

Joint Trauma System Clinical Practice Guideline

Global Snake Envenomation Management



Background

Snakebite, recently declared a neglected tropical disease and global health priority by the World Health Organization (WHO), results in an estimated 2.5 million envenomations, 138,000 deaths and over 500,000 cases of permanent disability worldwide every year.¹⁻¹⁰ Snake, spider, and scorpion envenomations are a common environmental and occupational hazard for military forces worldwide.¹¹⁻⁴⁶ The consequences of an envenomation range from mild local effects to permanent disability or death, and the outcome is largely determined by the time to antivenom treatment and the level of training of the medical providers involved.

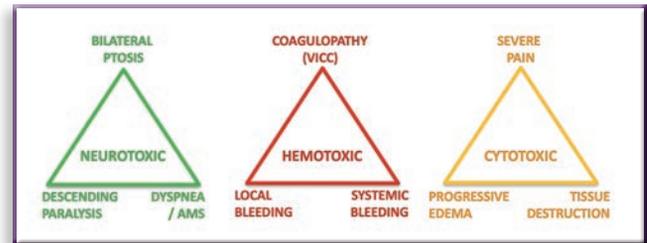
Once an envenomation has occurred, the provider and patient are racing against the clock to neutralize active venom components before extensive damage has occurred. Necrosis caused by cytotoxic venoms cannot be reversed, but it can be prevented by early antivenom administration or arrested before further damage can occur in cases of late antivenom treatment.^{1,7,47,48} Hemotoxic venoms can induce coagulopathies within 1 hour of the envenomation, which is quickly followed by a standard progression of worsening local and systemic external and internal bleeding. Neurotoxic venoms can act rapidly and be fatal. Africa is one of the few places in the world with snakes like the black mamba that are capable of killing a human within 1 hour due to direct effects of the venom, and most patients with mamba envenomation who are not rapidly treated with antivenom will die within 2-6 hours from respiratory arrest.^{1,49} When a neurotoxic bite occurs, rapid antivenom administration prior to the onset of respiratory muscle weakness can arrest the progression of descending paralysis before serious systemic manifestations develop.^{1,50,51} Every hour wasted between bite and antivenom administration is strongly associated with sharp increases in mortality and the development of chronic or permanent sequelae including amputation, disfigurement, PTSD, blindness, kidney injury, infections, and partial or complete loss of function of the bitten limb.^{4,7,8,52-58}

These guidelines will cover the continuum of snakebite care for snake envenomations in all combatant commands.

General Principles of Snakebite Management

Snakebite clinical triads: There are three major clinical syndromes of snakebite envenomation worldwide and three major signs and symptoms of each. All dangerous snakes capable of injuring or killing a human will produce at least one sign or symptom from at least one of the three major snakebite syndromes (neurotoxic, hemotoxic, and cytotoxic). Specific antivenoms required will vary regionally but the major triads are applicable globally.

Do not try to ID the snake: Snake identification is unreliable and should not be purposely attempted. DO NOT attempt to catch or



kill the snake; treatment is clinical and the snake species does not need to be identified.

Antivenom fundamentals: There are NO ABSOLUTE CONTRA-INDICATIONS TO ANTIVENOM for patients with symptomatic snake envenomations. The high risk of permanent damage posed by untreated venom in the body is far greater than the low risk of anaphylaxis associated with high-quality modern antivenoms.

Antivenom administration at the earliest possible opportunity is the gold standard of snakebite care and most effective way to reduce the risk of death or permanent disability in these patients.

- Early antivenom administration in the field at or near the point of injury may resolve the underlying envenomation before any serious systemic signs or symptoms develop.
- Ignore the packaging and manufacturer insert and treat according to the guidelines outlined in this CPG.
- Dosing and administration of recommended antivenoms in this CPG can vary significantly between products; refer to Appendix B for specific instructions for each product you have on hand.
- Antivenom may be given by IV or IO injection or infusion.^{54,59} IV is preferable but IO is an acceptable alternative and should not influence the efficacy of the medication.
- DO NOT give antivenom by IM or SQ injection, even if packaging says you can. The serum concentrations of antivenom given by IM or SQ injection will never achieve more than a fraction of the serum concentrations rapidly achieved from the intravascular route.
- DO NOT administer test doses of antivenom to check for hypersensitivity prior to giving the full dose. Test doses have no predictive value for identifying patients with hypersensitivity and waste both time and antivenom.⁶⁰⁻⁶³
- Antivenom dosage IS NOT WEIGHT-BASED and there is no difference in dosing between adults and children. The dose of antivenom needed to achieve control of the envenomation is proportional to the dose of venom injected into the patient. The quantity of venom injected into the patient corresponds to the severity of the envenomation syndrome(s).
- Antivenom should be given as many times as needed until control of envenomation is achieved.

- Overdosing antivenom is not a concern during the active treatment phase, and the worst-case scenario is an allergic reaction. If a patient did develop a reaction to large doses, it would most likely manifest as a late reaction called serum sickness (fever, rash, arthralgia, etc.) 1–3 weeks later and can be managed with antihistamines or steroids if the patient is uncomfortable. Serum sickness may be uncomfortable but is not life-threatening.

Establish a timeline and trend changes over time: Serial assessments and documentation are essential because the resolution of certain clinical findings will be used to determine when the right dose of antivenom has been given. At a minimum always document the following:

- Time and date when bite occurred
- Time elapsed from bite to presentation under your care (record as minutes, hours, days, etc)
- Time when the first dose of antivenom is given (defined as Hour 0, written as H0)
- Always repeat a complete snakebite assessment at hours 2, 4, 6, 12, and 24 (H2, H4, H6, H12, H24) since the first dose of antivenom was given in order to trend the clinical evolution of the syndrome over time

Snakebites are clinically dynamic emergencies: Patients can present with one syndrome initially and develop signs and symptoms of another later on. For example, a patient who presents with local pain and mild swelling at H0 could develop local bleeding or ptosis at H4. Always look for signs and symptoms of all three triads when reassessing.

Universal Approach to Snakebite Assessment, Diagnosis, and Treatment

Initial Approach to the Snakebite Patient – Universal Recommendations

1. Airway, breathing, circulation, and rapid antivenom administration are the critical priorities during stabilization and treatment of a snakebite casualty.
 - a. Assess ABCs; identify and address any immediate life threats before proceeding. Treat emergent secondary issues that may be present (such as anaphylaxis or hypovolemic shock) according to standard clinical protocols.
 - b. Establish IV or IO access in a non-bitten limb before proceeding.
2. DO NOT apply constricting bandages or tourniquets as these may worsen local tissue injury and increase the risk of permanent disability.^{64–66}
 - a. If a tourniquet is already in place, do not remove it until you are ready to treat and resuscitate the patient as a rapid decompensation can occur.^{67,68} When removing a tourniquet do so sequentially (loosen for several seconds–tighten–observe–repeat) over 20–30 minutes; if symptoms develop at any time administer antivenom and wait at least 30 minutes before resuming tourniquet release. Ideally, this should not be done until antivenom is available but prolonged evacuation times without antivenom may necessitate the risk of earlier removal to prevent limb death. Refer to TCCC guidelines for tourniquet conversion in these settings.
3. If and when conditions allow, minimize patient activity and loosely immobilize bitten limb to reduce movement without constricting tissues.
 - a. If antivenom is not available onsite, choose whichever evacuation option will safely get your patient to the antivenom in the shortest amount of time. This includes allowing the patient to walk to help when needed.
 - b. If conditions allow during transport, maintain the bitten limb in a position of comfort that is elevated above the level of the heart.

- c. Once the patient has arrived at the clinic and can be placed in a bed, aggressively elevate the bitten limb (aim for a minimum 60° angle in a supine patient if possible and tolerated by patient) to reduce oncotic pressure on swollen tissues.
4. Evaluate for specific signs and symptoms of snake envenomation. See Table 1 (page 47) and refer to **Specific Criteria for Initial Antivenom Treatment and Repeat Doses** for additional information.
 - a. Perform a physical examination and history focused on identifying signs and symptoms of neurotoxic, hemotoxic, and cytotoxic envenomations syndromes
 - i. Determine how long ago the bite occurred
 1. Circle the site of the bite wound and write the specific time that it occurred with a permanent marker on the patient
 - ii. Do not rely on fang marks to assess the possibility of a bite or envenomation. Snakebites can leave punctures, multiple lacerations, or even no obvious fang marks whatsoever.
 - iii. Rapid examination for signs of pain, swelling, or tissue destruction (cytotoxic syndrome)
 1. Separately mark the leading edge of both pain (dashed line) and edema (solid line) with a permanent marker and record time of observation next to each line
 - iv. Rapid examination for signs of local or systemic bleeding (hemotoxic syndrome)
 1. Inspect the bitten limb for persistent local bleeding > 30 minutes from the bite wound (if visible) or other lesions.^{1,69–71}
 2. Inspect the molar gingiva and other mucosa for signs of systemic bleeding.^{1,69,70}
 - v. Rapid examination for signs of neuromuscular weakness (neurotoxic syndrome)
 1. Evaluate respiratory muscle weakness by single breath count testing⁷² and repeat periodically to trend improvement or deterioration in respiratory function over time.
 - a. The single breath count (SBC) test requires no equipment to perform and is easily performed in austere settings:
 - i. Ask the patient to take a deep breath and count as high as possible in their normal speaking voice without taking another breath. Demonstrate the test to the patient, then have them repeat it and record the highest number reached.
 1. SBC correlates closely with spirometry. Normal SBC is approximately 50 and SBC < 20 is associated with the need for mechanical ventilation.
 - b. If spirometry is available, this can be used in place of the single breath count test by evaluating the negative inspiratory force (NIF) and/or forced vital capacity (FVC).
 2. Conduct gross assessment and pay particular attention to the following:
 - a. Signs and symptoms of descending flaccid paralysis:
 - i. Ptosis, diplopia, neck flexor muscle weakness, bulbar weakness, etc.^{1,54,73}
 - b. Signs and symptoms of parasympathetic/cholinergic crisis:
 - i. SLUDGE mnemonic–Salivation, Lacrimation, Urination, Defecation, GI distress, Emesis
 - b. Perform and/or check the clinical laboratory tests listed below (if available)

- i. Advanced laboratory tests
 1. Complete blood count (CBC)
 - a. Hemoglobin (Hb) or hematocrit (HCT) if no CBC but separate testing for either Hb or HCT is available
 2. Prothrombin time (PT), partial thromboplastin time (PTT), and international normalized ratio (INR)
 3. Fibrinogen
 4. Comprehensive metabolic panel (CMP)
 5. Creatine kinase (CK)
 - ii. Simple coagulation test for austere environments
 1. Use the whole blood clotting test (WBCT) as described in Appendix A to diagnose and monitor coagulopathy if advanced labs not available
5. If the patient is being medically evacuated from the field or between roles of care, confirm that the receiving facility has an adequate supply of the appropriate regionally specific antivenoms listed in this CPG to ensure treatment coverage against local species of concern.
 - a. Evacuation is not an alternative to antivenom administration. A patient whose snakebite warrants evacuation will require antivenom, and the earlier it can be given the greater the chance of a full recovery without permanent disability. DO NOT delay administration of antivenom in the field to a patient with an envenomation.
 6. If clinical evidence of envenomation is present and treatment is occurring in a hospital setting, always admit to a bed with continuous vital sign monitoring if available. If no initial clinical evidence of envenomation, admit for 24 hours for observation. If treating in the field, continuously monitor patient trends for signs of progression, improvement, or deterioration.
 7. Symptoms should be expected within 24 hours; if the patient is completely asymptomatic after 24 hours then they most likely received a dry bite and can be discharged as detailed in step 17.

Initial Antivenom Treatment – Universal Recommendations

Antivenom dosing, preparation, and administration recommendations vary by product and are detailed in **Appendix B: Coverage, initial dosing, preparation, and administration of antivenoms included in this CPG**. Refer to the specific guidelines for the included product you have available prior to administering the antivenom.

