health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Private Bag X828, PRETORIA, 0001 Dr AB Xuma Building1112 Voortrekker Road, Pretoria Townlands 351-JR, PRETORIA, 0187 Tel (012) 395 8000, Fax (012) 395 8918

Ms M Cloete
Imperial Market Access Healthcare SA (Pty) Ltd
57 Sarel Baard Crescent
Rooihuiskraal
Centurion
0157
Tshwane

Dear Ms Cloete

Section 21 Authorization for POLYVALENT SNAKEBITE ANTIVENOM INJ 20ML

Attached, please find the Authorization for exemption under Section 21 of the Medicines and Related Substances Act by SAHPRA granted for:

- **Polyvalent Snakebite Antivenom Injection 20mL**

The quantities for which approval was granted are only estimates based on procurement by provinces over the last 6 months. Please note that the National Department of Health (NDOH) cannot guarantee the procurement of these quantities, as NDOH has no control over orders being placed by provincial depots, and current stock holding might influence estimated quantities.

The following process will be followed to ensure the quality of the product being brought in:

1. Manufacturer will submit an assay and identification of every batch imported.
2. An additional assay of every batch will be done by a quality control laboratory.
3. A random sample will be assayed during the authorized period by a quality control laboratory.
4. Aggregate statistics to be submitted to NDOH in the first week of each month of all orders received and quantities supplied per province.
5. The NDOH needs to be advised of the quantities and date of arrival of stocks in terms of this authorization within 7 days after arrival.
6. The supplier will provide monthly reports, by the 7th of each month, using the attached format of orders received and issues done.
7. Participating Authorities (PAs) will provide a consolidated close out report of usage using the attached format on the date when an authorization lapses.

8. The full quantities imported in terms of this Section 21authorisation must be accounted for.
9. Note that this authorization DOES NOT cover supplies to the private sector.
10. Where this authorization is obtained to provide security of supply due to supply challenges from the contracted supplier, PAs are requested to buy out against contracted suppliers and ensure that related orders are cancelled accordingly to prevent overstocking once the contracted supplier gets back into stock.

It should be noted this authorization applies only for the use of the product in the public sector with estimated usage quantities for a period of six months. The authorization is expected to expire on **19 August 2025**.

Table 1: Provincial estimates

Province	Six Months Estimate
Correctional Services	11
EC-MT	600
EC-PE	300
FS	20
GP	0
KZN	2400
LP	400
MP	40
NC	90
NW	764
SAMHS	0
WC	0
Total	**4625**

Yours sincerely

KHADIJA JAMALOODIEN
CHIEF DIRECTOR: SECTOR WIDE PROCUREMENT
DATE: 20/2/2025

SAHPRA
SOUTH AFRICAN
HEALTH PRODUCTS
REGULATORY AUTHORITY

Section 21 Response Letter

2/19/2025 10:41 AM

Khadija Jamaloodien

National Department of Health
Dr AB Xuma Building
1112 Voortrekker Rd
Pretoria Townlands 351-JR
Pretoria
0187

Buhle.Mbongo@health.gov.za

Dear Khadija Jamaloodien,

REQUEST TO USE UNREGISTERED MEDICINE IN TERMS OF SECTION 21 OF THE MEDICINES AND RELATED SUBSTANCES ACT, 1965 (ACT 101 OF 1965):

Your application dated **2/18/2025 10:56 AM** refers

- ***A. STATUS: Approved***
- ***B. APPLICANT: Khadija Jamaloodien***
- ***C. IMPORTING COMPANY: Imperial Market Access Healthcare SA***
- ***D. PATIENT/(S):***
- ***E. UNREGISTERED MEDICINES:***

  GENERIC NAME: Lyophilized Polyvalent Enzymes Refined Equine

  TRADE NAME: PANAF-Premium Polyvalent Snake Venom Antiserum
- ***F. QUANTITY: Polyvalent Snakebite Antivenom Injection 20mL x 4600 vials***
- ***G. LETTER NUMBER: B-34612***

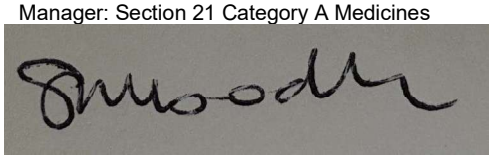
Section 21 authorization letters are valid for a period of six months from the letter date, unless otherwise specified.

Comments:

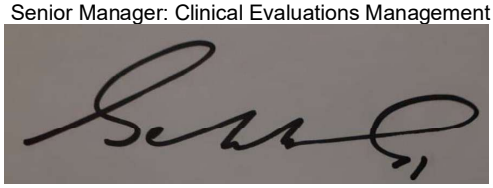
This application is approved with the following conditions:
1. Reporting of adverse events to the Section 21 unit (section21@sahpra.org.za) is required.
2. An update must be provided on the GMP status of the Indian manufacturer, when available. This is due to the significant number of Section 21 products that are requested from this manufacturer.
3. An update on the local manufacturer's renovation progress, when available.

