AUSTRALIAN PRODUCT INFORMATION – SEA SNAKE ANTIVENOM Injection

1. NAME OF THE MEDICINE

SEA SNAKE ANTIVENOM (equine)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

SEA SNAKE ANTIVENOM is prepared from the plasma of horses immunised with the venom of the sea snake (*Enhydrina schistosa*). Each vial contains 1,000 units of antivenom. Each 1 mL of the product also contains 2.2 mg phenol, 8 mg 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.

SEA SNAKE ANTIVENOM has been shown to be effective not only against the venom of *Enhydrina schistosa* but, to a varying degree, against the venoms of a wide variety of sea snakes present in northern Australian waters.

3. PHARMACEUTICAL FORM

SEA SNAKE ANTIVENOM is a concentrated injection for intravenous use available as vials containing 1,000 units in aqueous solution. 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 sea snake.

4.2 DOSE AND METHOD OF ADMINISTRATION

A large proportion of people bitten by sea snakes have minimal or no effects from the bite and antivenom is unnecessary. When there is evidence of systemic envenoming from a sea snake, the contents of one vial (1,000 units) should be administered slowly by intravenous infusion after dilution with Hartmann's Solution or normal saline. Once diluted, SEA SNAKE 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.

In cases of severe envenoming, when myalgia, muscle weakness, trismus, ptosis and ophthalmoplegia are present, an initial dose of 3,000 to 4,000 units should be given and up to 10,000 units may be required altogether. In less severe cases a total of 3,000 units will control most patients.

In the past, some authorities have advocated premedication with 0.25 mL of 1:1000 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 **4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

If the patient has the affected limb immobilised, the splint and pressure bandage should not be removed until the patient is in a unit where full resuscitation measures and antivenom are available.

Severe cases of systemic envenoming should be managed in an intensive care unit if possible and always in a setting where resuscitation facilities are immediately available.

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

Before starting the infusion of antivenom, adrenaline should be prepared ready for use, as anaphylactic reactions can occur rapidly (see 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.

SEA SNAKE 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.

See **4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE** for use of SEA SNAKE 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.

Most cases of sea snake bites are painless with no local swelling. A row of small teeth marks may be seen. Intense pain from underwater trauma is more likely to be due to a fish than a sea snake.

Up to two thirds of those bitten by a sea snake have little or no effect from the bite. Severely envenomed patients often develop symptoms soon after the bite, but in some, the potentially dangerous effects may be delayed for several hours. It is therefore essential to observe all those who have been bitten by a sea snake for at least 12 hours, prior to discharge. Such patients must be regularly monitored for signs of neuromuscular impairment, coagulopathy, myolysis, renal impairment and other abnormalities.

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. As immobilisation causes local retention of the venom, the requisite period of observation of the patient for a minimum of 12 hours commences when the splint and bandage are removed.

Severe cases of systemic envenoming should be managed in an intensive care unit, if possible and always in a setting where resuscitation facilities are immediately available.

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 may be more likely to occur in those who are atopic or 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 not be 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 the antivenom prior to infusion, although care should be taken to avoid fluid overload (see 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.

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.

Use in the elderly

No data available.

Paediatric use

See **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 no information on the safety of this 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 effect of this medicine on the 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 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 131 126 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Sea snakes are abundant throughout the warmer waters of the Indian and Pacific oceans. They require a sea temperature of at least 20°C and are therefore common in Australian tropical waters although there has been one confirmed sea snake bite at a Sydney beach.

The venom of the sea snake is very potent but in many cases of human bites, little venom is injected. In a study of 101 cases in Malaysia, only 22% of bites were considered to be serious. However, 6 of the 11 who were seriously envenomed died before antivenom was available and 2 of 11 after introduction of the antivenom.

Sea snake bites can occur from inadvertently standing on the snake or, more commonly, they occur as an occupational hazard to fishermen sorting fish in their nets. The venom of the sea snakes contains potent neurotoxins that can cause muscle paralysis and respiratory failure leading to death. The venom also has myolytic properties. The muscle destruction can cause myalgia and renal failure. Hyperkalaemia can be severe. Myolysis has been demonstrated in monkeys with considerable elevation of creatine kinase levels. There is also elevation of aspartate transaminase (AST) levels in humans.

As there is considerable similarity between the toxins of the sea snakes and the Australian elapids, TIGER SNAKE ANTIVENOM is often effective in cases of sea snake envenoming and may be used if SEA SNAKE ANTIVENOM is not available.

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

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

6.5 NATURE AND CONTENTS OF CONTAINER

SEA SNAKE ANTIVENOM is available as 1 x 1,000 units in 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 (POISON STANDARD)

Prescription Only Medicine (S4)

8 SPONSOR

Seqirus Pty Ltd
ABN: 26 160 735 035
63 Poplar Road
Parkville VIC 3052
Australia

9 DATE OF FIRST APPROVAL

21 July 2000

10 DATE OF REVISION

14 November 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	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.