

# Antivenom<sup>®</sup>

Snake Venom Antiserum BP

## Presentation

Antivenom<sup>®</sup>: Each vial contains lyophilized preparation of Snake Venom Antiserum BP. After reconstitution each ml Snake Venom Antiserum neutralizes not less than Cobra venom (*Naja naja*) 0.60 mg, Common Krait venom (*Bungarus caeruleus*) 0.45 mg, Russell's Viper venom (*Vipera russelli*) 0.60 mg, Saw-scaled Viper venom (*Echis carinatus*) 0.45 mg.

## Description

Snake Venom Antiserum lyophilized is a refined and concentrated preparation of serum globulins for intravenous administration, containing equine immunoglobulin fragments F(ab')<sub>2</sub>, obtained from the plasma of healthy equines, hyperimmunized against venoms of above species of snakes. In addition, it also contains the anti-microbial agent: cresol.

## Indications and uses

Antivenom is indicated for bites caused by Cobra, Common Krait, Russell's Viper and Saw-Scaled Viper, where the patient presents with one or more of following visible clinical signs and symptoms of envenomation –

1. Local envenomation-
  - a) Presence of bite marks with or without oozing of blood, blistering and change in color of skin.
  - b) Rapidly progressive or massive swelling involving more than half of the bitten limb within few hours of bite (without tourniquet)
  - c) Development of enlarged tender lymph nodes draining the bitten part within couple of hours after bite
2. Systemic envenomation-
  - a) Neurotoxic syndrome- signs of neuro-paralysis like blurring of vision, double vision, and difficulty in swallowing, sleepy feeling, drooping of head, slurring of speech and the voice may become indistinct with shallow breathing, ptosis, ataxia, respiratory paralysis and generalized flaccid paralysis.
  - b) Hemotoxic syndrome- spontaneous systemic bleeding, nausea, vomiting, abdominal pain and abdominal tenderness suggestive of gastro-intestinal or retro-peritoneal bleed and/or renal damage, coagulopathy detected by 20 min WBCT with or without external bleeding and shock.

Neurotoxic syndrome		Haemotoxic syndrome
Cobra bite	Common Krait bite	Russell's Viper bite or Saw Scaled Viper bite
Local envenoming present	Local envenoming absent	Local envenoming present
Local necrosis and blistering	Minimal or no swelling	Local pain, swelling and erythema at the bite site.
Rapidly progressive descending paralysis	Often presents early morning with paralysis	Tender & enlarged lymph nodes draining the bitten part
Ptosis, diplopia or ophthalmoplegia	H/O sleeping on floor bed	Local necrosis and/or blistering
Paralysis of jaw and tongue	Abdominal pain	Nausea, vomiting, abdominal pain and abdominal tenderness
Bulbar paralysis and respiratory failure	Neuro-paralysis	Low back ache or loin pain which suggest of the likelihood of developing renal failure
Hypoxia, altered sensorium and coma	Ptosis .Bulbar paralysis & respiratory failure	Passage of reddish or dark brown colored urine or a reduction in the amount of urine output
Intercostal muscle paralysis	-	Haemoptysis, epistaxis, hematuria, hematemesis and melena, chemosis, macular bleed, bleeding from the bite site or cannula, bleeding into the muscles, gingival bleed, bleeding into the skin and mucous membranes showing as purpura or petechia
Respiratory paralysis	-	An abnormal WBCT and PT / APTT above 1.5 times normal, DIC and shock
-	-	Neurological manifestations have been reported in Russell's Viper bites

(It has been reported that Snake Venom Antiserum also provides para-specific neutralization of venoms of related snake species, however, the extent of protection is uncertain).

## Immediate actions and first aid

Quick and positive measures should be taken to meet the emergency. Do not try to catch or kill the snake without proper tools and avoid unnecessary exposure to snack. Patient should be removed to a well-ventilated and quiet place and restrict his/her movement. Patient should be reassured to overcome fear. Immobilize the bitten part by applying immobilization bandage as done for a fracture and bitten part is kept below heart level. Ligation by applying tourniquets should be avoided, however, if applied it should be tied at moderate distance above the bitten part to prevent the entry of venom into the circulation. Patient should be immediately taken to nearby medical centre for treatment without loss of time.

## Direction for reconstitution

To reconstitute the Snake Venom Antiserum, transfer content of supplied diluents into the vial containing lyophilized preparation. Mix the contents gently by swirling action and avoid vigorous shaking. Serum should be used as soon as possible after reconstitution.