Yours faithfully,

Dr S Munbodh
Manager: Section 21 Category A Medicines



T Sehloho
Senior Manager: Clinical Evaluations Management



Imperial™
beyond possibility

Market Access

Att: **Buhle Mbongo**

National Department of Health
Dr AB Xuma Building1112
Voortrekker Road,
Pretoria Townlands 351-JR,
PRETORIA,
0187
Buhle.Mbongo@health.gov.za
012 395 9539

Subject: Quotation for Snakebite Antivenom Injection
Quotation number: QR010122024

Thank you for considering Imperial Market Access Healthcare SA (IMAHSA) as your service provider.
We are pleased to provide you with a detailed quotation based on your requirements.

Product code	Description	Pack Size	Quantity	Price Incl. Vat Per Unit	Total Price Incl. Vat
MH000374	PANAF Polyvalent Snake Venom Antiserum 20ml *HUMAN USE*	Each	4600 Vials	R1606.03	R7 387 738.00

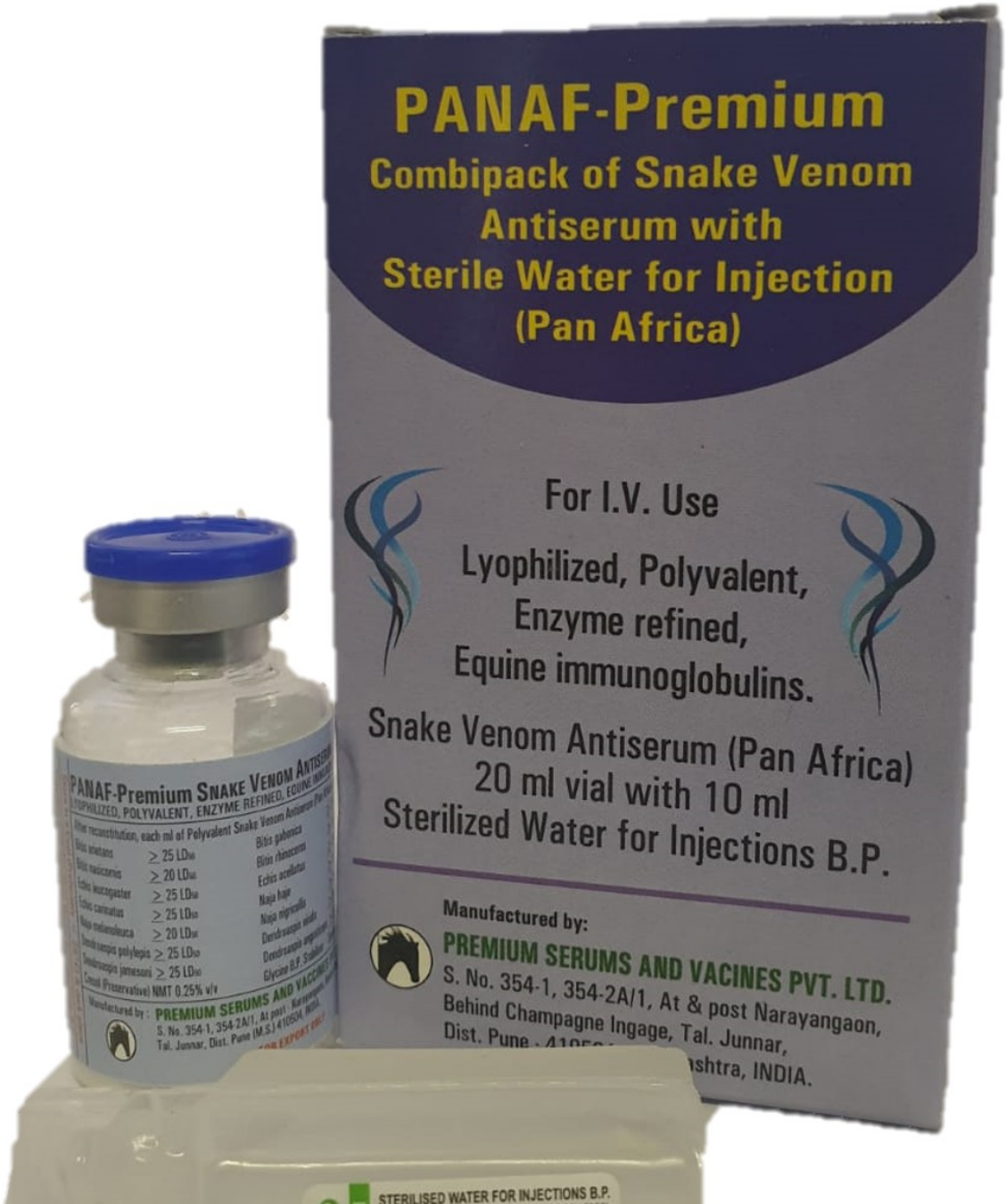
Please note that the prices quoted are subject to change based on any additional requirements or modifications. Quotations are valid for 90 days.
Delivery costs are included in pricing.

Lead times:
Lead time for state orders: 5 days

If you have any questions or need further clarification, please do not hesitate to contact us.

