For the use of Registered Medical Practitioner or a Hospital or a Laboratory

SNAKE VENOM ANTITOXIN

(BIOSNAKE)

(Lyophilised, Polyvalent, Enzyme refined, Equine Immunoglobulin Fragments)

Description:
Snake venom antitoxin polyvalent is prepared from purified plasma of healthy horses, which have been hyperimmunized against venoms of the most dangerous snakes mentioned below. The antitoxin is purified from whole equine immune serum by pepsin digestion, controlled heating and caprylic acid precipitation and ultra-filtration followed by sterile filtration. It is intended for either intramuscular injection or intravenous infusion according to the severity of the condition.

Composition:
Each mL upon reconstitution with Sterilised Water for Injection neutralises snake venoms of the following :

Naja haje	75 LD_{50}
Naja nigricollis	25 LD_{50}
Cerastes cerastes	75 LD_{50}

Paraspecificity
Walterinnesia aegyptia
Bitis gabonica (East, Central and Southern Africa)
Echis carinatus
Macrovipera xanthina
Macrovipera lebetina
Vipera ammodytes
Cerastes vipera
Naja naje oxiana
Naja mossambica
Naja melanoleuca
Bitis arietans
Vipera palestinae

Preservative: Cresol BP ≤0.25% v/v
Stabiliser: Glycine BP

Clinical Pharmacology:
Symptoms and signs of snakebite depends on species, size and age of the biting snake, location and number of bites, depth of fang penetration, period of snake fangs on and volume of venom injected. They also depend on age, size and general health of the victim. Some snake species are neurotoxic, others are haemotoxic therefore, the clinical picture shows a wide range of symptoms and signs.

Grades of severity:

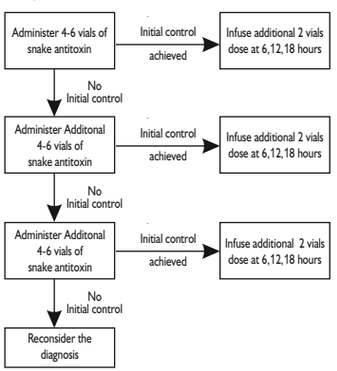
Grade 0 (no)	No local or systemic manifestations.
Grade I (Minimal)	Local swelling - no systemic manifestations normal laboratory results.
Grade II (Moderate)	Local swelling - one or more systemic manifestations abnormal laboratory results.
Grade III (Severe)	Marked local and systemic manifestations with significant changes in laboratory results.

N.B: Envenomation is a highly dynamic process which means that grade I state can very rapidly progress to grade III state.
The blood peak level is delayed up to 8 hours after intramuscular injection therefore; the intravenous route is preferred especially for moderate and severe envenomation and it is mandatory in venom induced shock. If adequate dose is given, cardiovascular effects respond within 10-20 minutes, spontaneous systemic bleeding stops within 15-30 minutes, blood coagulability is restored within about 6 hours and neurotoxic signs respond slowly after several hours. Snake bite victims must be given quick and positive first aid.

Indication:
Treatment of envenomation caused by snake bites of any of the mentioned species in composition.

Dosage and Administration:
A skin test should be performed prior to administration of this product (see under skin test).
The antivenom should be injected as soon as possible after the bite. It is given either intramuscularly or by intravenous drip according to severity of the condition. However, the subcutaneous route may be used in case of absence of anti-shock measures or an expert physician. The dose is neither age nor weight dependent however, it depends on severity of the condition with no recommended maximum dose. The total required dose is the amount needed to neutralize the venom as determined by cessation of progression of all components of envenomation (initial control).

For grade 0 : No treatment is required as the drug should never be administered prophylactically in asymptomatic patients.
For grade I : The recommended initial dose is 20-40 mL i.e., contents of 2-4 vials given by intramuscular route into a large muscle mass preferably the gluteal area, at different sites with care to avoid injury of nerve trunks.
For grades II and III : The recommended initial dose is 40–60 mL, given by intravenous drip after diluting the product 5-10 times with 0.9% Sodium chloride or 5% Dextrose. The product should be infused slowly for the first 10 minutes at a rate of 25–50 mL/h, with careful observation of any allergic reaction. If no reaction occurs, the infusion rate should be increased to the full 250 mL/h until completion.