## Dosage and administration

As of now Antivenom is the only specific antidote for snake envenomation and prompt administration of adequate dose of Antiserum is of paramount importance for neutralization of unbound circulating snake venom components for early response to treatment. Any delay in administration may result in increased dose requirement and decreased effectiveness. As the clinical signs can vary due to many factors such as type of snake, time of reporting after bite, size of snake, amount of venom injected during bite, seasonal & regional variation in venom composition etc., no accurate dosage can be recommended. However, considering the average quantity of venom injected by snake at the time of bite and degree of envenomation, it is recommended to administer initial dose of 5-10 vials of Antivenom by slow intravenous infusion either undiluted at a speed of not more than 2 ml per minute or after dilution with Normal /glucose saline at a rate of 5-10 ml/kg body weight over one hour. Children should receive the same dose as adults. Constant monitoring of the vital signs at frequent intervals during initial 1 hour is recommended. Requirement of further dosing depends on extent of

reversal of coagulopathy confirmed after 6 hours of Antiserum administration by WBCT in haemotoxic bite or if symptoms persist or worsen or in respiratory failure in neurotoxic bite after 1 hour of Antiserum administration. If the blood is still in coagulable or no signs of reversal of paralysis are seen, a further dose of 5 to 10 vials of Antiserum should be administered by slow IV route only. Administration by IM or locally around the bite wound is not recommended. In the majority of cases of both neurotoxic and haemotoxic bites, total dose of 15-20 vials is adequate unless a proven recurrence of envenomation is established. In such a scenario, further doses can be given as per clinical condition of the patient. Hypersensitivity skin test has no predictability value and hence should not be used.

## Supportive treatment

Hydration, ventilation (Maintenance of airway is essential in neurotoxic bites due to impending respiratory paralysis), dialysis (Renal failure is a common complication in haemotoxic bites and might require dialysis), neostigmine, pain management (Most of the bite sites are painful requiring administration of pain killers) and surgical intervention if required. In addition above, administration of antibiotics and Tetanus toxoid may be necessary as per the clinical condition of the patient.

## Pregnancy and lactation

Considering the risk associated with snake bite envenomation, pregnancy is not a contraindication for the administration of Snake Venom Antiserum subsequent to bite.

## Drug interactions

There are no known drug interactions reported.

## Adverse reactions

Antivenom being derived from equines is heterologous to human can give either early or late reaction. Adrenaline should be always kept handy, before starting the dose of Antivenom.

Antivenom reactions			
Type	Early (Within few hours)		Late (Five days or more)
	Anaphylactic	Pyrogenic	Serum Sickness
Timeline	Develops within 10 -180 minutes of starting anti-venom	Develops within 1-2 hours of starting anti-venom	Appear after about 1 to 12 (Av.7) days after injection of anti-venom
Symptoms	Urticaria, itching, dry cough, fever, nausea, vomiting, abdominal colic, diarrhoea, tachycardia	Chills, fever, vasodilatation and all of blood pressure	Fever, nausea, vomiting, diarrhoea, itching, urticarial rash, pain in joints and muscles, recurrent urticaria, enlargement of lymph glands, proteinuria and rarely encephalitis
Recommended treatment	1. Stop administration of Antivenom temporarily 2. Give Inj. Adrenaline 0.5 mg of 1:1000 for adults and 0.01 mg/kg for children by IM route 3. Repeat the dose if required every 5-10 minutes 4. In addition, administration of 10-25 mg of Chlorpheniramine maleate for adults or 0.2 mg/kg for children may be given by IV route followed by Hydrocortisone 100 mg for adults or 2 mg/kg for children by IV route 5. In pyrogenic reaction, may be physically cooled and with antipyretics (Paracetamol) 6. Hypovolaemia may be corrected by IV fluids		Serum sickness should be treated with 5 days course of antihistamines. Patients who fail to respond in 24 to 48 hours should be given 5 days course of Prednisolone <i>Chlorpheniramine dose:</i> Adults - 2 mg six hourly, children - 0.25 mg/kg/day in divided doses <i>Prednisolone dose:</i> Adults - 5 mg six hourly, children - 0.7 mg/kg/day in divided doses

Reduction in adverse reactions has been reported by use of adequate dilution of Antivenom with saline and controlling rate of infusion.

## Contraindications and precautions

There are no known contraindications for the administration of Antivenom. Proper precautions are necessary while dealing with persons with a known hypersensitivity to constituents of product. Few doctors prefer to premedicate patients with Inj. Adrenaline 0.25 ml s/c to prevent possibility of adverse reactions. In haemotoxic bites, IM injections should be avoided till correction of coagulopathy to avoid formation of haematoma and oozing of blood. In patients having tourniquet, it should be released slowly only after start of Antivenom administration.

## Storage

Lyophilized Antivenom is stable at room temperature and does not require special storage facilities. Ideally, it should be stored in a cool & dark place and do not expose to excessive heat.

## Commercial pack

Antivenom<sup>®</sup>: Each box contains 1 vial of Snake Venom Antiserum BP, 1 ampoule containing 10 ml WFI and one sterile disposable syringe.

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 Dhaka, Bangladesh  
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