Sincerely,

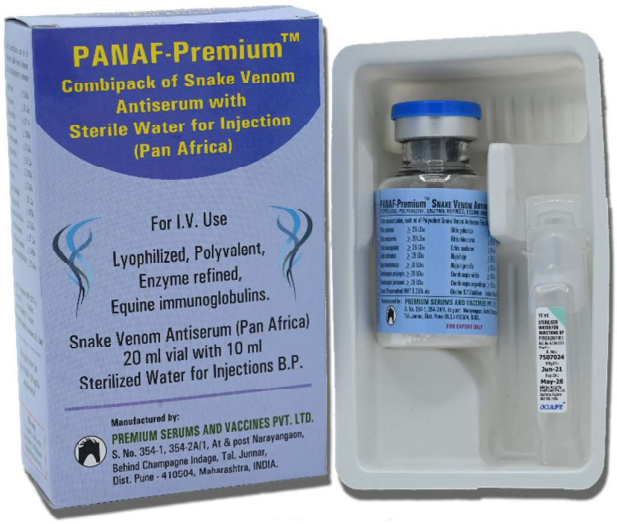
Kim Yearsley
Senior Manager: Commercial Operations| Imperial Market Access Healthcare SA
20/02/2025


PANAF-Premium
Combipack of Snake Venom Antiserum with Sterile Water for Injection (Pan Africa)
For I.V. Use
Lyophilized, Polyvalent, Enzyme refined, Equine immunoglobulins.
Snake Venom Antiserum (Pan Africa) 20 ml vial with 10 ml Sterilized Water for Injections B.P.
Manufactured by:
PREMIUM SERUMS AND VACINES PVT. LTD.
S. No. 354-1, 354-2A/1, At & post Narayangaon,
Behind Champagne Ingage, Tal. Junnar,
PANAF-Premium SNAKE VENOM ANTISERUM
PREMIUM SERUMS AND VACCINES
STERILISED WATER FOR INJECTIONS B.P.

Common Name	Species Name	Countries of Occurrence
Black-necked spitting cobra	*Naja nigricollis*	Angola, Benín, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo, Côte D'Ivoire, Democratic Republic of the Congo, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Malawi, Mali, Mauritania, Namibia, Niger, Nigeria, Rwanda, Senegal, Sierra Leone, South Sudan, Sudan, Togo, Uganda, United Republic of Tanzania, Zambia
Western barred spitting cobra	*Naja nigricincta*	Angola, Botswana, Namibia, South Africa
Red spitting cobra	*Naja pallida*	Djibouti, Ethiopia, Kenya, Somalia, South Sudan, United Republic of Tanzania
São Tomé Cobra	*Naja peroescobari*	São Tomé and Príncipe
West African banded cobra	*Naja savannula*	Benín, Burkina Faso, Cameroon, Central African Republic, Chad, Côte D'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Mali, Niger, Nigeria, Senegal, Sierra Leone, Togo
Senegalese cobra	*Naja senegalensis*	Benín, Burkina Faso, Côte D'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Mali, Mauritania, Niger, Nigeria, Senegal, Togo
Brown forest cobra	*Naja subfulva*	Angola, Burundi, Cameroon, Central African Republic, Chad, Congo, Democratic Republic of the Congo, Ethiopia, Kenya, Malawi, Mozambique, Nigeria, Rwanda, Somalia, South Africa, South Sudan, Sudan, Uganda, United Republic of Tanzania, Zambia, Zimbabwe

The manufacturer will not represent the WHO recommendation as applying to any other species that are not listed in ***Schedule 2*** of this notice. The recommendation is strictly limited to the listed species. Where the manufacturer obtains data supporting addition of new species to ***Schedule 2***, they will provide this data to WHO for review and validation. Where WHO can validate the data, additional species may be added to ***Schedule 2*** by WHO.

PRODUCT PACKAGING IMAGE



PANAF-Premium™
Combipack of Snake Venom Antiserum with Sterile Water for Injection (Pan Africa)

PRODUCT OVERVIEW

Type:	Snake Antivenom for sub-Saharan Africa
Commercial Name:	PANAF-Premium™ Combipack of Snake Venom Antiserum with Sterile Water for Injection (Pan Africa)
Manufacturer:	Premium Serums and Vaccines Pvt. Ltd.
Country:	India.
URL:	https://www.premiumserums.com/
Responsible NRA:	Central Drugs Standards Control Organization (CDSCO)
Country:	India
URL:	https://www.cdsco.gov.in

PRODUCT DESCRIPTION

Pharmaceutical Form:	Injectable solution
Presentation:	Lyophilized powder (vial) with diluent (SWFI) for reconstitution (ampoule).
Number of Doses:	1 (10 mL upon reconstitution)
Route of administration:	Intravenous
Shelf Life:	48 months
Storage temperature:	Store below 30°C, no refrigeration required.
Immunoglobulin content:	Not more than 10% w/v.
Packaging configuration:	Box containing one (1) vial lyophilized PANAF-Premium™, one (1) ampoule of diluent (SWFI), and instructions for use.

