AUSTRALIAN PRODUCT INFORMATION – DEATH ADDER ANTIVENOM Injection

1 NAME OF THE MEDICINE

DEATH ADDER ANTIVENOM (equine) as active ingredient

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

DEATH ADDER ANTIVENOM is prepared from the plasma of horses immunised with the venom of the common death adder (*Acanthophis antarcticus*). Each vial contains 6,000 units of antivenom which has been standardised to neutralise in vitro the average yield of venom from the death adder.

The product also contains 2.2mg phenol, 8mg sodium chloride and water for injections to 1 mL in an aqueous solution. Each vial contains ≤ 170 mg per mL of plasma protein of equine origin. The product volume is potency dependant thus it varies from batch to batch. Please refer to the product volume printed on the carton.

3 PHARMACEUTICAL FORM

DEATH ADDER ANTIVENOM is a concentrated solution for intravenous injection. It is a light straw coloured, slightly viscous transparent solution in a glass vial.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the treatment of patients who exhibit manifestations of systemic envenoming following a bite by a death adder.

4.2 DOSE AND METHOD OF ADMINISTRATION

When there is evidence of systemic envenoming and it has been established that DEATH ADDER ANTIVENOM is the appropriate treatment, the contents of one vial (6,000 units) should be administered slowly by intravenous infusion after dilution with Hartmann's Solution or 0.9%w/v Sodium Chloride. Once diluted, DEATH ADDER ANTIVENOM should be used immediately. Do not store diluted antivenom.

The dose is the same for adults and children.

The antivenom should be diluted 1 in 10, although a dilution of 1 in 5 may be more appropriate to avoid fluid overload in patients that are at risk (e.g. small children). Seek expert advice, regarding dilution of antivenom to avoid fluid overload, as required. It should not be administered by the intramuscular route.

In the past, 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 **Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

The patient should receive the antivenom in an intensive care unit if possible and always in a setting where resuscitation facilities are immediately available.

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 more than one vial of antivenom to control the paralysis caused by the neurotoxin. There are reports of patients receiving up to five vials.

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

Before starting the infusion of antivenom, adrenaline should be prepared ready to use, as anaphylactic reactions can occur rapidly (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Should an anaphylactic reaction occur, suspend administration of antivenom and implement treatment measures immediately according to an appropriate protocol or guideline.

As delayed serum sickness is relatively common following the use of large volumes of horse serum, patients who have received antivenom should be advised of the symptoms of serum sickness and warned to seek urgent medical attention if such symptoms develop.

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

DEATH ADDER ANTIVENOM contains no antimicrobial preservative. Use in one patient on one occasion only and discard any residue.

4.3 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.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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. With Death adders, however, the majority of patients will develop systemic envenoming. If a significant amount of venom has been introduced, clinical or laboratory evidence of envenoming is usually present within 2 hours but can be delayed, particularly if efficient first aid has been instituted with immobilisation and a firm pressure bandage.

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

Suspected cases of snake bite should be observed for at least 12 hours after being bitten or after removal of the bandage prior to discharge, preferably in an intensive care setting. Such patients must be regularly monitored for signs of neuromuscular impairment, coagulopathy, myolysis, renal impairment 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. Adrenaline must be available during antivenom therapy

and prepared ready for use prior to antivenom administration. 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). In the past, 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 anaphylactoid 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 prior to infusion, although care should be taken to avoid fluid overload (also see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

Should anaphylaxis occur, suspend administration of antivenom and implement treatment measures immediately according to an appropriate protocol or guideline. 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 can appear days or weeks after the use of antivenom but can occur as soon as 12 hours after a second injection of a similar animal protein. Patients who have received antivenom should be advised of the symptoms of serum sickness and warned to seek urgent medical attention if such symptoms develop.

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 the elderly

No data available.

Paediatric use

Please see Section **4.2 DOSE AND METHOD OF ADMINISTRATION**.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No data available.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

There is limited but inconclusive information on the safety of the product in pregnant women. It is advisable to carefully weigh the risks of untreated envenoming against the expected benefits and potential risks of antivenom administration.

Use in lactation

No information is available on the use of the product during lactation. It is advisable to carefully weigh the risks of untreated envenoming against the expected benefits and potential risks of antivenom administration.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The following adverse reactions, presented below according to System Organ Class and frequency, have been identified during post-approval use of all Seqirus snake 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

Nervous system disorders

Common: Headache

Gastrointestinal disorders

Uncommon: Abdominal pain, vomiting, nausea and diarrhoea

Skin and subcutaneous tissue disorders

Common: Urticaria, rash

Musculoskeletal and connective tissue disorders

Uncommon: Myalgia

General disorders and administration site conditions

Common: Pyrexia, chills

Uncommon: Local injection site reactions, chest pain

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 Pharmacological properties

5.1 Pharmacodynamic properties

Mechanism of action

The main effect of a bite by a death adder is from a neurotoxin. In a case series of 5 patients with paralysis as a result of death adder envenoming, antivenom was effective in reversing paralysis. The longest delay between envenoming and administration of antivenom was 7 hours. The maximum amount of antivenom required in this series was 5 vials.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

No specific information is available on absorption, distribution, metabolism or excretion of antivenom.

5.3 PRECLINICAL SAFETY DATA

Carcinogenicity

No data available.

Genotoxicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Refer to **Section 2 QUALITATIVE AND QUANTITATIVE COMPOSITION**.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

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

6.5 NATURE AND CONTENTS OF CONTAINER

DEATH ADDER ANTIVENOM is available as 1 x 6,000 units in a clear glass vial.

The vial and all associated components do not contain natural rubber latex.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Not applicable.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (S4)

8 SPONSOR

Seqirus Pty Ltd

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Parkville Victoria 3052

Australia

9 DATE OF FIRST APPROVAL

21 July 2000

10 DATE OF REVISION

03 February 2020

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Updated for compliance with TGA Form for providing PI (March 2018).
1 NAME OF THE MEDICINE	Inclusion of the snake species contained in the medicine for clarity to user.
2 QUALITATIVE AND QUANTITATIVE COMPOSITION	Addition of excipient quantities for clarity to user. Inclusion of statement to address labelling requirements of current Ph. Eur. Monograph Immunosera for Human Use, Ph. Eur. Monograph 0084.
3 PHARMACEUTICAL FORM	Inclusion of formulation and active description as per current ARTG records.
4.2 DOSE AND METHOD OF ADMINISTRATION	Single use statement revised for clarity and alignment with labelling.
6.5 NATURE AND CONTENTS OF CONTAINER	Container details included as per TGA Form for Providing PI, Note 36 (March 2018). Inclusion of latex free statement as per section 3.1.2, Medicine labels, Guidance on TGO 91 and TGO 92, Version 2, June 2018.

8 SPONSOR	Inclusion of company ABN for Corporate Compliance.