Product Information

APPROVED NAME

BROWN SNAKE ANTIVENOM AUST R 74897

DESCRIPTION

BROWN SNAKE ANTIVENOM is prepared from the plasma of horses immunised with the venom of the brown snake (*Pseudonaja textilis*). Each vial contains 1,000 units of antivenom which has been standardised to neutralise *in vitro* the average yield of venom from the brown snake.

The product also contains phenol, sodium chloride and other equine plasma proteins in an aqueous solution.

PHARMACOLOGY

Brown snakes were responsible for 11 of the 18 deaths from snake bite recorded in Australia between 1981 and 1991. Death after a brown snake bite is often sudden and unexpected. The venom can cause rapid onset of life-threatening coagulopathy, sometimes associated with respiratory paralysis and thrombocytopenia.

Although the amount of antivenom in each dose of BROWN SNAKE ANTIVENOM will neutralise the average yield of venom *in vitro*, the actual amount needed in clinical practice may be considerably more, particularly if gross coagulopathy or myocardial depression are present.

INDICATIONS

For the treatment of patients who exhibit manifestations of systemic envenoming following a bite by a snake of the genus *Pseudonaja*. This genus includes the Eastern brown snake, the dugite and the gwardar (Western brown snake).

CONTRAINDICATIONS

There are no absolute contraindications, but the product should not be used unless there is clear evidence of systemic envenoming with the potential for serious toxic effects.

PRECAUTIONS

When medicinal products prepared from animal plasma are administered, infectious diseases due to the transmission of infective agents cannot be totally excluded. This applies to pathogens of hitherto unknown origin. This possibility must always be considered and should be conveyed, whenever possible, to patients who may receive the product. Historically there have been no known recorded cases of transmission of viruses by this product.

In many cases of snake bite, little venom is injected and significant envenoming does not occur. If a significant amount of venom has been introduced, clinical or laboratory evidence of poisoning is usually present within 2 hours but can be delayed, particularly if efficient first aid has been instituted with immobilisation and a firm crepe bandage.

Removal of the bandage and splint will often precipitate the systemic effects of the poison in patients who have been bitten.

Suspected cases of snake bite should be observed for at least 6 hours after being bitten or after removal of the bandage and definite cases for at least 12 hours, preferably in an intensive care setting. Such patients must be regularly monitored for signs of neuromuscular impairment, coagulopathy, myolysis and other abnormalities.

A diagnosis of systemic envenoming should be based on clinical and, where possible, laboratory evidence.

The venom detection kits can be helpful in detecting and identifying specific venom at the bite site or in urine and can enable the selection of the appropriate monovalent antivenom. Tests of blood are less reliable.

As this product is prepared from animal serum, severe allergic reactions may follow, including anaphylactic shock. A syringe already loaded with 1:1000 adrenaline must be available during antivenom therapy. Anaphylactoid reactions may be more likely to occur in those who are atopic or who have previously received equine serum. This would include patients who have previously received equine Tetanus Antitoxin (prior to 1974 in Australia). Some authorities have advocated premedication with subcutaneous adrenaline and intravenous antihistamine, particularly in those patients who are known to be at risk, but such use is controversial.

The results of skin testing to determine patients who may have an allergic reaction are not satisfactory and should be not undertaken.

Antivenoms may bind complement and produce an anaphalactoid reaction in patients who have had no previous contact with equine protein. The risk of such a reaction can be reduced by adequate dilution of antivenom (1:10 in adults and 1:5 in small children) prior to infusion (also see DOSAGE AND ADMINISTRATION).

Symptoms and signs of anaphylaxis include pallor, tachycardia, urticaria, angioedema, cough and dyspnoea due to laryngeal oedema or bronchospasm. Nausea, vomiting and abdominal pain are less common. Typical signs of shock may develop in 1 to 2 minutes and the patient may convulse, become unresponsive and die.

Should anaphylaxis occur, cease administration of antivenom, administer oxygen and inject adrenaline 1:1,000 intramuscularly at the following dose rates: small adults (<50 kg) 0.25 mL, average adults (50-100 kg) 0.5 mL, large adults (>100 kg) 0.75 mL. For children (to age 12) use 1:10,000 and inject 0.25 mL per year of age. If there is little or no response to the initial intramuscular dose of adrenaline, administer the same dose (diluted to 1:10,000) slowly into an intravenous line. Repeat at 5 minute intervals depending on response. In severe cases, intravenous antihistamine and intravenous corticosteroids may also be given to reduce the chance of late reactions, but have a slower onset of action than adrenaline. Further administration of antivenom should be considered in the light of the relative problems of envenoming and anaphylaxis.

Severe cases of systemic envenoming should be managed in an intensive care unit.

Delayed serum sickness can occur following the use of animal derived antivenoms. The most common manifestations include fever, cutaneous eruptions, arthralgia, lymphadenopathy and albuminuria. Less commonly, arthritis, nephritis, neuropathy and vasculitis can occur. The condition usually appears 8-13 days after the use of antivenom but can occur as soon as 12 hours after a second injection of a similar animal protein.