WHO RECOMMENDATION

Based on the results of a comprehensive risk-benefit assessment, this product can be used, at the dose ranges indicated in **Schedule 1**, for the treatment of envenoming by snake species listed in **Schedule 2**.

The recommendation is subject to terms and conditions imposed by WHO upon the manufacturer, which include the implementation (within one year) of a post-marketing surveillance strategy to monitor the use of the product and the clinical outcomes, including reporting of deaths, disabilities and adverse drug reactions.

WHO reviews all recommendations annually, and considers all new data that becomes available, and may renew, revoke, or amend these recommendations, based on the information available at the time of the review.

SCHEDULE 1: INITIAL DOSES

Dose recommendations below are based on the recognition of the variable composition of snake venoms leading to differences in potency within and between species. They also recognize the wide variation in the amount of venom that may be injected by individual specimens, particularly by large cobras (*Naja*) and mambas (*Dendroaspis*). These dose recommendations may be updated as new data based on clinical practice or clinical trials experience becomes available, and subject to review and approval by WHO.

Species Group	Genus	Recommended Initial Dose
African adders	*Bitis*	3-6 vials
African carpet vipers	*Echis*	1-3 vials
African mambas	*Dendroaspis*	10-25 vials
African cobras	*Naja*	20-40 vials

SCHEDULE 2: SPECIES COVERED BY THIS RECOMMENDATION

1. African Adders **Genus: *Bitis***

Recommended dose: The manufacturer recommends an initial dose of 3-6 vials.

Common Name	Species Name	Countries of Occurrence
Puff adder	*Bitis arietans*	Angola, Benín, Botswana, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Djibouti, Eritrea, Eswatini, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Malawi, Mali, Mauritania, Morocco, Mozambique, Namibia, Niger, Nigeria, Oman, Rwanda, Saudi Arabia, Senegal, Sierra Leone, Somalia, South Africa, South Sudan, Sudan, Togo, Uganda, United Republic of Tanzania, *Western Sahara*, Yemen, Zambia, Zimbabwe
Gaboon viper	*Bitis gabonica*	Angola, Burundi, Cameroon, Central African Republic, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Kenya, Malawi, Mozambique, Nigeria, Rwanda, South Africa, South Sudan, Uganda, United Republic of Tanzania, Zambia, Zimbabwe
Rhinoceros viper	*Bitis nasicornis*	Angola, Burundi, Cameroon, Central African Republic, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Kenya, Liberia, Nigeria, Rwanda, Sierra Leone, South Sudan, Togo, Uganda, United Republic of Tanzania
West African Gaboon viper	*Bitis rhinoceros*	Côte d'Ivoire, Ghana, Guinea, Liberia, Sierra Leone, Togo

2. African Carpet Vipers **Genus: *Echis***

Recommended dose: The manufacturer recommends an initial dose of 1-3 vials.

Common Name	Species Name	Countries of Occurrence
White-bellied carpet viper	*Echis leucogaster*	Algeria, Benín, Burkina Faso, Cameroon, Chad, Gambia, Mali, Mauritania, Morocco, Niger, Nigeria, Senegal, Sudan, Tunisia, *Western Sahara*
West African carpet viper	*Echis ocellatus*	Benín, Burkina Faso, Côte d'Ivoire, Ghana, Guinea, Mali, Niger, Nigeria, Senegal, Togo
East African carpet viper	*Echis pyramidum*	Central African Republic (north-east), Djibouti, Egypt, Eritrea, Ethiopia, Kenya, Libya, Somalia, South Sudan, Sudan
Roman's carpet viper	*Echis romani*	Cameroon, Central African Republic (west), Chad, Niger, Nigeria, Sudan

3. African Mambas **Genus: *Dendroaspis***

Recommended dose: The manufacturer recommends an initial dose of 10-25 vials.

Common Name	Species Name	Countries of Occurrence
Eastern green mamba	*Dendroaspis angusticeps*	Kenya, Malawi, Mozambique, South Africa, United Republic of Tanzania, Zimbabwe
Jameson's mamba	*Dendroaspis jamesoni*	Angola, Benín, Burundi, Cameroon, Central African Republic, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Ghana, Kenya, Nigeria, Rwanda, São Tomé and Príncipe, South Sudan, Togo, Uganda, United Republic of Tanzania
Black mamba	*Dendroaspis polylepis*	Angola, Benín, Botswana, Burkina Faso, Burundi, Cameroon, Central African Republic, Côte d'Ivoire, Democratic Republic of Congo, Djibouti, Eritrea, Eswatini, Ethiopia, Gambia, Guinea, Guinea-Bissau, Kenya, Malawi, Mali, Mozambique, Namibia, Rwanda, Senegal, Sierra Leone, Somalia, South Africa, South Sudan, Sudan, Uganda, United Republic of Tanzania, Zambia, Zimbabwe
Western green mamba	*Dendroaspis viridis*	Benín, Côte D'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Nigeria, Senegal, Sierra Leone, Togo

4. African Cobras **Genus: *Naja***

Recommended dose: The manufacturer recommends an initial dose of 20-40 vials.