8. The presence of one or more of the criteria for each category in Table 1 is generally sufficient to diagnose the syndrome, determine severity, and initiate treatment. Patients who present with “mixed syndromes” (signs and symptoms of > 1 syndrome present) receive the same initial doses of antivenom as those presenting with a single syndrome.
 - a. To identify the appropriate antivenom and initial dosing for your patient, refer to the **Regionally Specific Snakebite Treatment for Each Combatant Command** (page 49) section later in this document. Once you have identified the appropriate product, refer to the detailed information sheets in **Appendix B** (page 63) for comprehensive instructions on preparation, dosing, and administration of each antivenom in the CPG.
9. In certain instances, pretreatment with a low dose of SQ epinephrine prior to antivenom administration may be recommended to reduce the risk of an adverse reaction to antivenom therapy. Refer to **Pretreatment with Epinephrine to Prevent Early Adverse Reactions** (page 47) for specific guidelines on pretreatment.
10. The majority of severe early reactions to antivenom occur within the first 5–60 minutes after antivenom administration. Observe and monitor the patient closely at the bedside for a minimum of 1 hour after each dose of antivenom has been given.
 - a. Refer to **Management of Mild, Moderate, and Severe Antivenom Reactions** (page 48) for specific guidelines on how to manage mild, moderate, or severe reactions to antivenom therapy

TABLE 1: Simplified Universal Diagnosis and Treatment Criteria for Snakebite Worldwide

	Neurotoxic Syndrome	Hemotoxic Syndrome	Cytotoxic Syndrome
Mild	Local S/Sx (paresthesias; neuropathic pain; piloerection; muscle spasm, fasciculations)	Coagulopathy ± persistence of local bleeding from bite wound > 30 mins after bite	Severe pain; edema below elbow or knee; limited blistering within several inches of the bite wound
Moderate	Systemic S/Sx (bilateral ptosis GI symptoms; visual, auditory, or other sensory disturbances; widespread hyperesthesia)	Moderate systemic bleeding (old scabs, gingival bleeding, epistaxis, etc); bruising distant from the bite wound	Edema above elbow or knee but not beyond shoulder or hip; moderate local blistering along bitten limb segment
Severe	Difficulty speaking; altered mental status; respiratory muscle weakness causing difficulty breathing; shock or otherwise unstable patient	Active GI bleed (usually hematemesis) or other internal bleeding; severe anemia; altered mental status; shock or otherwise unstable patient	Progressive edema beyond shoulder or hip; severe necrosis or widespread blistering; symptomatic bite to head, neck, or torso; altered mental status; shock or otherwise unstable patient
Initial Dose Antivenom	<i>Refer to Appendix B for dosing recommendations specific to each antivenom in this CPG</i>	<i>Refer to Appendix B for dosing recommendations specific to each antivenom in this CPG</i>	<i>Refer to Appendix B for dosing recommendations specific to each antivenom in this CPG</i>
Criteria for additional AV doses at hours 2, 4, 6, 12, 24 (as needed)	<i><u>Additional doses (Appendix E) if:</u> persistence or worsening of systemic neurotoxic S/Sx. Continue to re-administer 2 vial boluses as needed at hours 2, 4, 6, 12, and 24 until indications of improvement begin to appear (↑SBC, ↑LOC, ↑strength, etc.)</i>	<i><u>Additional doses (Appendix E) if:</u> persistence, resumption, or new onset of any active external or internal bleeding OR S/Sx of active venom confirmed by secondary recurrence of abnormal WBCT</i>	<i><u>Additional doses (Appendix E) if:</u> significant increase in edema (such as beyond major joint) OR significant increase in pain (severity of pain and/or how far pain radiates up the bitten limb)</i>

S/Sx = signs & symptoms; SBC = single breath count test; LOC = level of consciousness; WBCT = whole blood clotting test.

Supportive Care and Ongoing Management – Universal Recommendations

11. Provide supportive care and address secondary issues related to the envenomation as follows:
 - a. Anticipate the need for aggressive airway management with intubation and prolonged ventilation in all patients presenting with neurotoxic envenomation, particularly those who present late with impending respiratory failure or fail to respond to antivenom.
 - i. For any neurotoxic snakebite producing a cholinergic crisis, consider atropine 0.5 mg IV/IO titrated by auscultation to dry up bronchial and oral hypersecretions posing a risk to airway or breathing.
 1. Repeat original dose every 5 minutes until resolution of crackles, rales, bronchospasm has been achieved. Pediatric atropine doses should be weight based at a dose of 0.01 mg/kg, up to 0.25 mg.
 - ii. For neurotoxic snakebites in the Middle East, North Africa, and Central Asia without cholinergic crisis, but causing ptosis and respiratory muscle weakness, consider administering trial dose of 0.5 mg atropine followed by 1.0 mg neostigmine IV/IO to temporarily reverse neuromuscular weakness and delay the need for intubation. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to a maximum of 0.25 mg atropine with 0.5 mg neostigmine.^{54,74–77}
 1. Not all patients will respond, but those who do will show temporary improvement (reversal of ptosis, increased respiratory muscle strength, etc). If no response to neostigmine, do not reattempt. If positive response is achieved, repeat every 1–4 hours as needed (maximum dose in 24 hours = 10 mg adults/5 mg pediatric) until antivenom has definitively reversed the paralysis.
 - b. For hemotoxic envenomations, all internal and external active bleeding should cease within 30–60 minutes of antivenom administration once the appropriate dose has been given. Packed red blood cell or whole blood transfusion can be considered if the patient is in hemorrhagic shock.^{17,69,70,78–82} Platelets, fresh frozen plasma, cryoprecipitate, TXA, and other agents are NOT EFFECTIVE in these cases due to the mechanism of the venoms.
 - c. Ketamine and fentanyl are preferable for analgesia. Histamine release from morphine may mask signs of an allergic reaction or worsen hypotension.
 - d. It is important to keep the limb significantly elevated (> 60° is ideal) whenever possible to limit dependent edema and swelling.
 - e. DO NOT routinely de-roof or aspirate blisters, bullae, or blebs unless they are causing significant discomfort or uncontrolled rupture appears imminent. If abscess is suspected, treat according to existing protocols for abscess management.
 - f. DO NOT perform fasciotomy for snakebites. Compartment syndrome is rare in snakebites. Even in cases of confirmed elevated intracompartmental pressure, patients who received antivenom without fasciotomy experienced better outcomes (shorter recovery time and less long term morbidity) than those who received fasciotomy.^{83–86} Appropriate use of antivenom should resolve the underlying issue that is producing the elevated intracompartmental pressures.
 - g. DO NOT routinely administer antibiotics unless signs and symptoms of an infection are present. Direct infections are rare from most snakebites when prompt, appropriate treatment is given.⁵⁴
12. Monitor the patient closely for signs of progression in the initial hours of treatment until control of symptoms has been achieved.
 - a. Serial assessments for signs and symptoms of the neurotoxic, hemotoxic, and cytotoxic syndromes should be repeated at hours 2, 4, 6, 12, 24 (H2, H4, H6, H12, H24).
13. Within the first 24 hours, antivenom may be given at hours 0, 2, 4, 6, 12, and 24 according to the specific criteria for antivenom treatment listed under **Specific Criteria for Initial Antivenom Treatment and Repeat Doses** (page 47)
 - a. If the treatment criteria have not been resolved at any of these intervals, give an additional dose of antivenom at hours 2, 4, 6, 12, and 24 until control is achieved. Refer to **Appendix B: Coverage, initial dosing, preparation, and administration of antivenoms included in this CPG** (page 63) for specific dosage instructions for each product.
 - b. If symptoms reappear or persist for more than 24 hours after the first dose of antivenom was given, additional treatment intervals should be discussed with a physician expert.
 - c. If 10 or more vials of a single antivenom have been given without any indications of improvement, consider changing to second-line antivenom if possible as species may not be covered. If **any indications of improvement** have been observed, continue with the antivenom you are using.
14. If the patient is asymptomatic but coagulopathy persists 24 hours after the first dose of antivenom was given, administer a dose of antivenom and repeat laboratory tests every 24 hours until resolution.
15. Continuous monitoring for effectiveness of antivenom dose must be done. Occasionally, pockets of venom can be trapped in swollen tissue compartments and escape into the bloodstream once circulation has improved. This is called recurrent envenomation and is most common within the first 24–48 hours after a severe bite with extensive swelling and blistering.^{78,87–93}
 - a. Continuous clinical monitoring includes hourly checks of vital signs, urine output, and detailed assessment for new or worsening signs of neurotoxic, hemotoxic, or cytotoxic envenomation.
 - b. Serial laboratory studies including CBC, CMP, PT/PTT/INR, CK, fibrinogen levels (or WBCT if no advanced testing available) may be repeated every 2 hours while signs of envenomation persist.
 - c. After signs of clinical resolution, monitoring can decrease to every 6 hours.
16. If indications of recurrent envenomation are detected more than 24 hours after the first dose of antivenom was given, treat as follows:
 - i. Asymptomatic patient with coagulopathy and no other findings
 1. Treat according to Step No. 16
 - ii. Symptomatic patient with new or worsening pain, swelling, bleeding, neurotoxicity, or other indications of active envenomation:
 1. Administer an additional dose of antivenom every 2 hours until acute symptoms have resolved completely
17. Patients should be held for at least 24 hours after resolution of all signs and symptoms, and the following steps should be completed prior to discharge:
 - a. Repeat blood tests before releasing the patient to ensure resolution of coagulopathy.
 - b. Administer a booster dose of tetanus toxoid if needed.
 - c. Patients should be instructed to return if any new or worrying signs or symptoms develop.

18. Serum sickness is characterized by flu-like symptoms ± rash that typically develops between 1 and 3 weeks after antivenom administration. It is rare with highly purified modern antivenoms but may occur more frequently with some of the second and third line antivenoms listed in this CPG.⁹⁴⁻⁹⁷
 - a. Serum sickness may be uncomfortable but is not dangerous. Management is either symptomatic or with a course of oral steroids.^{94,95,97-99}
2. **H2, H4, H6, H12, H24:** A previously normal coagulation test that changes to abnormal in the presence of any new symptoms meets criteria to administer an additional dose of antivenom. This also applies to a WBCT that was abnormal, normalized several hours after antivenom, but then changes to abnormal again later (recurrent envenomation).⁷⁸
3. **Coagulopathy remains abnormal at H24:** If WBCT or other tests of coagulation remain abnormal at H24, administer an additional dose of antivenom and repeat every 24 hours until resolution of coagulopathy has occurred.

Specific Criteria for Initial Antivenom Treatment and Repeat Doses

Cytotoxicity: The presence of significant local pain OR progressive edema OR signs of tissue destruction (bruising, blistering, necrosis) is an indication for initial administration of antivenom.^{1,47,48,79,100-105} If any of these criteria (or other systemic signs and symptoms) are present, treat immediately and do not wait for irreversible damage to occur before deciding to give antivenom. Note that the progression of edema at any treatment interval is an indication to administer additional antivenom; however, edema may not begin to noticeably decrease for several days and severe edema may take 1–2 weeks or longer to completely resolve. **WORSENING** edema is therefore a treatment criteria, persistence of edema without any progression IS NOT a treatment criteria. Worsening pain that increases significantly in severity or moves proximally up the limb is another indicator for antivenom treatment.

Neurotoxicity: The onset, persistence, or resumption of systemic neurotoxic signs of envenomation (dyspnea, neck flexor muscle weakness, bulbar muscle weakness, reduced level of consciousness, ↓ respiratory muscle function, etc.) at any of the antivenom treatment intervals is always an indication to administer or re-administer antivenom.^{1,49,106-108} Monitor respiratory function using negative inspiratory force (NIF) or forced vital capacity (FVC), single breath count test (SBC), capnography, spirometry, peak flow meters, etc.^{1,54,72} In patients who have not reached the late stages of respiratory distress/arrest, the first indications that paralysis is improving may be apparent within 30–60 minutes once the right dose of antivenom has been achieved. In patients who are already intubated, it may take hours for reversal to occur after antivenom. This typically occurs within 1–3 hours but may take 6–12 hours or longer in some patients. There are numerous documented cases of patients who did not receive antivenom and required prolonged mechanical ventilation ranging from several days up to 13 weeks before recovery. Antivenom typically either reverses the syndrome before it progresses or dramatically shortens the duration of paralysis.

Bleeding: The onset, persistence, or resumption of any active local or systemic bleeding at any of the standard assessment intervals (0, 2, 4, 6, 12, 24 hours) is always an indication to administer or readminister antivenom regardless of the WBCT result at the time.^{1,70,78,106,109-111} All external and internal bleeding will cease when the appropriate dose of antivenom has been given and actively circulating venom has been neutralized.

Whole blood clotting test (WBCT) and other tests of coagulation: Tests of coagulation usually normalize within 2–6 hours after the effective dose of antivenom has been achieved but in some cases it may take longer for these labs to fully normalize after antivenom therapy.^{78,112-120} WBCT procedure and interpretation is covered in **Appendix A: Whole Blood Clotting Test (WBCT) for Venom-Induced Consumptive Coagulopathies (VICC)**. There are three situations where an abnormal WBCT or other abnormal laboratory tests of coagulation (e.g. fibrinogen, PT/PTT/INR, etc) should be treated with antivenom:

1. **Initial assessment at H0:** Coagulopathy after a snakebite is an indication to give antivenom. If the coagulation test is abnormal but the patient is otherwise asymptomatic, repeat the test

Sudden collapse syndrome: In rare cases, a patient may rapidly deteriorate in the first 5–30 minutes after the bite and present with profound hypotension, tachycardia, angioedema, altered level of consciousness, etc..^{1,122-130} These patients should be aggressively treated for severe anaphylaxis and severe envenomation simultaneously. Treat anaphylaxis aggressively according to anaphylaxis protocols. Treat the envenomation with an initial high dose (at least 6 vials) of antivenom by rapid IV push, and support the patient with airway management, fluids, and other interventions as appropriate.^{122,123,125,131,132} Most patients presenting with hypotension or angioedema are responsive to epinephrine, but may require IV epinephrine infusions to achieve this effect if they are unresponsive to IM epinephrine.¹²²

Sudden Collapse Syndrome Treatment Protocol

1. Patient presents within 30 minutes of the bite with rapid onset shock ± angioedema, altered mental status, systemic bleeding, and diarrhea.^{1,122-130}
 - a. Stabilize with IM or IV epinephrine and fluids as per anaphylaxis protocols
 - i. Intubate for airway edema not rapidly responsive to epinephrine
 - b. Follow epinephrine immediately with a high dose of the appropriate regional antivenom given by rapid IV or IO push during the resuscitation
 - c. Maintain blood pressure with IV or IO fluids and epinephrine until antivenom has taken effect to reverse the hypotension

Pretreatment With Epinephrine to Prevent Early Adverse Reactions

Epinephrine is the only prophylactic treatment (pretreatment) that has been shown to effectively reduce the incidence of early adverse reactions (EARs) such as anaphylaxis.^{60,98,133-136} **DO NOT** pretreat with steroids or antihistamines. **DO NOT** administer test doses of antivenom to check for hypersensitivity.⁶⁰⁻⁶³

Pretreatment Guidelines for Preventing Early Adverse Reactions (EARs) to Antivenom

Relative contraindications to epinephrine pretreatment include age > 70, hypertension, ischemic heart disease, history of stroke, suspected or confirmed intracranial hemorrhage. No absolute contraindications.

