Summary of Product Characteristics

1. Name of the medicinal product

Antivenom

Snake Venom Antiserum BP

Lyophilized0 powder and solvent for suspension for intravenous use, 10 ml

2. Qualitative and quantitative composition

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.

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Snake Venom Antiserum lyophilized is a refined and concentrated preparation of serum globulins for intravenous administration, containing equine immunoglobulin fragments F(ab')2, 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. It is Freeze-dried white or slightly yellow powders or solid friable masses. After reconstitution, clear colourless to pale yellow liquid.

4. Clinical particulars

4.1 Therapeutic indications

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

a) Local envenomation-

- Presence of bite marks with or without oozing of blood, blistering and change in color of skin.
- Rapidly progressive or massive swelling involving more than half of the bitten limb within few hours of bite (without tourniquet)
- Development of enlarged tender lymph nodes draining the bitten part within couple of hours after bite

b) Systemic envenomation-

- Neurotoxic syndrome– Signs of neuro-paralysis like blurring of vision, double vision, and difficulty in swallowing, sleepy felling, dropping of head, slurring of speech and the voice may become indistinct with shallow breathing, ptosis, ataxia, respiratory paralysis and generalized flaccid paralysis.
- 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 opthalmoplegia	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 sensoriumand 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 extant of protection is uncertain).

4.2 Posology and method of administration

4.2.1 Posology

Route of administration: Antivenom should be injected intravenously.

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:

Would include 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.

4.3 Contraindications

There are no known contraindications for the administration of Snake Venom Antiserum.

4.4 Special warnings and precautions for use

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 Snake Venom Antiserum administration.

4.5 Interaction with other medical products and forms of interaction

There are no known drug interactions reported.

4.6 Fertility, pregnancy and lactation

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

4.7 Effects on ability to drive and use machines

Nor relevant.

See section 4.8 “Undesirable effects” regarding the ability to drive or use machines

4.8 Undesirable effects

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

<table>
<tr><th colspan="4">Antivenom reactions</th></tr>
<tr><td>Type</td><td colspan="2">Early (Within few hours)</td><td>Late (Five days or more)</td></tr>
<tr><td></td><td>Anaphylactic</td><td>Pyrogenic</td><td>Serum Sickness</td></tr>
<tr><td>Timeline</td><td>Develops within
10 -180 minutes of
starting anti-venom</td><td>Develops within
1-2 hours of starting
anti-venom</td><td>Appear after about 1-12(Av.7) days after injection of anti-venom</td></tr>
<tr><td>Symptoms</td><td>Urticaria, itching, dry cough, fever, nausea, vomiting, abdominal colic, diarrhoea, tachycardia</td><td>Chills, fever, vasodilatation and all of blood pressure</td><td>Fever, nausea, vomiting, diarrhoea, itching, urticarial rash, pain in joints and muscles, recurrent urticaria, enlargement of lymph glands, proteinuria and rarely encephalitis</td></tr>
<tr><td>Recommended treatment</td><td colspan="2">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.</td><td>Serum sickness should be treated with 5 day course of antihistamines. Patients who fail to respond in 2448 hours should be given 5 day course of Prednisolone.
Chlorpheniramine dose: Adults - 2 mg six hourly, children - 0.25 mg/kg/day in divided doses.
Prednisolone dose: Adults-5 mg six hourly, children - 0.7 mg/kg/day in divided doses.</td></tr>
</table>

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

4.9 Overdose

Not applicable

5. Pharmacological properties

5.1 Pharmacodynamic properties

Immunoglobulin, Snake Venom Antiserum

Mechanism of action

Intravenously administered antivenom binds with snake toxins in the circulation and neutralizes the toxins. Binding of antivenom to venom in the central compartment prevents the distribution of venom to the peripheral tissues and enhances the elimination of venom.

5.2 Pharmacokinetic properties

Not applicable to vaccine products.

6. Pharmaceutical particulars

6.1 List of excipients

Cresol
Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years from the date of manufacturer when stored at 2 – 8 °C.

6.4 Special precautions for 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.

6.5 Nature and contents of container

Each box contains 1 vial of Snake Venom Antiserum BP, 1 ampoule containing 10 ml WFI and one sterile disposable syringe.

6.6 Special precautions for disposal and other handling

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 Snake Venom Antiserum administration.

7. Marketing authorization holder

Incepta Pharmaceuticals Limited
Vaccine Division
Savar, Dhaka,
Bangladesh

8. Drug authorization number(s)

363-16-069

9. Date of first authorization/Renewal of the authorization

12-Oct-2014

10. Date of revision of the text

11-Oct-2024