Common Name	Species Name	Countries of Occurrence
Snouted cobra	*Naja annulifera*	Botswana, Eswatini, Malawi, Mozambique, Namibia, South Africa, Zambia, Zimbabwe
Black forest cobra	*Naja guineensis*	Côte d'Ivoire, Ghana, Guinea, Guinea-Bissau, Liberia, Sierra Leone, Togo
Egyptian cobra	*Naja haje*	Algeria, Cameroon, Central African Republic, Chad, Democratic Republic of the Congo, Djibouti, Egypt, Eritrea, Ethiopia, Kenya, Libya, Mali, Morocco, Niger, Nigeria, Somalia, South Sudan, Sudan, Tunisia, Uganda, United Republic of Tanzania
Forest cobra	*Naja melanoleuca*	Angola, Benín, Cameroon, Central African Republic, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Nigeria, South Sudan, Uganda
Mozambique spitting cobra	*Naja mossambica*	Angola, Botswana, Eswatini, Malawi, Mozambique, Namibia, South Africa, United Republic of Tanzania, Zambia, Zimbabwe

Common Name	Species Name	Countries of Occurrence
Black-necked spitting cobra	*Naja nigricollis*	Angola, Benín, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo, Côte D'Ivoire, Democratic Republic of the Congo, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Malawi, Mali, Mauritania, Namibia, Niger, Nigeria, Rwanda, Senegal, Sierra Leone, South Sudan, Sudan, Togo, Uganda, United Republic of Tanzania, Zambia
Western barred spitting cobra	*Naja nigricincta*	Angola, Botswana, Namibia, South Africa
Red spitting cobra	*Naja pallida*	Djibouti, Ethiopia, Kenya, Somalia, South Sudan, United Republic of Tanzania
São Tomé Cobra	*Naja peroescobari*	São Tomé and Príncipe
West African banded cobra	*Naja savannula*	Benín, Burkina Faso, Cameroon, Central African Republic, Chad, Côte D'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Mali, Niger, Nigeria, Senegal, Sierra Leone, Togo
Senegalese cobra	*Naja senegalensis*	Benín, Burkina Faso, Côte D'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Mali, Mauritania, Niger, Nigeria, Senegal, Togo
Brown forest cobra	*Naja subfulva*	Angola, Burundi, Cameroon, Central African Republic, Chad, Congo, Democratic Republic of the Congo, Ethiopia, Kenya, Malawi, Mozambique, Nigeria, Rwanda, Somalia, South Africa, South Sudan, Sudan, Uganda, United Republic of Tanzania, Zambia, Zimbabwe

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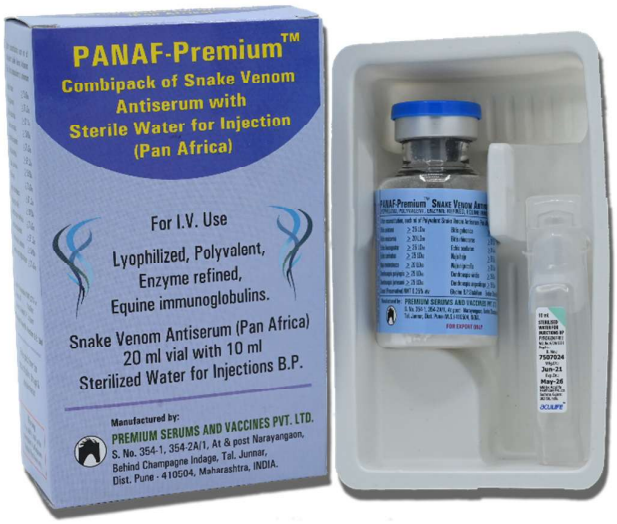
PRODUCT PACKAGING IMAGE



PACKAGE INSTRUCTIONS

English language copies of the Package Instructions appended to this notice are current as of the date of issue, but are subject to change in future, subject to review and approval by WHO. The Package Instructions included in the product have been reviewed by independent experts as part of the risk-benefit assessment by WHO and updated by the manufacturer on the basis of that review.

French, Spanish or Portuguese language versions of the Instructions will be included with product marketed in countries where these are the official languages of a country.

NOTICE ISSUED

Effective date: 01/03/2023

PANAF- Premium ™

SNAKE VENOM ANTISERUM (PAN AFRICA)

(For the use of only by a Registered Medical Practitioner or Hospital or Laboratory)

(LYOPHILIZED-POLYVALENT ENZYME REFINED EQUINE IMMUNOGLOBULINS)

COMPOSITION:

PANAF-Premium is a sterile solution containing enzyme refined anti-snake venom equine immunoglobulin $F(ab')_2$ fragments for parenteral administration. It contains glycine as a stabilizer, sodium chloride as an excipient and cresol as preservative. It is produced by pepsin digestion, heat inactivation at controlled temperature and caprylic acid treatment of hyper-immune plasma derived from healthy equines immunized with snake venoms sourced from Africa namely *Bitis arietans*, *Bitis gabonica*, *Bitis nasicornis*, *Bitis rhinoceros*, *Echis leucogaster*, *Echis ocellatus*, *Echis carinatus*, *Naja haje*, *Naja melanoleuca*, *Naja nigricollis*, *Dendroaspis polylepis*, *Dendroaspis viridis*, *Dendroaspis jamesoni* & *Dendroaspis angusticeps*. Protein content is not less than 6.0% w/v and is not more than 10% w/v protein (by Kjeldhal method).