The incidence of serum sickness is greater with larger volumes of antivenom, but can be expected to occur in at least 5% of patients receiving horse serum for the first time.

Use in pregnancy
There is limited but inconclusive information on the safety of the product in pregnant women.

Use in lactation
No information is available on the use of the product during lactation.

ADVERSE REACTIONS

As the product is of animal origin, severe allergic reactions can occur (see PRECAUTIONS). There have been 17 spontaneous reports in Australia of hypersensitivity to snake antivenoms produced by CSL between 1978 and 2003 and of these, 4 involved BROWN SNAKE ANTIVENOM. Publications in which adverse events to all snake antivenoms are reported give rates ranging from 5 to 39%. The rates related to the monovalent antivenoms appear to be lower than those to the polyvalent antivenom. There have been 4 published reports of hypersensitivity reactions in 43 patients following the administration of BROWN SNAKE ANTIVENOM. The overall rate for monovalent antivenoms appears to be in the vicinity of 9%.

Following the treatment of snake bite in Australia, there were 3 deaths which were attributed to serum reactions to snake antivenoms between 1952 and 1961. No deaths specifically attributed to the use of snake antivenoms have been reported since that time.

Adverse events to all snake antivenoms manufactured by CSL are compiled below:

Hypersensitivity and skin	*Common:*	Urticaria Rash Hypotension Bronchospasm Anaphylaxis Delayed serum sickness
	Uncommon:	Angioedema
Neurological	*Common:*	Headache
Musculoskeletal	*Uncommon:*	Arthralgia Myalgia
Gastrointestinal	*Uncommon:*	Abdominal pain Vomiting
Cardiovascular	*Uncommon:*	Chest pain Cyanosis
General	*Common:*	Pyrexia
	Uncommon:	Pain at infusion site

As the recording of adverse events was by means of forms which were, in most cases, returned within 24 hours of administration of the antivenom, the actual incidence of serum sickness may be higher than is reported here.

DOSAGE AND ADMINISTRATION

A proportion of people bitten by snakes have symptoms that are so mild that antivenom is not necessary. When there is evidence of systemic envenoming and it has been established that BROWN SNAKE ANTIVENOM is the appropriate treatment, the contents of one vial (1,000 units) should be administered slowly by intravenous infusion after dilution with Hartmann's Solution. The dose is the same for adults and children.

The antivenom should be diluted 1 in 10, although in small children a dilution of 1 in 5 may be more appropriate to avoid fluid overload. It should not be administered by the intramuscular route.

Some authorities have advocated premedication with 0.25 mL of 1:1,000 adrenaline subcutaneously and intravenous antihistamine to reduce the chance of anaphylactic shock, particularly in those patients who are known to be at risk, but such use is controversial (see PRECAUTIONS).

The patient should receive the antivenom in an intensive care unit if possible.
If the patient has received adequate first aid treatment, the splint and pressure bandage should not be removed until antivenom is available for infusion, as removal can precipitate significant effects of systemic envenoming.

The aim of antivenom therapy is to neutralise the venom. Sufficient antivenom must be given to neutralise further venom migrating from the bite site. Deterioration in the patient's condition may indicate that treatment is inadequate and more may be required. Children may become critically ill sooner than adults and may need more antivenom.

Patients with severe systemic envenoming may require several vials of antivenom to control the effects, particularly if coagulopathy or myocardial depression are present which does not resolve with initial antivenom therapy. Most patients require at least 3 vials and the use of 13 vials has been recorded.

The patient must be monitored for at least 6 hours after antivenom is administered.

Before starting the infusion of antivenom, a separate syringe should be loaded with 1:1,000 adrenaline, as anaphylactic reactions can occur rapidly (see PRECAUTIONS).

Should an anaphylactic reaction occur, cease administration of antivenom, administer oxygen and inject adrenaline 1:1,000 intramuscularly at the following dose rates: small adults (<50 kg) 0.25 mL, average adults (50-100 kg) 0.5 mL, large adults (>100 kg) 0.75 mL. For children (to age 12) use 1:10,000 and inject 0.25 mL per year of age. If there is little or no response to the initial intramuscular dose of adrenaline, administer the same dose (diluted to 1:10,000) slowly into an intravenous line. Repeat at 5 minute intervals depending on response.

As delayed serum sickness is relatively common following the use of large volumes of horse serum, it is advisable to administer a corticosteroid either by a single intravenous injection or orally for 4 to 5 days to children and to those receiving multiple vials of antivenom.

It may occasionally be necessary to treat both envenoming and anaphylaxis simultaneously.

BROWN SNAKE ANTIVENOM contains no antimicrobial preservative. Use once only and discard any residue.

OVERDOSAGE

No information is available on overdosage.

PRESENTATION

BROWN SNAKE ANTIVENOM is available as vials containing 1000 units of antivenom in 4 to 9 mL of aqueous solution.

STORAGE

BROWN SNAKE ANTIVENOM should be protected from light and stored at 2-8°C. Do not freeze.

NAME AND ADDRESS OF SPONSOR

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