1. Pretreatment with epinephrine prior to antivenom administration is not indicated by default for all antivenoms, and is recommended only under the following circumstances:
 - a. Unstable snakebite patients with signs of shock.
 - b. Known history of atopy (asthma, eczema, etc.), equine hypersensitivity, or severe reactions to antivenom in the past.
 - c. Use of certain second or third line antivenom due to the high rate of serious EARs associated with these products. Refer to Appendix B for specific recommendations for each product.

2. Standard epinephrine pretreatment protocol:
 - a. Adult dose is 0.25 mg of 1:1000 epinephrine given by SQ injection several minutes prior to antivenom administration.
 - b. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to 0.25 mg.^{60,134,135,137,138}
 - c. Patients with signs of shock should be given epinephrine by IM injection in the lateral thigh

Management of Mild, Moderate, and Severe Antivenom Reactions

If signs and symptoms of an early adverse reaction develop during administration of antivenom:

- a. Mild or moderate reaction during infusion:
 - i. Stop the infusion and manage mild or moderate reactions (e.g. nausea, vomiting, urticaria, pruritus, chills, fever, etc) symptomatically as needed with antiemetics, antihistamines, steroids, etc. Reassess the patient once the reaction has been controlled; if the antivenom treatment criteria for cytotoxic, hemotoxic, or neurotoxic syndromes have not resolved completely then resume the infusion at a slower rate over 30 minutes.
 - ii. If giving via push, dilute the remaining dose of antivenom in a 100 mL bag of normal saline and give as 30-minute infusion.
- b. Severe reaction (anaphylaxis) during infusion:
 - i. Stop the infusion and treat according to the anaphylaxis treatment protocol. Reassess the patient once the reaction has been controlled; if the antivenom treatment criteria for cytotoxic, hemotoxic, or neurotoxic syndromes have not resolved completely then resume the infusion at a slower rate over 30 minutes.
 - ii. If giving via push, dilute the remaining dose of antivenom in a 100–250 mL bag of normal saline and give as 30-minute infusion.
- c. If the reaction reoccurs:
 - i. Stop the infusion and consult a physician expert via telemedicine to discuss next steps for management.

Anaphylaxis Treatment Protocol^{15,60,94,98,127,128,139–145}

NOTE: Intubate for airway edema not rapidly responsive to epinephrine.

1. If anaphylaxis occurs after antivenom administration, treat according to the following protocol:
 - a. First line treatment of anaphylaxis is rapid administration of 1:1000 epinephrine (initial adult dose = 0.5 mg IM in the lateral thigh for rapid absorption). Epinephrine can be repeated as needed until the patient has stabilized and/or an intravenous or intraosseous infusion administered as per standard protocols if the patient fails to respond to IM doses.
 - i. Epinephrine should always be given prior to antihistamines or steroids to counter the immediate life-threats of bronchospasm and vasodilation.
 - b. After epinephrine has been given:
 - i. Give methylprednisolone 125 mg IV.
 - ii. Give diphenhydramine or promethazine 50 mg IV.
 - iii. Consider adding an H2 antihistamine such as ranitidine.
2. If anaphylaxis occurs during administration of antivenom, stop the antivenom administration to treat the reaction then resume the antivenom administration as described below.

Management of Late Reactions to Antivenom (Serum Sickness)

Serum sickness is characterized by flu-like symptoms ± rash that typically develops between 1–3 weeks after antivenom administration. Serum sickness may be uncomfortable but it is not dangerous.

1. Serum sickness may be uncomfortable but it is not dangerous.
 - a. Management is either symptomatic with antihistamines, acetaminophen, etc or with a course of oral steroids for patients who are in significant discomfort^{94,95,97–99}

Special Situations

How to Proceed if Antivenom Is Not Available

- Antivenom is the gold standard of care for symptomatic snake envenomations and early treatment is the best strategy to prevent death, amputation, or other serious disability. Management of snake envenomations when antivenom is not available should be directed at getting the patient to the antivenom (or vice versa) as quickly as possible to prevent irreversible damage to organs and tissues.
- Mission planning before deployment should include research and procurement of the appropriate regionally specific antivenom(s) recommended in this CPG for your area of operation. If currently deployed without antivenom, efforts to acquire the appropriate antivenom(s) recommended in this CPG for your area of operations should be initiated through proper channels as fake or low-quality antivenoms are frequently found in local pharmacies throughout Africa and elsewhere in the developing world.
- For specific management until antivenom can be obtained, follow the checklist and skip the steps related to antivenom administration until it has been obtained.
- Refer to step No. 11 for specific recommendations on supportive care measures

Military Working Dogs/Multipurpose Canines

- All antivenoms can be administered to MWDs/MPCs according to the same treatment criteria and initial doses listed in this CPG; all other management should be based on the MWD CPG.

Late Presentations and Treatment Delays

- There is NO DEFINED TIME LIMIT to antivenom therapy for a symptomatic snakebite. Early antivenom within the first minutes or hours after a bite is the best means of preventing morbidity or mortality, but antivenom remains effective at resolving reversible issues like coagulopathy and preventing further irreversible tissue damage even in patients who present many hours or days after the snakebite.^{56,69,78,146,147}

Outdated Interventions That Should Not Be Performed

- DO NOT cut, suck, electrocute, burn, or use chemicals on the envenomation site.
- DO NOT apply constricting bandages, tourniquets or other circulation-reducing interventions
- DO NOT use venom extractors or other commercial snakebite first aid kits^{148–152}
- DO NOT administer test doses of antivenom to check for hypersensitivity as these are ineffective and waste both time and antivenom.^{60–63}
- DO NOT administer antihistamines or steroids as prophylactic pretreatment for prevention of anaphylaxis or other early adverse reactions (EARs) to antivenom as neither is effective as a premedication.^{133,134}

Management of Ocular Envenomation by Spitting Cobras (Venom Ophthalmia)

Spitting cobras have modified fangs that allow them to spray venom into the eyes of a predator or perceived threat.^{153–155} The venom spray widens like buckshot as it travels and the snakes aim at the glint of sunlight reflecting off of the target's eyes. The venom is harmless unless it enters the eyes (causing instantaneous burning, lacrimation, blurred vision, etc.) or the bloodstream by injection

(such as a bite), through open wounds on the skin or inside of the mouth, or by ingestion (such as drinking a glass of venom with an ulcer). If a significant amount of venom enters the bloodstream through an open wound and produces typical symptoms of a snakebite, it is treated with antivenom like any other envenomation. For ocular exposure alone without signs of systemic envenomation, antivenom is not indicated and the management is like any ocular chemical exposure with copious irrigation. Spitting cobras can also deliver a venomous bite, so it is important to rule out an actual snakebite in patients who have encountered one of these snakes.

Signs and Symptoms: Immediate signs and symptoms of venom ophthalmia include intense local pain, swelling and/or spasms of the eyelid, lacrimation, and leukorrhea.¹⁵⁶ The primary concern is corneal epithelial injury which can lead to blindness by secondary infection or scarring if not treated correctly.^{7,25,54,156-158} Treatment of venom ophthalmia is relatively simple and similar to managing a patient who has been splashed in the eyes with a harmful chemical solution.

First Aid: Confirm that the patient did not experience a snakebite in addition to the ophthalmia. Immediately irrigate the eye with copious quantities of water, normal saline, or a bland fluid such as milk if nothing else is available. Remove clothing and decontaminate the patient from head to toe with soap and water to prevent second re-exposure to dried venom.⁵⁴

Clinical Management: Apply topical anesthetic eye drops (tetracaine) to facilitate thorough irrigation and examination of the affected eyes. Irrigate the eyes thoroughly using water or normal saline for ≥ 15 minutes.¹⁵⁶

Fluorescein Stain and Examination Using a Slit Lamp or Ophthalmoscope for Corneal Injury: If present, treat with antimicrobial eye drops (such as tetracycline and chloramphenicol) or ointments and mydriatics. Reassess daily with slit lamp examination. If absent, consider benefits vs risks of antimicrobial eye drops.

Additional Treatments to Consider: Topical eye drops containing either epinephrine (1:1000) or phenylephrine (10%) are reported to immediately relieve the burning sensation produced by the venom.^{54,156}

Contraindicated Treatments: Antivenom (topical or systemic) is not indicated for patients with ocular exposure to snake venom.^{54,156,159} Topical steroids are contraindicated for these patients.

Regionally Specific Snakebite Treatment for Each Combatant Command

Whenever possible, broad-spectrum, field-stable antivenoms are recommended to enable syndromic diagnosis and treatment at the point of injury without the need to identify the species responsible for the bite. Citations of the relevant literature on safety, efficacy, and dosing for each product are provided at the end of **Appendix B**.

Determine the appropriate first line antivenom for your area of operations prior to deployment using this section, then refer back to the **Universal Approach to Snakebite Assessment, Diagnosis, and Treatment** on page 44 for detailed instructions and a stepwise approach to snakebite management throughout the course of care. Abbreviated antivenom guidelines for each regional combatant command are included below.

AFRICOM – Abbreviated Treatment Guidelines

Safe and effective broad-spectrum, field-stable antivenoms are available for all three syndromes of snake envenomation in this AOR and treatment does not require identification of the species responsible. Snakebite treatment at the point of injury is recommended for AFRICOM due to prolonged evacuation times, high incidence of snakebites, and the high risk of death or permanent disability from many venomous snakes in the AOR if early antivenom treatment is not available.

1. First line (AFRICOM–SUB-SAHARAN AFRICA):

POLYSERP-P

- FIELD-STABLE. BROAD-SPECTRUM COVERAGE FOR 24+ SPECIES CYTO/HEMO/NEURO.
- Single-source treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in sub-Saharan Africa when the causative species is either unknown or among the 24 snakes for which this product is directly indicated. Only polyvalent to include boomslangs and only antivenom for mole viper envenomations. Directly or indirectly covers all of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.
- Initial dose = 6 vials all syndromes, additional doses = 2 vials as needed.

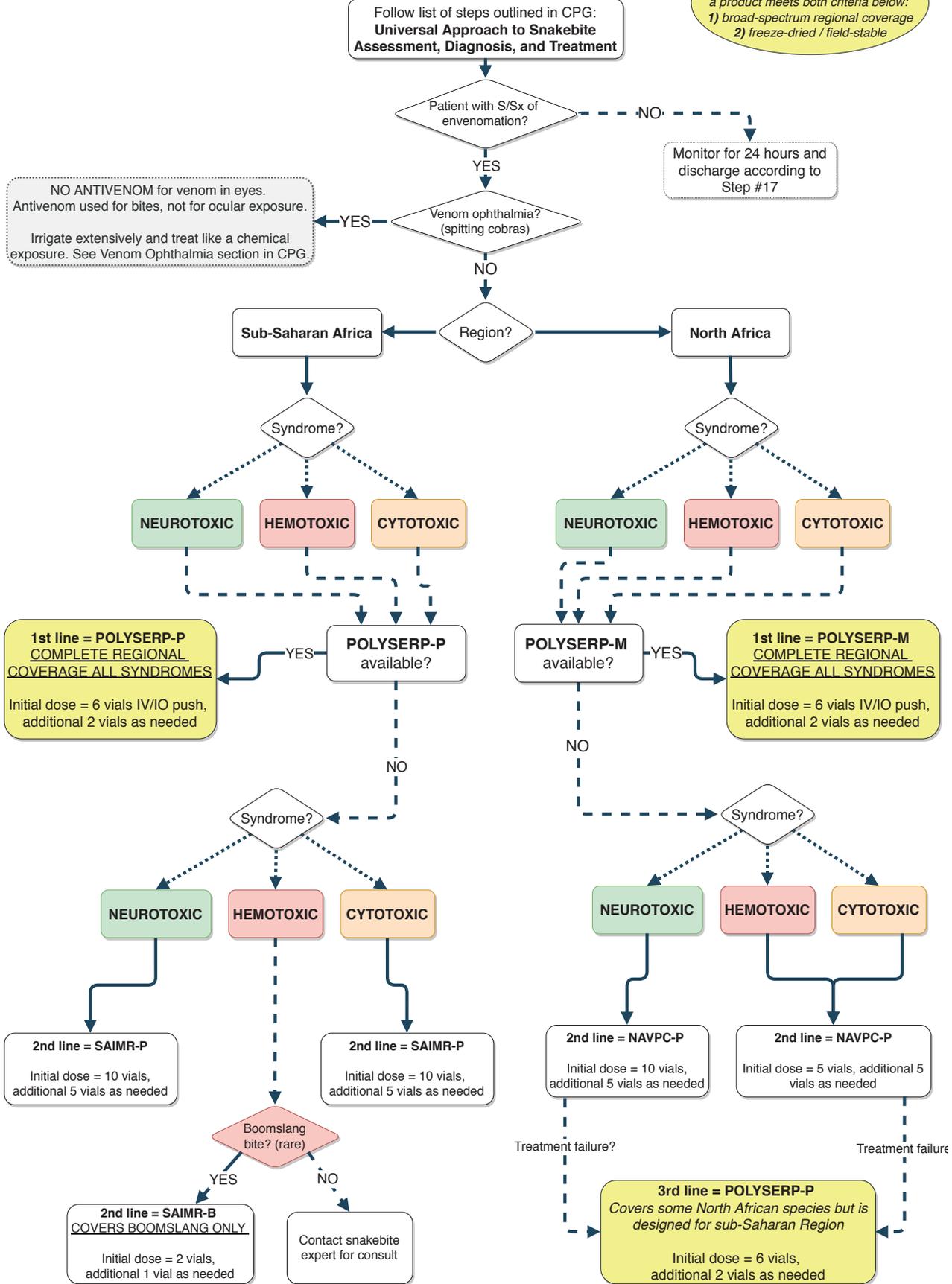
2. First line (AFRICOM–NORTH AFRICA): POLYSERP-M

- FIELD-STABLE. BROAD-SPECTRUM COVERAGE FOR 27+ SPECIES CYTO/HEMO/NEURO.