INDICATIONS:

PANAF-Premium is indicated for bites caused by several species of African snakes in line with WHO recommendations, including *Bitis arietans*, *Bitis gabonica*, *Bitis nasicornis*, *Bitis rhinoceros*, *Echis leucogaster*, *Echis ocellatus*, *Echis pyramidum, Echis romani, Dendroaspis angusticeps, Dendroaspis jamesoni, Dendroaspis polylepis, Dendroaspis viridis*, *Naja annulifera, Naja guineenesis, Naja haje*, *Naja melanoleuca, Naja mossambica, Naja nigricollis*, *Naja nigricincta, Naja pallida*, *Naja peroescobari, Naja savannula*, *Naja senegalensis and Naja subfulva,* where the patients present with visible clinical signs and symptoms of envenoming: -

Systematic envenomation:

(i) Neurotoxic envenoming – Moderate or no local swelling, progressive descending paralysis with ptosis and paralysis of eye movements. Earlier symptoms of neurotoxicity include blurred vision/double vision, feeling of heaviness of eyelids and apparent drowsiness, difficulty raising the eye brows and puckering the forehead even before ptosis. High risk of respiratory failure is suggested by poor mouth opening and limited tongue protrusion, dysarthria, dysphagia, dyspnoea, distress, restlessness, sweating, respiratory muscle weakness and impaired consciousness as a result of respiratory paralysis or airway obstruction and/or circulatory failure.

(ii) Non-Neurotoxic envenoming - (Haemorrhagic & Cytotoxic envenoming) Painful and progressive swelling with blood-stained tissue fluid leaking from bite wound and spontaneous systemic bleeding from gums (gingival sulci), coagulopathy detected by 20 min WBCT with or without external bleeding, persistent bleeding from fang marks, nausea, vomiting and shock. Hypovolaemic shock, blistering and bruising. Severe pain at bite site and throughout affected limb and painful tender enlargement of local lymph glands and irreversible tissue death (necrosis/ gangrene).

(iii) Spitting cobra ophthalmia - venom spat into the eyes should be washed out as soon as possible using copious amounts of water or other bland fluids (e.g., milk). Local anaesthetic eyedrops may need to be applied once only if eyes are being held shut due to pain, after which a protective eye pad dressing should be applied. Topical antibiotics should be applied as for corneal injuries. Antivenom is not indicated.

RECONSTITUTION AND ADMINISTRATION:

PANAF-Premium is supplied in 20ml glass vial with 10ml sterilized Water for Injection BP as diluent. Withdraw diluent in 10ml sterile syringe and insert needle through vial stopper and inject into the vial. Mix the contents gently by swirling action and avoid vigorous shaking. Serum should be used as soon as possible after reconstitution.

DOSAGE AND ADMINISTRATIONS:

Currently, snake antivenom is the only specific antidote for snake envenoming and prompt administration of an adequate dose of antivenom is of paramount importance for neutralization of unbound circulating snake venom components for early response to treatment. Antivenom is most effective when given intravenously. Any delay in administration may result in increased dose requirement and decreased effectiveness.

Snake antivenom is effective in preventing or reversing many of the harmful effects of snakebite envenoming. When administered early, antivenoms are not just lifesaving, but can prevent some irreversible effects such as

local tissue damage (necrosis, gangrene) so sparing patients some of the suffering caused by snake venom, and allowing faster recovery, less time in hospital and a more rapid transition back to a productive life.

Snake antivenom should be administered intravenously and not by other routes. It can be given by intravenous infusion after dilution 1:1 in isotonic fluid over 30 – 60 minutes, or by intravenous injection at a rate of about 5ml per minute after dilution 1:1 in isotonic fluid. Total volume of antivenom and diluent administered should not exceed 500 ml/hr. If giving more than 25 vials, the dose should be diluted 1:1 with isotonic fluid and administered over 90-120 minutes. **Children should receive the same dose of antivenom as adults, but it is imperative to avoid fluid overload**.

Correct identification of the biting snake is usually very difficult or impossible unless a dead snake is brought with the patient or an adequate photograph of the actual snake for expert assessment. There may be variability in clinical signs and symptoms due to many factors such as size of victim, comorbidities, body part bitten, activity after bite, individual sensitivity to venom components, bite characteristics (bite number, depth, interposition of clothing, amount of venom injected, condition of fangs, duration of snake's clinging to the victim and chewing), biting snake species, nature of first aid given, and time to antivenom administration after bite. As the clinical signs vary due to many factors, a syndromic approach (supported by epidemiological data about prevalence of snake species prevalent in that region) is recommended for initiating appropriate clinical management.

