

AUSTRALIAN PRODUCT INFORMATION – POLYVALENT SNAKE ANTIVENOM (AUSTRALIA – PAPUA NEW GUINEA) Injection

1 NAME OF THE MEDICINE

POLYVALENT SNAKE ANTIVENOM (equine) containing the following active ingredients:

Black snake antivenom
Taipan antivenom
Death adder antivenom
Tiger snake antivenom
Brown snake antivenom

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

POLYVALENT SNAKE ANTIVENOM contains antibodies to the venom of the following snakes:

King brown or mulga snake	(<i>Pseudechis australis</i>)
Mainland tiger snake	(<i>Notechis scutatus</i>)
Eastern brown snake	(<i>Pseudonaja textilis</i>)
Common death adder	(<i>Acanthophis antarcticus</i>)
Coastal taipan	(<i>Oxyuranus scutellatus</i>)

The antivenom is prepared from the plasma of horses immunised with the venom of the snakes. The amount of antivenom has been standardised to neutralise *in vitro* the average yield of venom from each snake. The minimum amount of each antivenom is as follows:

Black snake antivenom	18,000 units
Taipan antivenom	12,000 units
Death adder antivenom	6,000 units
Tiger snake antivenom	3,000 units
Brown snake antivenom	1,000 units
Total	40,000 units

Each 1 mL of 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 dependent thus it varies from batch to batch. Please refer to the product volume printed on the carton.

3 PHARMACEUTICAL FORM

POLYVALENT SNAKE ANTIVENOM is a concentrated injection for intravenous use. 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 in Papua New Guinea and in all Australian states except Victoria and Tasmania who exhibit manifestations of systemic snake envenoming and the snake has not been definitely identified. In Tasmania, Tiger Snake Antivenom should be used rather than polyvalent antivenom whilst in Victoria a combination of Tiger Snake Antivenom and Brown Snake Antivenom is the preferred treatment.

POLYVALENT SNAKE ANTIVENOM should not be used when the snake has been identified, as appropriate monovalent antivenom provides similar neutralisation of the venom without introducing the larger amounts of equine protein present in the polyvalent product.

4.2 DOSE AND METHOD OF 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 the snake has not been identified, the contents of one vial (40,000 units) of POLYVALENT SNAKE ANTIVENOM should be administered slowly by intravenous infusion after dilution with Hartmann's Solution or 0.9% w/v sodium chloride. Once diluted, POLYVALENT 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 for patients at risk of fluid overload. 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 **P4.4 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 several vials of antivenom to control the effects, particularly if coagulopathy is present. Amounts as high as 6 vials have been used in the treatment of severe systemic envenoming; it should be remembered that such high doses of this product contain large amounts of horse protein. 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 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. POLYVALENT 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 POLYVALENT SNAKE ANTIVENOM in patients with a known allergy.

4.4 SPECIAL WARNING 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 systemic envenoming does not occur. 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, and 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 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 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.

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 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.

To minimise the amounts of equine protein administered, the appropriate monovalent antivenom should be used wherever possible for an identified snake (See **4.1 THERAPEUTIC INDICATIONS**). However, if the appropriate monovalent antivenom is not available or in insufficient quantity, POLYVALENT SNAKE ANTIVENOM may be useful, as it contains components against five venom immunotypes. Seek expert advice in the case of an identified snake, where supply of monovalent antivenom is an issue.

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 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: $\geq 1/10$; common: $\geq 1/100$ and $< 1/10$; uncommon: $\geq 1/1000$ and $< 1/100$; rare: $\geq 1/10,000$ 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

The venoms of some snakes from Australia and Papua New Guinea contain neurotoxins which can cause respiratory paralysis, and coagulants (except in the death adder) which convert prothrombin to thrombin, which in turn produces a secondary afibrinogenaemia with resultant haemorrhage. The venoms of some snakes also contain a myolytic toxin which can cause renal failure.

Although the amount of antivenom in each dose of POLYVALENT SNAKE ANTIVENOM will neutralise the average yield of venom from each snake in vitro, the actual amount needed in clinical practice may be considerably more, particularly if treatment is delayed and the effects of the venom are already evident.

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

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

6.5 NATURE AND CONTENTS OF CONTAINER

POLYVALENT SNAKE ANTIVENOM is available as 1 x 40,000 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 (POISON STANDARD)

Prescription Only Medicine (S4)

8 SPONSOR

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63 Poplar Road
Parkville, VIC 3052
Australia

9 DATE OF FIRST APPROVAL

21 July 2000

10 DATE OF REVISION

30 October 2019

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.