AFRICA COMMAND – FIRST LINE ANTIVENOMS			
	Neurotoxic Syndrome	Hemotoxic Syndrome	Cytotoxic Syndrome
Mild	Local S/Sx (paresthesias; neuropathic pain; piloerection; muscle spasm, fasciculations)	Coagulopathy ± persistence of local bleeding from bite wound > 30 mins after bite	Severe pain; edema below elbow or knee; limited blistering within several inches of the bite wound
Moderate	Systemic S/Sx (bilateral ptosis GI symptoms; visual, auditory, or other sensory disturbances; widespread hyperesthesia)	Moderate systemic bleeding (old scabs, gingival bleeding, epistaxis, etc); bruising distant from the bite wound	Edema above elbow or knee but not beyond shoulder or hip; moderate local blistering along bitten limb segment
Severe	Difficulty speaking; altered mental status; respiratory muscle weakness causing difficulty breathing; shock or otherwise unstable patient	Active GI bleed (usually hematemesis) or other internal bleeding; severe anemia; altered mental status; shock or otherwise unstable patient	Progressive edema beyond shoulder or hip; severe necrosis or widespread blistering; symptomatic bite to head, neck, or torso; altered mental status; shock or otherwise unstable patient
General Criteria for additional AV doses at hours 2, 4, 6, 12, 24 (as needed)	Additional doses of antivenom if: persistence or worsening of systemic neurotoxic S/Sx. Continue to re-administer 2 vial boluses as needed at hours 2, 4, 6, 12, and 24 until indications of improvement begin to appear (↑SBC, ↑LOC, ↑strength, etc.)	Additional doses of antivenom if: persistence, resumption, or new onset of any active external or internal bleeding OR S/Sx of active venom confirmed by secondary recurrence of abnormal WBCT	Additional doses of antivenom if: significant increase in edema (such as beyond major joint) OR significant increase in pain (severity of pain and/or how far pain radiates up the bitten limb)
AFRICOM 1st Line Antivenoms	Sub-Saharan Africa: Broad-spectrum coverage for all neurotoxic/hemotoxic/cytotoxic snakebite syndromes by known or unknown species - POLYSERP-P: Initial dose = 6 vials / Additional doses = 2 vials as needed North Africa: Broad-spectrum coverage for all neurotoxic/hemotoxic/cytotoxic snakebite syndromes by known or unknown species - POLYSERP-M: Initial dose = 6 vials / Additional doses = 2 vials as needed		
Antivenom Abbreviations AFRICOM	POLYSERP-P = POLYSERP PAN-AFRICA - (POLYSERP Therapeutics S.L, Spain) POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain)	POLYSERP-P = POLYSERP PAN-AFRICA - (POLYSERP Therapeutics S.L, Spain) POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain)	POLYSERP-P = POLYSERP PAN-AFRICA - (POLYSERP Therapeutics S.L, Spain) POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain)

Antivenom Algorithm: AFRICOM AOR

NOTE:
Yellow background indicates that a product meets both criteria below:
1) broad-spectrum regional coverage
2) freeze-dried / field-stable



- b. Single-source treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in North Africa (Algeria, Egypt, Libya, Morocco, Tunisia, Western Sahara) when the causative species is either unknown or among the 27 snakes for which this product is directly indicated. Directly or indirectly covers all of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.
 - c. Initial dose = 6 vials all syndromes, additional doses = 2 vials as needed.
3. **Second line (AFRICOM-SUB-SAHARAN AFRICA): SAIMR-P**
- a. NOT FIELD STABLE. BROAD-SPECTRUM AGAINST 10+ SPECIES NEUROTOXIC AND CYTOTOXIC ONLY.
 - b. Unknown neurotoxic and/or cytotoxic envenomation in sub-Saharan Africa or with no indications of improvement after 10 vials of POLYSERP-P. Will not treat hemotoxic envenomations. SOUTHERN AFRICA: Directly or indirectly covers all WHO category 1 and category 2 species for which an antivenom currently exists. EAST/CENTRAL/WEST AFRICA: Covers many cytotoxic and neurotoxic snakes in West, Central, and East Africa but has major coverage gaps with no efficacy against all WHO category 1 or category 2 hemotoxic snake species.
 - c. Initial dose = 10 vials neurotoxic/cytotoxic only, additional doses = 5 vials
4. **Second line, boomslang only (AFRICOM-SUB-SAHARAN AFRICA): SAIMR-B**
- a. NOT FIELD-STABLE. NOT BROAD-SPECTRUM. SINGLE SPECIES COVERAGE.
 - b. Confirmed or suspected boomslang bite with no indications of improvement after 10 vials of POLYSERP-P. Monovalent that can only be used to treat the WHO category 2 boomslang. Does not provide coverage against any other WHO category 1 or category 2 species.
 - c. Initial dose = 2 vials boomslang only, additional doses = 1 vial as needed
5. **Second line (AFRICOM-NORTH AFRICA): NAVPC-C**
- a. NOT FIELD-STABLE. BROAD-SPECTRUM COVERAGE 6+ SPECIES OF NEURO/HEMO/CYTO.
 - b. Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 10 vials of POLYSERP-M. Directly or indirectly covers some of the

WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.

- c. Initial dose neuro = 10 vials. Initial dose hemo/cyto = 5 vials. All additional doses = 5 vials.

CENTCOM – Abbreviated Treatment Guidelines

Safe and effective broad-spectrum, field-stable antivenoms are available for all three syndromes of snake envenomation in this AOR and treatment does not require identification of the species responsible. Snakebite treatment at the point of injury is recommended for CENTCOM due to potential for prolonged evacuation times, high incidence of snakebites, and the high risk of death or permanent disability from many venomous snakes in the AOR if early antivenom treatment is not available.

1. First line (CENTCOM-ARABIAN PENINSULA/MIDDLE EAST/CENTRAL ASIA): POLYSERP-M

- a. FIELD-STABLE. BROAD-SPECTRUM COVERAGE 27+ SPECIES OF CYTO/HEMO/NEURO.
- b. Single source treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in the Arabian Peninsula, the Middle East, and Central Asia when the causative species is either unknown or among the 27 snakes for which this product is directly indicated. Directly or indirectly covers all WHO category 1 species in the region. Directly or indirectly covers all category 2 snakes in this region for which an antivenom currently exists except for *Gloydius halys*, which is covered by Shanghai SIOBP-G or Iranian RAZI-P. Paraspecific neutralization against *Gloydius* unknown but not anticipated.
- c. Initial dose = 6 vials all syndromes, additional doses = 2 vials as needed.

2. First line Gloydius Halys only (CENTCOM-MIDDLE EAST/CENTRAL ASIA): SIOBP-G

- a. NOT FIELD-STABLE. NOT BROAD-SPECTRUM. SINGLE SPECIES COVERAGE.
- b. Monovalent for the WHO category 2 species *Gloydius halys*. Indicated as first line only for confirmed envenomation by *Gloydius halys* or related *Gloydius* species. Indicated as second line for unknown cytotoxic and/or hemotoxic envenomation in Middle East or Central Asia with no signs of improvement after 10 vials of POLYSERP-M. Does not provide coverage against any other WHO category 1 or category 2 species.

CENTRAL COMMAND – FIRST LINE ANTIVENOMS			
	Neurotoxic Syndrome	Hemotoxic Syndrome	Cytotoxic Syndrome
Mild	Local S/Sx (paresthesias; neuropathic pain; piloerection; muscle spasm, fasciculations)	Coagulopathy ± persistence of local bleeding from bite wound > 30 mins after bite	Severe pain; edema below elbow or knee; limited blistering within several inches of the bite wound
Moderate	Systemic S/Sx (bilateral ptosis GI symptoms; visual, auditory, or other sensory disturbances; widespread hyperesthesia)	Moderate systemic bleeding (old scabs, gingival bleeding, epistaxis, etc); bruising distant from the bite wound	Edema above elbow or knee but not beyond shoulder or hip; moderate local blistering along bitten limb segment
Severe	Difficulty speaking; altered mental status; respiratory muscle weakness causing difficulty breathing; shock or otherwise unstable patient	Active GI bleed (usually hematemesis) or other internal bleeding; severe anemia; altered mental status; shock or otherwise unstable patient	Progressive edema beyond shoulder or hip; severe necrosis or widespread blistering; symptomatic bite to head, neck, or torso; altered mental status; shock or otherwise unstable patient
General Criteria for additional AV doses at hours 2, 4, 6, 12, 24 (as needed)	Additional doses of antivenom if: persistence or worsening of systemic neurotoxic S/Sx. Continue to re-administer 2 vial boluses as needed at hours 2, 4, 6, 12, and 24 until indications of improvement begin to appear (↑SBC, ↑LOC, ↑strength, etc.)	Additional doses of antivenom if: persistence, resumption, or new onset of any active external or internal bleeding OR S/Sx of active venom confirmed by secondary recurrence of abnormal WBCT	Additional doses of antivenom if: significant increase in edema (such as beyond major joint) OR significant increase in pain (severity of pain and/or how far pain radiates up the bitten limb)
CENTCOM 1st Line Antivenoms	CENTCOM: Broad-spectrum coverage for all neurotoxic/hemotoxic/cytotoxic snakebite syndromes by known* or unknown species - POLYSERP-M: Initial dose = 6 vials regardless of severity / Additional doses = 2 vials as needed CENTRAL ASIA: *If patient has a confirmed <i>Gloydius halys</i> bite (rare!), use SIOBP-G as 1st line if available. If unavailable or unconfirmed ID give POLYSERP-M - SIOBP-G: Initial dose = 2 vials / Additional doses = 2 vials as needed		
Antivenom Abbreviations CENTCOM	POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain)	POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain) SIOBP-G = <i>Gloydius halys</i> monovalent - (Shanghai Institute of Biological Products, China)	POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain) SIOBP-G = <i>Gloydius halys</i> monovalent - (Shanghai Institute of Biological Products, China)

Antivenom Algorithm: CENTCOM AOR

NOTE:
Yellow background indicates that a product meets both criteria below:
1) broad-spectrum regional coverage
2) freeze-dried / field-stable

Follow list of steps outlined in CPG:
**Universal Approach to Snakebite
Assessment, Diagnosis, and Treatment**

Patient with S/Sx of envenomation?

Monitor for 24 hours and discharge according to Step #17

Yes

Region?

CENTCOM AOR
(except Central Asia)

CENTRAL ASIA ONLY

Snake ID known?

Syndrome?

Confirmed *Gloydius halys* or other *Gloydius* species? (rare)

NEUROTOXIC

HEMOTOXIC

CYTOTOXIC

1st line = SIOBP-G
Gloydius halys or related *Gloydius* species only!

Initial dose = 2 vials,
additional 2 vials as needed

1st line = POLYSERP-M
COMPLETE REGIONAL COVERAGE

Initial dose = 6 vials,
additional 2 vials as needed

POLYSERP-M available?

NO

Region?

MIDDLE EAST /
CENTRAL ASIA

ARABIAN PENINSULA

RAZI-P available?

NAVPC-P available?