(1) Non-Neurotoxic Envenoming Syndrome-the clinical syndrome of envenoming is dominated by haemorrhagic, cytotoxic or procoagulant effects by African adders/vipers (*Bitis* spp.), or carpet vipers (*Echis* spp.) and African spitting cobras (e.g., *Naja nigricollis, N. pallida, N. ashei, N. mossambica,* etc.). The amount of injected venom can vary greatly from one species to another. For carpet vipers it is generally less than 20 mg, but African adders and spitting cobras commonly inject >300 mg of venom. Considering worst case scenario, the following doses are recommended for each species-

For bites by carpet vipers (*Echis* spp).-It is recommended to administer initial dose of 1-3 vials

For bites by African adders (*Bitis* spp)-It is recommended to administer initial dose of 3-6 vials

For bites by African spitting cobras (*Naja* spp.) -It is recommended to administer initial dose of 20-40 vials.

(2) Neurotoxic Envenoming Syndrome-the clinical syndrome of envenoming is dominated by neurotoxic effects potentially causing rapid death through paralysis of airway and breathing muscles and is caused by neurotoxic species of cobra (e.g., *Naja haje*, *N. senegalensis*, *N.melanoleuca*, etc.) or mamba (*Dendroaspis polylepis*, *D.viridis*, *D.angusticeps* and *D.jamesoni*). Neurotoxic cobras can inject >300 mg venom and mambas may inject >100 mg venom. Considering worst case scenario, the following doses are recommended for each species-

For bites by mambas (*Dendroaspis* spp.)- It is recommended to administer initial dose of 10-25 vials.

For bites by neurotoxic cobras (*Naja* spp.)- It is recommended to administer initial dose of 20-40 vials.

Administration of repeat doses should be based on the clinical picture post-antivenom and decided by the treating clinician. For non-neurotoxic snakebites progression of local or systemic signs of envenoming more than 6 hours post-antivenom indicates need for additional antivenom. In particular, continued spontaneous bleeding or positive 20 minutes WBCT at 6 hours after presumed *Echis* spp. or *Bitis* spp. envenoming indicates need for repeat dosing. For neurotoxic snakebites any worsening of paralysis (particularly related to airway and breathing) more than 1 hour post-antivenom indicates need for additional antivenom.

SUPPORTIVE TREATMENT:

Antivenom alone cannot be relied upon to reverse neurotoxicity or prevent its progression to respiratory paralysis. It is essential that close attention be given to protecting and maintaining airway and breathing. Basic airway management and assisted breathing is lifesaving. Appropriate interventions such as Guedel airways, laryngeal mask airways, supplementary oxygen, bag-mask ventilation and if available endotracheal intubation and initiation of mechanical ventilation should be implemented as soon as indicated. For bites by neurotoxic cobras the use of anticholinesterase drugs like Neostigmine can temporarily reverse paralysis, but these drugs are not safe or appropriate for treatment of mamba bites. When used for cobra bites the co-administration of atropine is essential to block potentially serious muscarinic effects, such as bradycardia, bronchospasm, and an increase in secretions. Two anticholinergic drugs are available for this purpose, namely, atropine and glycopyrrolate. Atropine or glycopyrrolate may be used as anticholinergic agents.

In non-neurotoxic syndrome, recovery of normal haemostatic function may be accelerated by giving fresh whole blood, fresh frozen plasma, cryoprecipitates, or platelet concentrates but only after administration of an effective dose of antivenom. Acute kidney injury is uncommon after snakebites in Africa but may be a complication of prolonged hypotension (shock) or sepsis. Ideally, urine output should be monitored closely from time of presentation and if urine output falls below 1.5 mg/kg/hr in 24 hours, then appropriate renal therapy should be instituted. Cautious rehydration with isotonic fluids can be attempted but diuretics such as furosemide and mannitol are not recommended. If these measures fail, dialysis may be indicated.

Massive local swelling (e.g., after bites by large *Bitis* spp.) may cause hypovolaemic shock (fall in blood pressure, especially orthostatic) from fluid extravasation. Fluid replacement is essential, commonly after puff adder (*B. arietans*) envenoming.

Other measures include pain management (most of the bite sites are painful requiring administration of pain killers such as paracetamol) and surgical intervention if required. In addition to above, routine administration of tetanus toxoid is recommended. Antibiotics are indicated if the wound is already necrotic, has been tampered with or when signs of infection appear. Expert surgical advice should be sought where debridement of necrotic tissue in needed. Rapidly-evolving secondary bacterial necrotizing fasciitis is a dangerous complication requiring urgent parenteral antibiotics and surgical debridement.