Skin Test:
The skin test is preferable to be performed and interpreted prior to administration of antitoxin in order to be ready for early interference and close observation. In case of severe symptoms, it is not recommended to wait for 30 minutes to observe the skin test result therefore; it is advisable to initiate serum therapy with simultaneous injection of 0.5-1mL of 1:1000 adrenaline subcutaneous and parallel infusion of hydrocortisone and antihistamine to decrease the acute allergic reactions.

Steps and Interpretation:
Inject 0.1-0.2 mL (1:10 dilution) of antitoxin intradermally. A positive reaction occurs within 5-30 minutes manifested by a wheal with or without surrounding erythema accompanied by increased risk of systemic reactions in sensitive patients. If history is positive for allergy and the test is positive, administration may be dangerous especially if the test is accompanied by systemic allergic manifestations. In such instances, the benefit of administration must be weighed against the risk of withholding the drug keeping in mind that severe envenomation can be fatal. The anti-shock measures should be loaded in syringes in such cases.
If history is negative for allergy and the result of test is negative, administer the drug, however, these do not rule out the possibility of an immediate reaction as 10% of false negative reactions have been reported.

N.B: Use of larger amount of skin test dose, increases the likelihood of false positive reactions.

Reconstitution of the Lyophilised Antitoxin:

Remove the flip off on the seal over the diaphragms of the vials of antivenin. Sterilize the rubber diaphragm with alcohol. Withdraw the diluent in a 10 mL sterile syringe. Insert the needle through the stopper of the vial containing antitoxin and point the diluent jet to the center of lyophilised pellet to be dissolved and in order to prevent floating. Swirl the vial gently for one to five minutes and do not shake to avoid foaming.

Adverse Effects:
Immediate systemic reactions (anaphylaxis or allergy) may occur with horse serum. It may include flushing, itching, urticaria, cough, dyspnea, cyanosis, vomiting, hypotension, edema of the face, tongue, and throat and collapse. Cardiac arrest and death are very rare. Serum Sickness may develop after 7-10 days and is manifested by fever, urticaria, lymphadenopathy, arthralgia and muscle pain. Occasional meningism or peripheral neuritis may occur.

Contraindications:
In case of severe envenomation threatening life or limb there is no contraindication for a history of allergy however, careful evaluation and expert management is required.

Precautions:
Before giving any horse serum, history of allergy or previous exposure to horse serum should be reviewed.
As recommended by the WHO, anti-shock measures including: Epinephrine 1:1000, corticosteroids, airway, oxygen, calcium salts and antihistamines should be readily available prior to administration of the antitoxin. If any systemic reaction occurs, serum administration should be discontinued immediately and appropriate antishock measures must be initiated.
Constant attendance and monitoring of vital signs, any untoward reaction is mandatory during antitoxin administration for at least 2 hours. The type of electrolyte solution used for dilution and the rate of intravenous delivery of the antitoxin must take into consideration - the age, weight, cardiac status of the patient, severity of envenomation and interval between the bite and initiation of therapy. Safety of the product during pregnancy and lactation has not been established; therefore the risk should be outweighed against the benefit.
Therapy with beta adrenergic blockers has been associated with an increased severity of acute anaphylaxis. The antitoxin should not be used if turbid, expired or showing precipitation.

Shelf Life:
Four years from the date of manufacturing.

Storage:
Store the freeze dried vial below 30°C. Reconstituted liquid shall be used immediately and shall not be freezed

Presentation:
Snake Venom Antitoxin is supplied as freeze dried powder in a 20mL glass vial.

Disposal:
Left over antitoxin and used empty vials should be discarded as biomedical waste.

Manufactured by:
VINS BIOPRODUCTS LTD.
Survey No:117,Thimmapur (V), Kothur(M),
Mahaboobnagar Dist.- 509 325.
Telangana,India.

Recommended to neutralize snake bites by species as mentioned above in 'Composition'.