YES

NO

YES

NO

2nd line = NAVPC-P
Moderate coverage for
NEURO / HEMO / CYTO syndromes

Initial dose varies by syndrome, see below

2nd line = RAZI-P

Initial dose = 10 vials,
additional 2 vials as needed

Contact snakebite expert for consult

Contact snakebite expert for consult

2nd line = NAVPC-P

Initial dose neurotoxic = 10 vials,
additional 5 vials as needed

2nd line = NAVPC-P

Initial dose hemotoxic and/or
cytotoxic = 10 vials,
additional 5 vials as needed

- c. Initial dose = 6 vials hemotoxic/cytotoxic only, additional doses = 2 vials as needed.
- 3. **Second line (CENTCOM–MIDDLE EAST/CENTRAL ASIA): RAZI-P**
 - a. NOT FIELD-STABLE. BROAD-SPECTRUM COVERAGE 6+ SPECIES CYTO/HEMO/NEURO.
 - b. Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 10 vials of POLYSERP-M. Directly or indirectly covers all WHO category 1 species in the region. Directly or indirectly covers some of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists. Covers fewer species than POLYSERP-M.
 - c. Initial dose = 10 vials all syndromes, additional doses = 5 vials as needed.
- 4. **Second line (CENTCOM–ARABIAN PENINSULA): NAVPC-C**
 - a. NOT FIELD-STABLE. BROAD-SPECTRUM COVERAGE 6+ SPECIES OF NEURO/HEMO/CYTO.
 - b. Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 10 vials of POLYSERP-M. Directly or indirectly covers some of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.
 - c. Initial dose neuro = 10 vials. Initial dose hemo/cyto = 5 vials. All additional doses = 5 vials.

EUCOM – Abbreviated Treatment Guidelines

Safe and effective broad-spectrum, refrigerated antivenoms are available for all three syndromes of snake envenomation due to European viper species in this AOR and treatment does not require identification of the species responsible. Snakebite treatment at the point of injury is not routinely recommended for EUCOM.

- 1. **First line (EUCOM–EUCOM OUTSIDE UK/ SCANDINAVIA): VIPERFAV**
 - a. NOT FIELD-STABLE. BROAD-SPECTRUM COVERAGE AGAINST MULTIPLE EUROPEAN VIPERS.
 - b. Single-source treatment option for neurotoxic, hemotoxic, and cytotoxic snake envenomations by the most medically and epidemiologically significant species in Europe (*Vipera berus*, *V. aspis*, *V. ammodytes*) with paraspecific coverage against other European *Vipera* species. Can be used in the

EUCOM AOR when the causative species is unknown or species for which this product is directly indicated. Second line treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations within the UK and Scandinavia if first line (VIPERATAB) is not available.

- c. Initial dose = 1–2 vials all syndromes, additional doses = 1 vial as needed.
- 2. **First line (EUCOM–UK/SCANDINAVIA): VIPERATAB**
 - a. NOT FIELD-STABLE. BROAD-SPECTRUM COVERAGE AGAINST SEVERAL EUROPEAN VIPERS.
 - b. Single-source treatment option for neurotoxic, hemotoxic, and cytotoxic snake envenomations by the most medically and epidemiologically significant species in the UK and Scandinavia (*Vipera berus*) with paraspecific coverage against some other European *Vipera* species. Second line treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in the EUCOM AOR outside of the UK and Scandinavia if first line (VIPERFAV) is not available.
 - c. Initial dose = 2 vials all syndromes, additional doses = 2 vials as needed. Each box = 2 vials.

INDOPACOM – Abbreviated Treatment Guidelines

Safe and effective broad-spectrum, field-stable antivenoms are available for all three syndromes of snake envenomation in Southeast Asia and several other areas within this AOR. Snakebite treatment in INDOPACOM as a whole is more complex than AFRICOM or CENTCOM due to the lack of a truly pan-Asian polyvalent product. Treatment in many places does not require identification of the species responsible, but products are syndrome specific and there is no single product for all 3 syndromes. Snakebite treatment at the point of injury is recommended for areas within the INDOPACOM AOR where field-stable antivenoms are available.

- 1. **First line (INDOPACOM–SOUTHEAST ASIA): TRC-HPAV**
 - a. FIELD-STABLE. BROAD-SPECTRUM COVERAGE MULTIPLE SPECIES OF HEMO/CYTO.
 - b. Broad-spectrum treatment option for all hemotoxic and cytotoxic snake envenomations by known or unknown species in Southeast Asia. Best regional polyvalent.
 - c. Initial dose hemotoxic/cytotoxic only = 10 vials, additional doses = 5 vials as needed.

EUROPEAN COMMAND – FIRST LINE ANTIVENOMS			
	Neurotoxic Syndrome	Hemotoxic Syndrome	Cytotoxic Syndrome
Mild	Local S/Sx (paresthesias; neuropathic pain; piloerection; muscle spasm, fasciculations)	Coagulopathy ± persistence of local bleeding from bite wound > 30 mins after bite	Severe pain; edema below elbow or knee; limited blistering within several inches of the bite wound
Moderate	Systemic S/Sx (bilateral ptosis GI symptoms; visual, auditory, or other sensory disturbances; widespread hyperesthesia)	Moderate systemic bleeding (old scabs, gingival bleeding, epistaxis, etc); bruising distant from the bite wound	Edema above elbow or knee but not beyond shoulder or hip; moderate local blistering along bitten limb segment
Severe	Difficulty speaking; altered mental status; respiratory muscle weakness causing difficulty breathing; shock or otherwise unstable patient	Active GI bleed (usually hematemesis) or other internal bleeding; severe anemia; altered mental status; shock or otherwise unstable patient	Progressive edema beyond shoulder or hip; severe necrosis or widespread blistering; symptomatic bite to head, neck, or torso; altered mental status; shock or otherwise unstable patient
General Criteria for additional AV doses at hours 2, 4, 6, 12, 24 (as needed)	Additional doses of antivenom if: persistence or worsening of systemic neurotoxic S/Sx. Continue to re-administer 2 vial boluses as needed at hours 2, 4, 6, 12, and 24 until indications of improvement begin to appear (↑SBC, ↑LOC, ↑strength, etc.)	Additional doses of antivenom if: persistence, resumption, or new onset of any active external or internal bleeding OR S/Sx of active venom confirmed by secondary recurrence of abnormal WBCT	Additional doses of antivenom if: significant increase in edema (such as beyond major joint) OR significant increase in pain (severity of pain and/or how far pain radiates up the bitten limb)
EUCOM 1st Line Antivenoms	UK or Scandinavia: Broad-spectrum coverage all neurotoxic/hemotoxic/cytotoxic syndromes from European Vipera species - VIPERATAB (1st line): Initial dose = 2 vials (one box), additional doses = 1–2 vials as needed - VIPERFAV (2nd line): Initial dose = 1–2 vials, additional doses = 1 vial as needed Outside UK/Scandinavia: Broad-spectrum coverage all neurotoxic/hemotoxic/cytotoxic syndromes from European Vipera species - VIPERFAV (1st line): Initial dose = 1–2 vials, additional doses = 1 vial as needed - VIPERATAB (2nd line): Initial dose = 2 vials (one box), additional doses = 1–2 vials as needed		
Antivenom Abbreviations EUCOM	VIPERFAV = VIPERFAV - (Sanofi-Pasteur, France) VIPERATAB = ViperaTAb - (Micropharm, UK)	VIPERFAV = VIPERFAV - (Sanofi-Pasteur, France) VIPERATAB = ViperaTAb - (Micropharm, UK)	VIPERFAV = VIPERFAV - (Sanofi-Pasteur, France) VIPERATAB = ViperaTAb - (Micropharm, UK)

**Antivenom Algorithm:
EUCOM AOR**

NOTE:
Yellow background indicates that a product meets both criteria below:
1) broad-spectrum regional coverage
2) freeze-dried / field-stable

Follow list of steps outlined in CPG:
**Universal Approach to Snakebite
Assessment, Diagnosis, and Treatment**

Patient with S/Sx of envenomation?
NO → Monitor for 24 hours and discharge according to Step #17

YES

**WITHIN UK /
SCANDINAVIA**

**OUTSIDE UK /
SCANDINAVIA**

Region?

Syndrome?

Syndrome?

NEUROTOXIC **HEMOTOXIC** **CYTOTOXIC**

NEUROTOXIC **HEMOTOXIC** **CYTOTOXIC**

VIPERATAB available?

VIPERFAV available?

1st line = VIPERATAB
COMPLETE REGIONAL
COVERAGE
Initial dose = 2 vials,
additional 2 vials as needed

1st line = VIPERFAV
COMPLETE REGIONAL
COVERAGE
Initial dose = 1 - 2 vials,
additional 1 vial as needed

VIPERFAV available?

VIPERATAB available?

2nd line = VIPERFAV
COMPLETE REGIONAL
COVERAGE
Initial dose = 1 - 2 vials,
additional 1 vial as needed

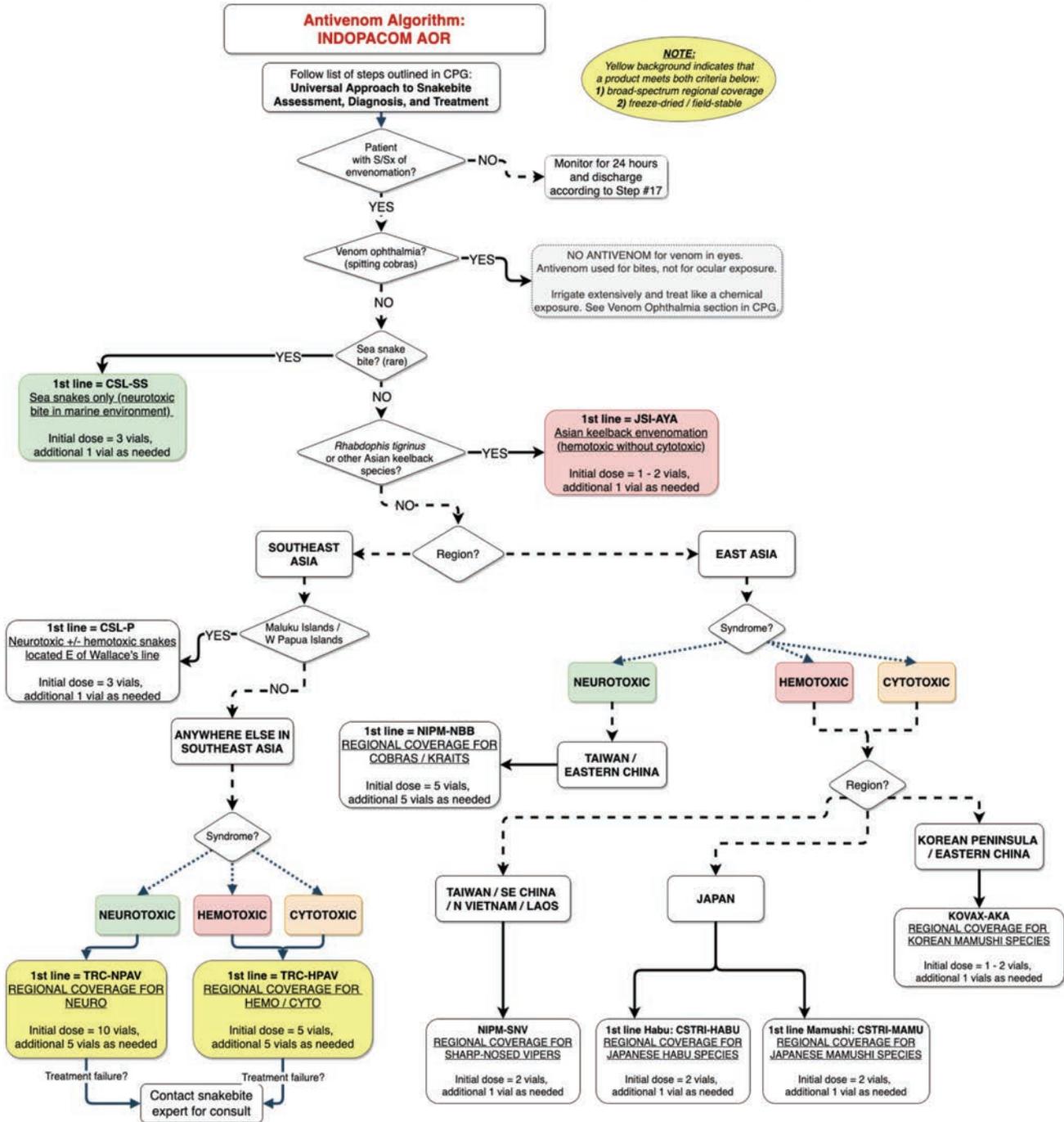
2nd line = VIPERATAB
COMPLETE REGIONAL
COVERAGE
Initial dose = 2 vials,
additional 2 vials as needed