IMMEDIATE ACTIONS AND FIRST AID:

Quick and positive measures should be taken to meet the emergency. Do not try to catch or kill the snake. Avoid further contact with the snake by the victim and bystanders. The patient should not be allowed to walk or run but should be carried by stretcher and kept as still as possible, ideally in the (left-lateral) recovery position. Reassure the patient to address anxiety and fear. Immobilizing the bitten limb with a splint and firm (but not tight) bandages is appropriate. Ligatures and tight tourniquets should be avoided. A pressure pad applied firmly over the bite site may be beneficial without exposing the patient to risk of local ischemia. Small sips of water may be given but eating and drinking should be avoided due to risk of vomiting and aspiration of vomitus into the airway in neurotoxic snakebites. Patient should be taken to the nearest medical facility without delay.

ADVERSE REACTIONS:

PANAF-Premium derived from equines, is heterologous to humans and can give either early or late reactions. Inj. Adrenaline should be always kept handy, before starting the doses of Snake Venom Antiserum.

ANTIVENOM REACTIONS			
Type	Early (within few hours)		Late 5 days or more
	Anaphylactic	Pyrogenic	Serum Sickness
Time Line	Develops within 3 - 60 minutes of starting antivenom	Develops within 1 – 2 Hours of starting antivenom	Appear after about 5 to 24 (avg. 7) days after injection of antivenom
Symptoms	Cough, tachycardia, itching (especially of scalp) urticaria, fever, nausea, vomiting and headache	Chills, fever, vasodilatation and fall of blood pressure	Itching, urticaria, fever, arthralgia, peri-articular swelling, proteinuria, and sometimes neurological symptoms
Recommended Treatment	1. Stop administration of antivenom temporarily. 2. Give inj. Adrenaline (1:1000) 0.5 to 1 ml for adults and 0.01 mg/kg for children by I.M. route. 3. Repeat the dose if required every 5 to 10 minutes. 4. In addition, administration of 10- 25 mg of chlorpheniramine maleate for adults / 0.2mg/kg for children may be given by I.V. route followed by Hydrocortisone 100 mg for adults / 2 mg/kg for children by I.V. route. 5. In pyrogenic reaction patient may be physically cooled (tepid sponging of the skin and fanning and given antipyretics (paracetamol). 6. Hypovolaemia should be corrected by I.V. fluids.		Serum sickness should be treated 5-day course of anti-H1 histamines such as chlorphenamine. Patients who failed to respond in 24 - 48 hours should be given 5-day course of once daily prednisolone. Chlorphenamine dose: Adults 2 mg 6 hourly, children 0.25 mg/kg/day in divided doses. Prednisolone dose: Adults 20mg, children 0.7 mg/kg/day as a single daily dose.

PREGNANCY AND LACTATION:
Considering the risk associated with snake bite envenoming, pregnancy is not a contraindication for the administration of PANAF-Premium subsequent to snake bite.

DRUG INTERACTIONS:
There are no known drug interactions reported.

HOW IT IS SUPPLIED:
Lyophilized PANAF-Premium is supplied in 20 ml glass vials along with Sterilized Water for Injections B.P. 10ml for the purpose of reconstitution.
After reconstitution, each ml of PANAF-Premium neutralizes the following number of murine median lethal doses (LD_{50}) and micrograms of venom neutralized, at a minimum–

Bitis arietans	≥ 25 LD_{50} (338 ug)	*Bitis gabonica*	≥25 LD_{50} (458 ug)
Bitis nasicornis	≥ 20 LD_{50} (529 ug)	*Bitis rhinoceros*	≥ 25 LD_{50} (615 ug)
Echis leucogaster	≥ 25 LD_{50} (872 ug)	*Echis ocellatus*	≥ 25 LD_{50} (556 ug)
Echis carinatus	≥ 25 LD_{50} (384 ug)	*Naja haje*	≥25 LD_{50} (152 ug)
Naja melanoleuca	≥20 LD_{50} (204 ug)	*Naja nigricollis*	≥ 20 LD_{50} (552 ug)
Dendroaspis polylepis	≥25 LD_{50} (168 ug)	*Dendroaspis viridis*	≥ 25 LD_{50} (310 ug)
Dendroaspis jamesoni	≥ 25 LD_{50} (277 ug)	*Dendroaspis angusticeps*	≥ 25 LD_{50} (796 ug)

Cresol (Preservative) NMT 0.25% v/v
Glycine B.P stabilizer, Sodium Chloride B.P excipient

STORAGE:
Lyophilized PANAF-Premium is stable at room temperature and should be stored preferably at a temperature below 30°C.

SHELF LIFE-Four years from manufacturing

CONTRAINDICATIONS AND PRECAUTIONS:
There are no known contraindications for the administration of Snake Venom Antiserum (Pan Africa). Proper precautions are necessary when dealing with patients with known hypersensitivity to constituents of the product. Premedication with Inj. Adrenaline (250 mcg 1:1000 for adults, 100-200 mcg 1:1000 for children) has been shown to reduce the risk of severe early adverse reactions to equine immunoglobulin-based antivenoms in a clinical trial. In hemotoxic bites, intramuscular injections should be avoided until coagulopathy has been corrected to avoid formation of haematoma and oozing of blood. Tight (arterial) tourniquets are contraindicated after snakebite because of their well-established risk of causing gangrene of the affected limb.

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