthmiform crisis, glottic edema and shock, immediately administer aqueous adrenaline 1:1000, via subcutaneous or intramuscular route, in a dose of 0.3 to 0.5 mL for adults and 0.01 ml/kg for children, which can be repeated every 5-10 minutes, as necessary. In the event of asthmiform crisis, it is also recommended the parenteral administration of

inhalation bronchodilators or aminophyllines. The corticosteroids and antihistamines play a secondary role in the control of the reactions, and can also be used. Resume serum therapy after hypersensitivity remission.

**b) Late reactions**

In general, they are benign and occur between 5 and 24 days after the administration of the serum. They are characterized by fever, urticaria, arthralgia, adenomegaly and, more rarely, neurological or renal compromise. This reaction is also known as "Serum sickness" and treated with corticosteroids, analgesics and antihistamines.

**DOSAGE**

The ANTIBOTHROPS-CROTALUS SERUM should be administered as soon as possible according to recommended doses.

**DOSES AND ROUTE OF ADMINISTRATION**

**BOTHROPS POISONING: CLASSIFICATION ACCORDING TO SEVERITY AND RECOMMENDED SERUM THERAPY**

SYMPTOMS AND TREATMENT	CLASSIFICATION		
	MILD	MODERATE	SEVERE
Local:			
<ul style="list-style-type: none"> <li>• pain</li> <li>• edema</li> <li>• ecchymosis</li> </ul>	Absent or Mild	Evident	Intense**
Systemic: <ul style="list-style-type: none"> <li>• severe hemorrhage</li> <li>• shock</li> <li>• anuria</li> </ul>	Absent	Absent	Present
Coagulation Time (CT)*	Normal or Altered	Normal or Altered	Normal or Altered
Serum Therapy (n° of ampoules)	2 to 4	4 to 8	12
Route of administration	Intravenous		

\* normal CT up to 10 min.; prolonged CT from 10 to 30 min.; CT "unable to clot" above 30 min.

\*\* Intense local manifestations may be the only criterion to classify severity

**CROTALUS POISONING: CLASSIFICATION ACCORDING TO GRAVITY AND APPROPRIATE SERUM THERAPY**

SYMPTOMS TREATMENT	CLASSIFICATION (INITIAL EVALUATION)		
	MILD	MODERATE	SEVERE

Myasthenic facies/ Visual disturbance	Absent or Late	Mild or Evident	Evident
Myalgia	Absent or mild	Mild	Severe
Redish or brown- coloured urine	Absent	Little evident Or absent	Present
Oliguria / Anuria	Absent	Absent	Present Or Absent
Coagulation Time (CT)*	Normal or Altered	Normal or Altered	Normal or Altered
Serum Therapy (n <sup>o</sup> of ampoules)	5	10	20
Route of administration	Intravenous		

\* CT normal up to 10 min.; CT prolonged from 10 to 30 min.; CT unable to clot above 30 min.

It is recommended to administer the serum intravenously, and the serum, diluted or not, should be infused for 20 to 60 minutes under strict medical and nursing supervision. When this route of administration is not possible, the serum should be administered subcutaneously. The need for additional doses should be considered based on the development of the clinical picture and Coagulation Time (CT). If CT remains "unable to clot" the 24 hours after serum therapy, an additional dose is recommended.

### **SPECIAL RECOMMENDATIONS**

Acute renal insufficiency (ARI) is the most serious complication in *Bothrops* and *Crotalus* poisoning. Special attention should be given to the patient's hydration status and renal function as soon as possible. A simple way to monitor renal function is through the urine eliminated. If renal function is compromised, the patient should be re-evaluated. In such case, a dialytic treatment may be indicated.

In *Bothrops* poisoning the local lesion may evolve into secondary infection, cases in which antimicrobial agents are recommended. Tetanus prophylaxis is recommended.

### **STORAGE**

Store at 2 °C to 8 °C. **DO NOT FREEZE.**

### **EXPIRATION DATE**

The expiration date of the ANTIBOTHROPS-CROTALUS SERUM is three years from the manufacturing date when stored at 2 to 8°C as indicated on the packaging.

**Registration Number: 1.2234.0003**

**PHARMACIST-IN-CHARGE**

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