Contact snakebite expert for consult

Contact snakebite expert for consult

INDO-PACIFIC COMMAND – FIRST LINE ANTIVENOMS			
	Neurotoxic Syndrome	Hemotoxic Syndrome	Cytotoxic Syndrome
Mild	Local S/Sx (paresthesias; neuropathic pain; piloerection; muscle spasm, fasciculations)	Coagulopathy ± persistence of local bleeding from bite wound > 30 mins after bite	Severe pain; edema below elbow or knee; limited blistering within several inches of the bite wound
Moderate	Systemic S/Sx (bilateral ptosis GI symptoms; visual, auditory, or other sensory disturbances; widespread hyperesthesia)	Moderate systemic bleeding (old scabs, gingival bleeding, epistaxis, etc); bruising distant from the bite wound	Edema above elbow or knee but not beyond shoulder or hip; moderate local blistering along bitten limb segment
Severe	Difficulty speaking; altered mental status; respiratory muscle weakness causing difficulty breathing; shock or otherwise unstable patient	Active GI bleed (usually hematemesis) or other internal bleeding; severe anemia; altered mental status; shock or otherwise unstable patient	Progressive edema beyond shoulder or hip; severe necrosis or widespread blistering; symptomatic bite to head, neck, or torso; altered mental status; shock or otherwise unstable patient
General Criteria for additional AV doses at hours 2, 4, 6, 12, 24 (as needed)	Additional doses of antivenom if: persistence or worsening of systemic neurotoxic S/Sx. Continue to re-administer 2 vial boluses as needed at hours 2, 4, 6, 12, and 24 until indications of improvement begin to appear (↑SBC, ↑LOC, ↑strength, etc.)	Additional doses of antivenom if: persistence, resumption, or new onset of any active external or internal bleeding OR S/Sx of active venom confirmed by secondary recurrence of abnormal WBCT	Additional doses of antivenom if: significant increase in edema (such as beyond major joint) OR significant increase in pain (severity of pain and/or how far pain radiates up the bitten limb)
INDOPACOM 1st Line Antivenoms	Southeast Asia: Broad-spectrum for all neurotoxic - TRC-NPAV: Initial dose 10 vials - Additional doses = 5 vials as needed TRC-NPAV is the 1 st line for all neurotoxic bites in SE Asia outside of the circumstances listed below: Marine environments: Sea snake envenomations - CSL-SS: Initial dose = 3 vials o Additional doses = 1 vial as needed Maluku/West Papua islands: Neurotoxic - CSL-P: Initial dose = 3 vials - Additional doses = 1 vial as needed Eastern China/Taiwan: Neurotoxic - NIPM-NBB: Initial dose = 5 vials - Additional doses = 5 vials as needed	Southeast Asia: Broad-spectrum for all hemotoxic/cytotoxic (1st line in SE Asia) - TRC-HPAV: Initial dose = 10 vials, additional doses = 2 vials as needed. TRC-HPAV is the 1 st line for all hemotoxic/cytotoxic bites in SE Asia outside of circumstances listed below: Korean Peninsula/Eastern China: Viper envenomations (Cytotoxic +/- Hemotoxic) Korean Mamushi species (<i>Gloydius brevicaudus</i> , <i>G. ussuriensis</i> , <i>G. intermedius</i>) - KOVAX-AMA: Initial dose = 1 - 2 vials, additional doses = 1 vial as needed Taiwan / Se China / N Vietnam / Laos: Sharp-nosed viper (<i>Deinagkistrodon acutus</i>) - NIPB-SNV: Initial dose = 2 vials, additional doses = 1 vial as needed Japan: Viper envenomations (Cytotoxic +/- Hemotoxic) If Japanese Habu (<i>Protobothrops spp.</i>) envenomation: - CSTRI-HABU: Initial dose = 1 - 2 vials, additional doses = 1 vial as needed If Japanese Mamushi (<i>Gloydius blomhoffii</i>) envenomation: - CSTRI-MAMU: Initial dose = 1 - 2 vials, additional doses = 1 vial as needed Japan / China / N & S Korea / Vietnam / E Russia: Rhabdophis spp. Hemotoxic without Cytotoxic Spontaneous bleeding develops within several days of bite without cytotoxicity. - JSI-AYA: Initial dose = 1 - 2 vials, additional doses = 1 vial as needed	
Antivenom Abbreviations INDOPACOM	TRC-NPAV = Neuro Polyvalent Antivenom - (Thai Red Cross, Thailand) CSL-P (CSL Polyvalent) / CSL-SS (CSL Sea Snake) - (Commonwealth Serum Laboratories, Australia) NIPM-NBB = <i>Naja atra</i> - <i>Bungarus multicinctus</i> Bivalent - (National Institute Preventative Medicine, Taiwan)	TRC-HPAV = Hemato Polyvalent Antivenom - (Thai Red Cross, Thailand) KOVAX-AKA = Agkistrodon Mamushi Antivenom - (Korea Vaccine, Korea) JSI-AYA = Anti-Yamakagashi Antivenom - (Japan Snake Institute, Japan) CSTRI-HABU = Kaketsuken Habu Antivenom CSTRI-MAMU = Kaketsuken Mamushi Antivenom - (Chemo-Sero Therapeutic Research Institute, Japan) NIPM-SNV = Sharp-nosed Viper Monovalent - (National Institute Preventative Medicine, Taiwan)	TRC-HPAV = Hemato Polyvalent Antivenom - (Thai Red Cross, Thailand) KOVAX-AKA = Agkistrodon Mamushi Antivenom - (Korea Vaccine, Korea) CSTRI-HABU = Kaketsuken Habu Antivenom / CSTRI-MAMU = Kaketsuken Mamushi Antivenom - (Chemo-Sero Therapeutic Research Institute, Japan) NIPM-SNV = Sharp-nosed Viper Monovalent - (National Institute Preventative Medicine, Taiwan)

2. First line (INDOPACOM–SOUTHEAST ASIA): **TRC-NPAV**
 - a. FIELD-STABLE. BROAD-SPECTRUM COVERAGE MULTIPLE SPECIES OF NEURO.
 - b. Broad-spectrum treatment option for all neurotoxic snake envenomations by known or unknown species in Southeast Asia. Best regional polyvalent.
 - c. Initial dose = 10 vials neurotoxic only, additional doses = 5 vials as needed.
3. First line (INDOPACOM–TAIWAN/SOUTHEAST CHINA/N LAOS/N VIETNAM): **NIPM-NBB**
 - a. LIQUID PRODUCT BUT FIELD-STABLE FOR SHORT EXCURSIONS. BROAD-SPECTRUM COVERAGE MULTIPLE SPECIES OF NEURO.
 - b. Bivalent treatment option for neurotoxic cobra and krait envenomations in East Asia.
 - c. Initial dose = 5 vials neurotoxic only, additional doses = 5 vials as needed.
4. First line (INDOPACOM–JAPAN): **CSTRI-HABU**
 - a. NOT FIELD-STABLE. NOT BROAD-SPECTRUM. HABU COVERAGE ONLY.
 - b. First line treatment option for Habu envenomation (*Protobothrops spp.*).
 - c. Initial dose = 1–2 vials, additional doses = 1 vial as needed
5. First line (INDOPACOM–JAPAN): **CSTRI-MAMU**
 - a. NOT FIELD-STABLE. NOT BROAD-SPECTRUM. JAPANESE MAMUSHI COVERAGE ONLY.
 - b. First line treatment option for hemotoxic and cytotoxic envenomation syndromes caused by the Japanese Mamushi (*Gloydius blomhoffii*).
6. First line (INDOPACOM–JAPAN/CHINA/N KOREA/S KOREA/VIETNAM/E RUSSIA): **JSI-AYA**
 - a. NOT FIELD-STABLE. NOT BROAD-SPECTRUM. KEELBACK COVERAGE ONLY.
 - b. First line treatment option for hemotoxic and cytotoxic envenomation syndromes caused by the Tiger Keelback (*Rhabdophis tigrinus*) and other East Asian keelback species.
 - c. Initial dose = 1–2 vials, additional doses = 1 vial as needed
7. First line (INDOPACOM–N KOREA/S KOREA): **KOVAX-AKA**
 - a. NOT FIELD-STABLE. NOT BROAD-SPECTRUM. KOREAN MAMUSHI COVERAGE ONLY.
 - b. First line treatment option of hemotoxic and cytotoxic envenomation syndromes caused by the major species of Mamushi in the Korean Peninsula (*Gloydius brevicaudus*, *G. ussuriensis*, *G. intermedius*). May neutralize other related species.
 - c. Initial dose = 1–2 vials, additional doses = 1 vial as needed
8. First line (INDOPACOM–TAIWAN/SOUTHEAST CHINA/N VIETNAM/LAOS): **NIPM-SNV**
 - a. FREEZE-DRIED PRODUCT REQUIRING COLD CHAIN BUT LIKELY TO BE FIELD-STABLE FOR SHORT EXCURSIONS. NOT BROAD-SPECTRUM. SHARP-NOSED VIPER ONLY.
 - b. First line monovalent antivenom directly indicated for the treatment of hemotoxic and cytotoxic envenomation syndromes caused by the sharp-nosed viper (*Deinagkistrodon acutus*).
 - c. Initial dose = 2 vials, additional doses = 1 vial as needed



9. **First Line (INDOPACOM–MARINE ENVIRONMENTS ONLY): CSL-SS**
- NOT FIELD-STABLE. BROAD-SPECTRUM COVERAGE AGAINST INDO-PACIFIC SEA SNAKES ONLY.
 - Neurotoxic envenomation in INDOPACOM by sea snakes or unknown species occurring in a strictly marine environment.
 - Initial dose = 3 vials, additional doses = 1 vial as needed
10. **First Line (INDOPACOM–MALUKU/WEST PAPUA ISLANDS ONLY): CSL-P**
- NOT FIELD-STABLE. BROAD-SPECTRUM COVERAGE.
 - First line antivenom indicated for neurotoxic/hemotoxic envenomation in INDOPACOM by Australasian elapids or unknown species occurring East of Wallace's line.
 - Initial dose = 3 vials, additional doses = 1 vial as needed

RDT/Instituto Bioclon, United States/Mexico:

ANAVIP (ANAVIP)

- FREEZE-DRIED/UNREFRIGERATED
- Indications:** Currently only indicated by FDA for rattlesnake envenomations. Not currently indicated for copperhead or cottonmouth envenomations, although this may change in the near future depending on results of upcoming studies. Freeze dried and field-stable at room temperature of 25° C/77° F.
- Initial dosing:** 10 vials

Pfizer, United States: North American Coral Snake Antivenom (NACSA)

- FREEZE-DRIED/REFRIGERATED
- Indications:** Indicated for neurotoxic envenomations by North American coral snake species in the United States including Eastern coral snake (*Micrurus fulvius*) and Texas coral snake (*Micrurus tener*). Store between 2–8° C/35.6–46.4° F; however, likely retains stability for short excursions in the field.
- Initial dosing:** 3–5 vials

NORTHCOM – Abbreviated Treatment Guidelines

Safe and effective antivenoms are available for all neurotoxic/hemo/cytotoxic pit viper envenomations and for neurotoxic coral snake envenomations in this AOR. Treatment does not require identification of the species responsible. Snakebite treatment at the point of injury is not routinely recommended for NORTHCOM. For all NORTHCOM antivenoms, refer to the package insert in the antivenom box for specific usage instructions as per FDA regulations for domestically approved products. Also see Unified treatment algorithm for the management of crotaline snakebite in the United States (Lavonas et al. 2011) for specific dosing and management guidelines on pit viper bites.

BTG Therapeutics, United States: CroFab (CROFAB)

- FREEZE-DRIED/REFRIGERATED
- Indications:** Envenomation by all Pit Viper species (rattlesnakes, copperheads, cottonmouths) in North America. Freeze-dried; requires refrigeration but one study has demonstrated that it will maintain efficacy under field conditions for ≥ 90 days if needed.
- Initial dosing:** 4–6 vials

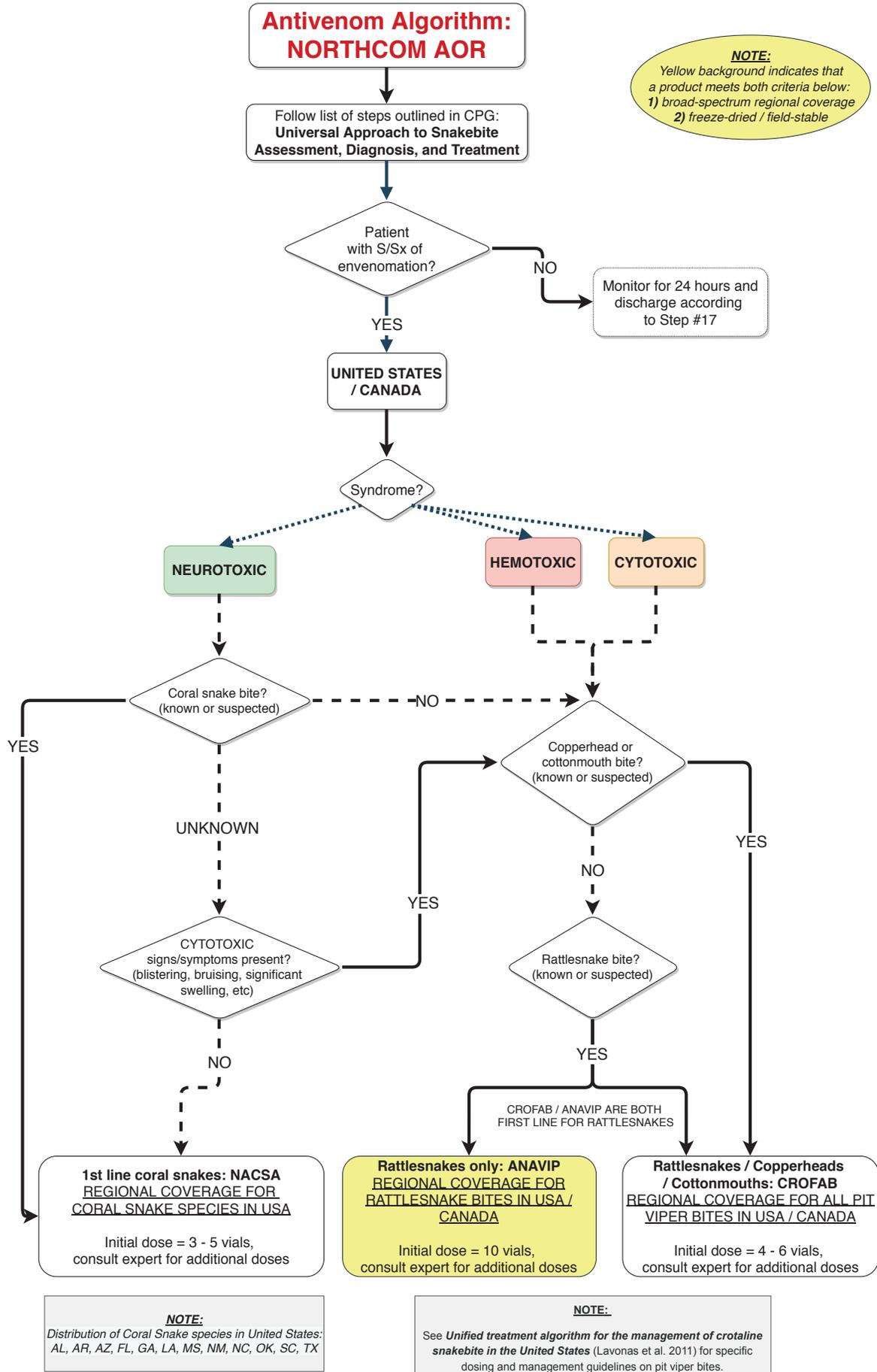
SOUTHCOM – Abbreviated Treatment Guidelines

Safe and effective antivenoms are available for all hemo/cytotoxic pit viper envenomations and for neurotoxic coral snake envenomations in this AOR. Treatment does not require identification of the species responsible but does require identification of the syndrome. Snakebite treatment at the point of injury is recommended for SOUTHCOM.

