Product Information

NAME OF THE MEDICINE

BOX JELLYFISH ANTIVENOM AUST R 74891

DESCRIPTION

BOX JELLYFISH ANTIVENOM is prepared from the plasma of sheep immunised with the venom of the box jellyfish (*Chironex fleckeri*). Each vial contains 20,000 units of antivenom. The product also contains phenol, sodium chloride and other ovine plasma proteins in an aqueous solution.

Pharmacology

Box jellyfish are present in Australian tropical waters from December to March, but stinging has been reported at other times of the year. In the Northern Territory, the box jellyfish stinging season extends from 1 October to 31 May.

They favour calm water close to shore with an unobstructed sandy sea floor . Fully grown specimens are 30 cm in diameter, have a curtain of very long tentacles which they trail along the sea floor and are virtually invisible. Each tentacle contains many thousands of nematocysts.

Each nematocyst discharges venom in response to mechanical or chemical stimulation and can penetrate human skin. Swimmers who come into contact with the box jellyfish may have several metres of adherent tentacles which cause serious and intense pain. They leave typical linear red weals on the skin which can, in some cases, progress to full thickness skin necrosis. The pain can be severe enough to cause screaming, panic and irrational behaviour. The muscular exertion involved tends to disseminate the venom.

The box jellyfish venom contains toxins, which affect the myocardium and the neuromuscular mechanisms of the respiratory system as well as causing dermatonecrosis. Death can occur in as little as 20 minutes.

Not all box jellyfish stings cause severe symptoms. The severity depends mainly on the surface area of tentacular contact and the age of the recipient. Contact of several metres in a small child can be fatal.

In most cases of severe envenoming, intravenous use of the antivenom, given soon after the sting, has produced a diminution of pain and inflammation in the skin wheals within a few minutes. Larger doses given intramuscularly have evoked a slower response.

INDICATIONS

For the treatment of patients who exhibit manifestations of systemic envenoming or who have extensive local involvement causing extreme pain which does not respond to routine analgesic therapy.

CONTRAINDICATIONS

There are no absolute contraindications, but the product should not be used unless there is clear evidence of systemic envenoming or extensive local involvement with intractable pain.

See PRECAUTIONS for use of BOX JELLYFISH ANTIVENOM in patients with a known allergy.

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.

Most stings from box jellyfish are not life threatening although the initial pain following tentacle contact may be severe. Severe envenoming following extensive tentacle contact over one or more limbs can cause death within 20 minutes.

In serious cases of envenoming, cessation of respiration and cardiac arrest can occur very soon after the sting. In these cases it is essential to initiate cardiopulmonary resuscitation and other first aid measures before commencing antivenom therapy. Liberal dousing of the tentacles with vinegar will prevent further dissemination of the venom from the nematocysts.

If the limb has been immobilised and a firm bandage applied, removal of the bandage and splint may precipitate the systemic effects of the venom. The bandage and splint should not be removed until the patient is in hospital with appropriate antivenom treatment available and an intravenous line in place.

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

As this product is prepared from animal plasma, severe allergic reactions may follow, including anaphylactic shock. A syringe already loaded with 1:1,000 adrenaline must be available during antivenom therapy. Anaphylactic reactions may be more likely to occur in those who are atopic or have previously received ovine plasma. 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 not be undertaken.

Antivenoms may bind complement and produce an anaphylactoid reaction in patients who have had no previous contact with ovine protein.

The risk of such a reaction can be reduced by adequate dilution of the antivenom (1:10 in adults and 1:5 in small children) prior to infusion (see also DOSAGE AND ADMINISTRATION).

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.

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 to 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.

Use in pregnancy

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

Use in lactation

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

ADVERSE REACTIONS

The following adverse reactions, presented below according to System Organ Class and frequency, have been identified during post-approval use of CSL antivenoms. Adverse event frequencies are defined as follows:

Very common: ≥1/10; common: ≥1/100 and < 1/10; uncommon: ≥1/1000 and <1/100; rare: ≥1/10,000 and <1/1000; and very rare: <1/10,000.

Immune system disorders
Common: Allergic reactions including anaphylactic shock and delayed serum sickness

Skin and subcutaneous tissue disorders
Common: Urticaria, rash

DOSAGE AND ADMINISTRATION

Not everyone who is stung by a box jellyfish needs antivenom. In cases of severe systemic envenoming, cardiopulmonary resuscitation and other first aid measures must be instituted when necessary before giving antivenom. All adherent tentacles must be doused with vinegar which will prevent further damage from the venom but will not ease the pain. **Antivenom should be administered as soon as possible after resuscitation has commenced. Ideally this will be in an intensive care facility.**

The contents of one vial (20,000 units) should be administered slowly by intravenous infusion after dilution with an intravenous solution. The dose is the same for both 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.

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).

If intravenous administration is not practical, 3 ampoules should be given undiluted by the intramuscular route at 3 separate sites.

If the affected limb is immobilised, the splint and pressure bandage should not be removed until antivenom is available for infusion and an intravenous line is in place, as removal can precipitate significant effects of envenoming.

The aim of antivenom therapy is to neutralise the venom. Sufficient antivenom must be given to combat the effects of the venom. Lack of response to the antivenom may indicate that treatment is inadequate and more antivenom may be required.

The patient must be monitored for at least 6 hours after conclusion of the antivenom infusion.

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 foreign protein, 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 doses of antivenom.

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

BOX JELLYFISH ANTIVENOM contains no antimicrobial preservative. Use once only and discard any residue.

OVERDOSAGE

No information is available on overdosage. Contact the Poisons Information Centre on 131 126 for further advice on overdosage management.

PRESENTATION

BOX JELLYFISH ANTIVENOM is available as vials containing 20,000 units in aqueous solution. The product volume is potency dependant thus it varies from batch to batch. Please refer to the product volume printed on the carton.

STORAGE

BOX JELLYFISH ANTIVENOM should be protected from light and stored between 2 to 8°C. Do not freeze.

NAME AND ADDRESS OF SPONSOR

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