AUSTRALIAN PRODUCT INFORMATION – STONEFISH ANTIVENOM SOLUTION FOR INJECTION

1 NAME OF THE MEDICINE

STONEFISH ANTIVENOM (equine) as the active ingredient.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

STONEFISH ANTIVENOM is prepared from the plasma of horses immunised with the venom of stonefish *(Synanceia verrucosa* and/or *Synanceia horrida)*. Each vial contains 2,000 units of antivenom. The product also contains 2.2 mg phenol, 8 mg sodium chloride, and water for injections to 1.0 mL. 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

STONEFISH ANTIVENOM is a solution for injection. It is a colourless to light straw coloured, slightly viscous, transparent solution in a glass vial.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the treatment of patients who, following envenoming by a stonefish, have systemic manifestations or severe oedema and pain which do not respond to first aid measures.

4.2 DOSE AND METHOD OF ADMINISTRATION

The majority of people who stand on stonefish and whose feet are pierced by their spines will need antivenom for relief of the pain and oedema. However appropriate first aid measures recommended by local guidelines must be instituted when necessary before giving antivenom.

The initial dose of antivenom depends on the number of visible puncture sites:

- 1 - 2 punctures 1 vial (2,000 units)
- 3 - 4 punctures 2 vials (4,000 units)

5 or more punctures 3 vials (6,000 units)

The dose is the same for both adults and children.

The antivenom should be given by intramuscular injection but may be given by intravenous infusion in extreme cases after diluting the antivenom 1:10 in an intravenous solution such as Hartmann's Solution or 0.9% w/v Sodium Chloride. Seek expert advice regarding dilution of antivenom to avoid fluid overload, as required. **NOTE: The intravenous route is more likely to precipitate anaphylactoid reactions.**

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 initial dose of antivenom is insufficient to control the effects of the venom and the identity of the stonefish is assured, the initial dose of antivenom should be repeated.
The patient must be monitored for at least 6 hours after the receiving the antivenom.

Before giving the 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 foreign 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.

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

STONEFISH 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 stonefish envenoming with severe effects.

See **Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE** for the use of STONEFISH ANTIVENOM in patients with a known allergy.

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.

Appropriate first aid measures recommended by local guidelines must be instituted when necessary before giving antivenom.

As this product is prepared from animal plasma, severe allergic reactions may follow, including anaphylactic shock. Adrenaline must be available during antivenom therapy and prepared ready for use prior to antivenom administration. Anaphylactic reactions are 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 initial skin testing to determine patients who may have an allergic reaction to antivenom are not satisfactory and should not be undertaken.

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 envenoming should be managed in an intensive care unit, if possible.

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 horse protein. Patients 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.

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

No data available.

Effects on fertility

No data available.

Use in pregnancy

There is no 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 this 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 Seqirus 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

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 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

Stonefish are found throughout Australian tropical waters. They prefer calm, shallow water around coral islands, estuaries and sheltered bays. They settle into depressions in the mud or sand of the sea bed and become almost indistinguishable from surrounding rock or coral. The stonefish has poisonous spines along its back which are used only in defence. Those who are stung are usually people who inadvertently stand on the fish; less commonly, the damage is caused when an attempt is made to pick up a stonefish believing it to be a piece of rock or coral.

The stonefish has thirteen dorsal spines, each of which possesses a pair of venom glands. The venom of the stonefish is heat labile. It possesses a permeability-increasing enzyme, which causes considerable local oedema. This enzyme is believed to be also responsible for pulmonary oedema, which can occur following a stonefish sting. Other systemic effects which have been described include hypotension, bradycardia, arrhythmia, fever, muscle weakness and paralysis.

The first and overwhelming local effect of the sting is excruciating pain. The pain, together with redness and swelling, will often spread up the limb and involve regional lymph nodes.

The systemic effects described earlier can also occur but do not appear to be common.

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

Genotoxicity

No data available.

Carcinogenicity

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

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

6.5 NATURE AND CONTENTS OF CONTAINER

STONEFISH ANTIVENOM is available as 1 x 2,000 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

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9 DATE OF FIRST APPROVAL

15 December 2009

10 DATE OF REVISION

1 October 2019

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Updated for compliance with TGA Form for providing PI (March 2018).
2 QUALITATIVE AND QUANTITATIVE COMPOSITION	• Statement included to address the labelling requirements of current Ph. Eur. Monograph • Addition of quantitative composition information as per Module 3.2.P.1 and to align with outer carton
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.