1. First Line (SOUTHCOM–ENTIRE SOUTHCOM AOR): BIOCL-AVT

- FIELD-STABLE. BROAD-SPECTRUM COVERAGE 14 SPECIES HEMO/CYTO.
- First line treatment option for all hemotoxic and cytotoxic snake envenomations anywhere in the SOUTHCOM AOR when the causative species is either unknown or among the ≥ 14 snakes for which this product is directly indicated. Directly or indirectly covers most of the WHO category 1 and category 2 snakes in this region.

NORTHERN COMMAND – FIRST LINE ANTIVENOMS			
	Neurotoxic Syndrome	Hemotoxic Syndrome	Cytotoxic Syndrome
Mild	Local S/Sx (paresthesias; neuropathic pain; piloerection; muscle spasm, fasciculations)	Coagulopathy ± persistence of local bleeding from bite wound > 30 mins after bite	Severe pain; edema below elbow or knee; limited blistering within several inches of the bite wound
Moderate	Systemic S/Sx (bilateral ptosis GI symptoms; visual, auditory, or other sensory disturbances; widespread hyperesthesia)	Moderate systemic bleeding (old scabs, gingival bleeding, epistaxis, etc); bruising distant from the bite wound	Edema above elbow or knee but not beyond shoulder or hip; moderate local blistering along bitten limb segment
Severe	Difficulty speaking; altered mental status; respiratory muscle weakness causing difficulty breathing; shock or otherwise unstable patient	Active GI bleed (usually hematemesis) or other internal bleeding; severe anemia; altered mental status; shock or otherwise unstable patient	Progressive edema beyond shoulder or hip; severe necrosis or widespread blistering; symptomatic bite to head, neck, or torso; altered mental status; shock or otherwise unstable patient
General Criteria for additional AV doses at hours 2, 4, 6, 12, 24 (as needed)	Additional doses of antivenom if: persistence or worsening of systemic neurotoxic S/Sx. Continue to re-administer 2 vial boluses as needed at hours 2, 4, 6, 12, and 24 until indications of improvement begin to appear (↑SBC, ↑LOC, ↑strength, etc.)	Additional doses of antivenom if: persistence, resumption, or new onset of any active external or internal bleeding OR S/Sx of active venom confirmed by secondary recurrence of abnormal WBCT	Additional doses of antivenom if: significant increase in edema (such as beyond major joint) OR significant increase in pain (severity of pain and/or how far pain radiates up the bitten limb)
NORTHCOM 1st Line Antivenoms	United States: Coral snake envenomations - Initial 3-5 vials NACSA, additional doses not needed if 5 vial initial dose given United States/Canada: Pit viper envenomations* - CROFAB: Initial dose = 4-6 vials, additional doses = 4-6 vial as needed - ANAVIP (rattlesnakes only): Initial dose = 10 vials, additional doses = 10 vials as needed *Follow unified treatment algorithm (Lavonas et al. 2011)	United States/Canada: Broad spectrum coverage all hemotoxic/cytotoxic syndromes* Any pit viper envenomation (rattlesnake, copperhead, cottonmouth): - CROFAB: Initial dose = 4-6 vials, additional doses = 4-6 vials as needed Rattlesnake envenomations only: - ANAVIP: Initial dose = 10 vials, additional doses = 10 vials as needed NOTE: Anavip is only indicated by FDA for rattlesnake envenomations; not for copperheads or cottonmouths at this time; however, it is likely effective against all North American pit vipers. Follow <i>Unified treatment algorithm for the management of crotaline snakebite in the United States</i> (Lavonas et al. 2011) for specific dosing and management guidelines on pit viper bites.	
Antivenom Abbreviations NORTHCOM	CROFAB = CroFab - (BTG Therapeutics, United States) ANAVIP = ANAVIP - (RDT / Bioclon, United States / Mexico) NACSA = North American Coral Snake Antivenom - (Pfizer, United States)	CROFAB = CroFab - (BTG Therapeutics, United States) ANAVIP = ANAVIP (RDT / Bioclon, United States / Mexico)	CROFAB = CroFab - (BTG Therapeutics, United States) ANAVIP = ANAVIP - (RDT / Bioclon, United States / Mexico)



SOUTHERN COMMAND – FIRST LINE ANTIVENOMS			
	Neurotoxic Syndrome	Hemotoxic Syndrome	Cytotoxic Syndrome
Mild	Local S/Sx (paresthesias; neuropathic pain; piloerection; muscle spasm, fasciculations)	Coagulopathy ± persistence of local bleeding from bite wound > 30 mins after bite	Severe pain; edema below elbow or knee; limited blistering within several inches of the bite wound
Moderate	Systemic S/Sx (bilateral ptosis GI symptoms; visual, auditory, or other sensory disturbances; widespread hyperesthesia)	Moderate systemic bleeding (old scabs, gingival bleeding, epistaxis, etc); bruising distant from the bite wound	Edema above elbow or knee but not beyond shoulder or hip; moderate local blistering along bitten limb segment
Severe	Difficulty speaking; altered mental status; respiratory muscle weakness causing difficulty breathing; shock or otherwise unstable patient	Active GI bleed (usually hematemesis) or other internal bleeding; severe anemia; altered mental status; shock or otherwise unstable patient	Progressive edema beyond shoulder or hip; severe necrosis or widespread blistering; symptomatic bite to head, neck, or torso; altered mental status; shock or otherwise unstable patient
General Criteria for additional AV doses at hours 2, 4, 6, 12, 24 (as needed)	Additional doses of antivenom if: persistence or worsening of systemic neurotoxic S/Sx. Continue to re-administer 2 vial boluses as needed at hours 2, 4, 6, 12, and 24 until indications of improvement begin to appear (↑SBC, ↑LOC, ↑strength, etc.)	Additional doses of antivenom if: persistence, resumption, or new onset of any active external or internal bleeding OR S/Sx of active venom confirmed by secondary recurrence of abnormal WBCT	Additional doses of antivenom if: significant increase in edema (such as beyond major joint) OR significant increase in pain (severity of pain and/or how far pain radiates up the bitten limb)
SOUTHCOM 1st Line Antivenoms	Central America: Neurotoxic polyvalent - BIOCL-COR: Any severity = initial 10 vials • Additional 5 vials as needed South America: Neurotoxic polyvalent - INS-AAP: Any Severity = 10 vials • Additional 5 vials as needed	Central and South America: Broad-spectrum all hemotoxic/cytotoxic syndromes BIOCL-AVT: Initial dosing of this antivenom is based on severity - Mild – moderate: Initial dose = 10 vials BIOCL-AVT - Additional doses = 5 vials as needed - Severe: Initial dose = 15 vials BIOCL-AVT - Additional doses = 5 vials as needed	
Antivenom Abbreviations SOUTHCOM	BIOCL-COR = CORALMYN - (Instituto Bioclon, Mexico) INS-AAP = Antiveneno Anticoral Polivalente - (Instituto Nacional de Salud, Colombia)	BIOCL-AVT = Antivipmyn Tri - (Instituto Bioclon, Mexico)	BIOCL-AVT = Antivipmyn Tri - (Instituto Bioclon, Mexico)

- c. Initial dose = 10 vials hemotoxic/cytotoxic only, additional doses = 5 vials as needed.
2. First Line (SOUTHCOM-CENTRAL AMERICA): **BIOCL-COR**
 - a. NOT FIELD-STABLE. BROAD-SPECTRUM COVERAGE NEURO IN CENTRAL AMERICA.
 - b. First line treatment option for neurotoxic envenomation in Central America by coral snakes or unknown species (coral snakes are only strictly neurotoxic snakes in SOUTHCOM AOR). Second line treatment option for coral snake/unknown neurotoxic envenomation in South America if first line (INS-AAP) is not available.
3. First Line (SOUTHCOM-SOUTH AMERICA): **INS-AAP**
 - a. NOT FIELD-STABLE. BROAD-SPECTRUM COVERAGE NEURO IN SOUTH AMERICA.
 - b. First line treatment option for neurotoxic envenomation in South America by coral snakes or unknown species (coral snakes are only strictly neurotoxic snakes in SOUTHCOM AOR). Second line treatment option for coral snake/unknown neurotoxic envenomation in Central America if first line (INS-AAP) is not available.
 - c. Initial dose = 10 vials neurotoxic only, additional doses = 5 vials as needed.

Antivenom Algorithm: SOUTHCOM AOR

NOTE:
Yellow background indicates that a product meets both criteria below:
1) broad-spectrum regional coverage
2) freeze-dried / field-stable

Follow list of steps outlined in CPG:
**Universal Approach to Snakebite
Assessment, Diagnosis, and Treatment**

Patient with S/Sx of envenomation?

-NO → Monitor for 24 hours and discharge according to Step #17

Syndrome?

NEUROTOXIC

HEMOTOXIC

CYTOTOXIC

Region?

CENTRAL AMERICA

SOUTH AMERICA

1st line = BIOCL-COR
CENTRAL AMERICAN CORAL SNAKE SPECIES
Initial dose = 10 vials, additional 5 vials as needed

1st line = INS-AAP
SOUTH AMERICAN CORAL SNAKE SPECIES
Initial dose = 10 vials, additional 5 vials as needed

1st line = BIOCL-AVT
COVERS ALL HEMO / CYTO
Initial dosing is based on severity:

Mild - moderate hemo/cyto:
initial dose = 10 vials, additional 5 vials as needed

Severe hemo/cyto:
Initial dose = 15 vials, additional 5 vials as needed

INTENT (EXPECTED OUTCOMES)

1. All snakebite patients should be managed according to the steps outlined in the “Universal Approach to Snakebite Assessment, Diagnosis, and Treatment”
2. Assessment, diagnosis, and treatment of snakebite patients should be based on the clinical syndrome of envenomation and not the identity of the snake species responsible for the bite.
 - a. When a broad-spectrum antivenom does not exist for a given syndrome in a given area, follow the steps outlined in the regional algorithms to determine the most appropriate antivenom therapy for the patient.
3. Snakebites are dynamic events and patients must be frequently reassessed for signs of neurotoxic, hemotoxic, and cytotoxic syndromes throughout the course of care as some syndromes will develop than others.
4. There are no absolute contraindications to antivenom administration for a patient with a symptomatic snake envenomation.
5. Antivenom administration should be performed by medical providers capable of providing advanced life support and trained to a minimum level of paramedic (or DoD equivalent) and higher (i.e. SOCM, 18D, PJ, IDC, IDMT, RN, PA, MD or DO, etc.)
6. Early antivenom treatment is the standard of care for snake envenomations worldwide. Whenever possible, the appropriate antivenom should be administered in the field prior to medevac to neutralize circulating venom before significant and potentially irreversible damage has occurred.
 - a. Field-stable, broad-spectrum antivenom options are included in this CPG for all combatant commands except for EUCCOM.
 - i. Appropriate regional products listed in the CPG should be stocked in role 2 and role 3 medical facilities. Far-forward units with paramedic level providers should be equipped with field-stable, broad-spectrum antivenoms that can be stocked in the aid station and carried into the field for extended periods of times at high temperatures without loss of efficacy.
7. If antivenom is not available, the patient should be transferred to a facility that maintains a stock of the appropriate antivenom. Confirm that the receiving facility has the correct antivenom in stock prior to transfer. If the receiving facility does not have the correct product(s) in stock, then that facility should be bypassed for a facility that is stocking the appropriate products.
8. Antivenom dosage, preparation, and administration procedures for each product should be performed as detailed for each specific product in Appendix B.
9. Tetanus prophylaxis should be given prior to discharge when needed.
10. Fasciotomy is contraindicated for snakebite and all cases of suspected compartment syndrome should be managed with additional doses of antivenom and elevation ≥ 60 degrees to reduce oncotic pressure in the bitten limb.
11. Initiate a telemedicine consult with a qualified snakebite expert for any questions, concerns, or unusual manifestations that arise.
12. Do not attempt to kill or capture the snake for identification purposes as treatment is based on clinical findings. If a photo of the snake is available it can be sent to an expert for identification, but this should not delay antivenom treatment in a symptomatic patient with signs and symptoms of any envenomation syndrome.

PERFORMANCE/ADHERENCE MEASURES

1. Administration of antivenom to any patients with clinical signs and symptoms of neurotoxic, hemotoxic, or cytotoxic envenomations

2. Early administration of appropriate antivenoms to symptomatic patients in the field
3. Rapid transfer of patients to a facility stocking the appropriate antivenom if not available on site
4. Antivenom administration should be performed by an advanced life support qualified provider trained to the paramedic level (or DoD equivalent) or higher
5. Tetanus prophylaxis as needed
6. Manage elevated intracompartmental pressures with antivenom and do not perform fasciotomies.

DATA SOURCE

1. Patient record
2. Department of Defense Trauma Registry (DODTR)

SYSTEM REPORTING & FREQUENCY

The above constitutes the minimum criteria for PI monitoring of this CPG. System reporting will be performed annually; additional PI monitoring and system reporting may be performed as needed. The system review and data analysis will be performed by the Joint Trauma System (JTS) Director and the JTS Performance Improvement Branch.

Performance Improvement (PI) Monitoring

RESPONSIBILITIES

It is the trauma team leader's responsibility to ensure familiarity, appropriate compliance and PI monitoring at the local level with this CPG.

Acknowledgments

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**APPENDIX A:
WHOLE BLOOD CLOTTING TEST (WBCT)
FOR VENOM-INDUCED CONSUMPTIVE COAGULOPATHIES (VICC)**

The whole blood clotting test (WBCT) is a simple but critical bedside gross examination used in the assessment, diagnosis, and therapeutic monitoring of snakebite patients in the developing world and remote environments.^{78,112-120} Refer to the diagram below regarding instructions for performing the test. At minutes 20 and 30, the tube is gently picked up and tilted 90 degrees; a stable solid clot retained within the tube is scored “Grade 0” and indicates normal coagulation. Abnormal results are scored “Grade 1” for a partial, semisolid clot that breaks apart and detaches from the glass tube shortly after it is turned or “Grade 2” for completely incoagulable liquid blood that pours out of the tube immediately. Attempting to score the test earlier than 20 minutes will not yield accurate results due to the consumptive mechanism of the coagulopathy. Using a healthy donor as a control is ideal to confirm questionable findings.

WBCT testing should continue throughout the course of care to monitor for secondary resumption of venom-induced consumptive coagulopathy.^{1,70,114} After control of the envenomation has been achieved, reassess WBCT every 24 hours throughout the course of hospitalization. It is important to remember that the WBCT must be interpreted in the context of the larger clinical picture. If a patient has improved in all parameters except for a persistent abnormal WBCT, it may reflect an inertia in replenishment of depleted clotting factors after a severe hemotoxic envenomation.⁷⁸ If the venom is active then hematocrit should continue to decrease or signs of ongoing hemolysis or bleeding should be present.

WHOLE BLOOD CLOTTING TEST (WBCT)

<p>Draw 2 mL of venous blood and transfer directly into a clean and dry glass tube. Leave it upright, open and undisturbed for 20 and/or 30 minutes at room temperature.</p>	<p>After exactly 20 minutes, pick up the tube and invert it. If a solid clot is retained, the test indicates normal coagulation.</p>	<p>If clot breaks down quickly upon inversion of the tube or fails to coagulate, the test indicates a coagulopathy.</p>
		
<p>Collection: a blood sample for WBCT testing immediately after collection.</p>	<p>Normal: a solid clot is retained upon inversion of the tube at 20 or 30 minutes (Grade 0, no coagulopathy).</p>	<p>Abnormal: clot degrades rapidly (Grade 1, friable clot) or fails to coagulate whatsoever (Grade 2).</p>

APPENDIX B: COVERAGE, INITIAL DOSING, PREPARATION, AND ADMINISTRATION OF ALL ANTIVENOMS INCLUDED IN THIS CPG

There are a number of different antivenoms included in this CPG for snakebite treatment in AFRICOM, CENTCOM, INDOPACOM, EUCOM, NORTHCOM, and SOUTHCOM. The coverage, initial dosing, preparation, and administration vary between products and details for each of them have been included in this appendix. Simplified algorithms for selecting and dosing each antivenom are included within the Regionally Specific Snakebite Treatment Guidelines for Each Combatant Command on pages 49–60.

World Health Organization:

Categorization of Medically Significant Snake Species¹⁶⁰

The World Health Organization (WHO) classifies the risk posed by various venomous snakes by designating each species as either Category 1 or Category 2 as described below. WHO guidelines state that the “species listed in Category 1 within a country, territory or area should be considered as being of highest priority for antivenom production on the basis that available knowledge implicates them as being responsible for the greater burden in that particular setting.”

WHO Category 1: Venomous snakes of highest medical importance.

Defined as “highly venomous snakes which are common or widespread and cause numerous snakebites, resulting in high levels of morbidity, disability or mortality.”

WHO Category 2: Venomous snakes of secondary medical importance.

Defined as “highly venomous snakes capable of causing morbidity, disability or death, for which exact epidemiological or clinical data may be lacking; and/or which are less frequently implicated (due to their activity cycles, behavior, habitat preferences or occurrence in areas remote to large human populations).”

NOTE ANTIVENOM INFUSION VS. DIRECT PUSH: *For most first line antivenoms in this CPG, administration using a 100–250 mL IV bag and 10-minute IV/IO infusion is recommended in order to get a full dose of antivenom onboard as quickly as possible and neutralize venom before further damage has occurred. However, if this is not possible it is acceptable to dilute antivenom in 250 mL or 500 mL bags of isotonic solution and give over 10–30 minutes.*

Reference Table: Product name abbreviations for all first line antivenoms recommended in this CPG

ALL COMBATANT COMMANDS – FIRST LINE ANTIVENOM ABBREVIATIONS			
	Neurotoxic Syndrome	Hemotoxic Syndrome	Cytotoxic Syndrome
Antivenom Abbreviations AFRICOM	POLYSERP-P = POLYSERP PAN-AFRICA - (POLYSERP Therapeutics S.L., Spain) POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain)	POLYSERP-P = POLYSERP PAN-AFRICA - (POLYSERP Therapeutics S.L., Spain) POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain)	POLYSERP-P = POLYSERP PAN-AFRICA - (POLYSERP Therapeutics S.L., Spain) POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain)
Antivenom Abbreviations CENTCOM	POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain)	POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain) SIOPB-G = <i>Gloydius halys</i> monovalent - (Shanghai Institute of Biological Products, China)	POLYSERP-M = POLYSERP MENA - (POLYSERP Therapeutics S.L., Spain) SIOPB-G = <i>Gloydius halys</i> monovalent - (Shanghai Institute of Biological Products, China)
Antivenom Abbreviations EUCOM	VIPERFAV = VIPERFAV - (Sanofi-Pasteur, France) VIPERATAB = ViperaTAB - (Micropharm, UK)	VIPERFAV = VIPERFAV - (Sanofi-Pasteur, France) VIPERATAB = ViperaTAB - (Micropharm, UK)	VIPERFAV = VIPERFAV - (Sanofi-Pasteur, France) VIPERATAB = ViperaTAB - (Micropharm, UK)
Antivenom Abbreviations INDOPACOM	TRC-NPAV = Neuro Polyvalent Antivenom - (Thai Red Cross, Thailand) CSL-P (CSL Polyvalent) / CSL-SS (CSL Sea Snake) - (Commonwealth Serum Laboratories, Australia) NIPM-NBB = <i>Naja atra</i> - <i>Bungarus multicinctus</i> Bivalent - (National Institute Preventative Medicine, Taiwan)	TRC-HPAV = Hemato Polyvalent Antivenom - (Thai Red Cross, Thailand) KOVAX-AKA = Agkistrodon Mamushi Antivenom - (Korea Vaccine, Korea) JSI-AYA = Anti-Yamakagashi Antivenom - (Japan Snake Institute, Japan) CSTRI-HABU = Kaketsuken Habu Antivenom CSTRI-MAMU = Kaketsuken Mamushi Antivenom - (Chemo-Sero Therapeutic Research Institute, Japan) NIPM-SNV = Sharp-nosed Viper Monovalent - (National Institute Preventative Medicine, Taiwan)	TRC-HPAV = Hemato Polyvalent Antivenom - (Thai Red Cross, Thailand) KOVAX-AKA = Agkistrodon Mamushi Antivenom - (Korea Vaccine, Korea) CSTRI-HABU = Kaketsuken Habu Antivenom / CSTRI-MAMU = Kaketsuken Mamushi Antivenom - (Chemo-Sero Therapeutic Research Institute, Japan) NIPM-SNV = Sharp-nosed Viper Monovalent - (National Institute Preventative Medicine, Taiwan)
Antivenom Abbreviations NORTHCOM	CROFAB = CroFab - (BTG Therapeutics, United States) ANAVIP = ANAVIP - (RDT / Bioclon, United States / Mexico) NACSA = North American Coral Snake Antivenin - (Pfizer, United States)	CROFAB = CroFab - (BTG Therapeutics, United States) ANAVIP = ANAVIP - (RDT / Bioclon, United States / Mexico)	CROFAB = CroFab - (BTG Therapeutics, United States) ANAVIP = ANAVIP - (RDT / Bioclon, United States / Mexico)
Antivenom Abbreviations SOUTHCOM	BIOCL-COR = CORALMYN - (Instituto Bioclon, Mexico) INS-AAP = Antiveneno Anticoral Polivalente - (Instituto Nacional de Salud, Colombia)	BIOCL-AVT = Antivipmyn Tri - (Instituto Bioclon, Mexico)	BIOCL-AVT = Antivipmyn Tri - (Instituto Bioclon, Mexico)

AFRICOM – ANTIVENOM RECOMMENDATIONS

AFRICOM – SUB-SAHARAN AFRICA/NORTH AFRICA FREEZE-DRIED/UNREFRIGERATED

POLYSERP/Inosan, Spain: POLYSERP PAN-AFRICA Polyvalent (POLYSERP-P)

First line (AFRICOM–SUB-SAHARAN AFRICA): Single-source treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in sub-Saharan Africa when the causative species is either unknown or among the 24 snakes for which this product is directly indicated. Only polyvalent to include boomslangs and only antivenom for mole viper envenomations. Directly or indirectly covers all of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.

Third line (AFRICOM–NORTH AFRICA): Indicated for all neurotoxic, hemotoxic, or cytotoxic envenomations in North Africa with no signs of improvement after 10 vials of POLYSERP-M and/or NAVPC-P. Directly or indirectly covers some of the WHO category 1 and category 2 snakes in North Africa.

Feasibility of use in austere environments: RECOMMENDED for use in operational settings and specifically designed to fill the capability gap for ground medics operating in these areas. Updated version of Inoserp Pan-Africa made specifically for the austere and operational medicine environment. Freeze-dried, unrefrigerated, stable at temperatures > 100° F for at least 180 days without loss of efficacy. Broad coverage and simple dosing enable administration in the field for any symptomatic snakebite by unknown species in this region. Special operations and conventional units deploying to austere operational environments and areas with critical threat venomous species should carry 8 vials per medic. It is recommended that a reserve quantity is stocked in all role 2 and role 3 facilities in AFRICOM in case additional antivenom is needed upon arrival, and also to restock field medics that have used their supply.

Adverse reactions: High efficacy against all major syndromes and very low 0.2% incidence of serious adverse reactions based on current publications.^{1,106,161–164}

- 1. Indications:** Broad spectrum polyvalent directly indicated for the treatment of neurotoxic, hemotoxic, and cytotoxic envenomation syndromes caused by 24 different species of African snakes from the families *Elapidae*, *Viperidae*, *Colubridae*, and *Atractaspididae*.
 - a. NEUROTOXIC:** *Dendroaspis angusticeps*, *D. jamesoni*, *D. polylepis*, *D. viridis*; *Naja anchieta*, *N. annulifera*, *N. haje*, *N. senegalensis*; *Naja melanoleuca*
 - b. CYTOTOXIC and/or HEMOTOXIC:** *Atractaspis irregularis*; *Bitis arietans*, *B. gabonica*, *B. nasicornis*, *B. rhinoceros*; *Cerastes cerastes*; *Dispholidus typus*; *Echis leucogaster*, *E. ocellatus*, *E. pyramidum*; *Naja katiensis*, *N. mossambica*, *N. nigricollis*, *N. nubiae*, *N. pallida*
- 2. Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
- 3. Initial dosing by syndrome:**
 - a. NEUROTOXIC** initial dose = 6 vials
 - b. HEMOTOXIC** initial dose = 6 vials
 - c. CYTOTOXIC** initial dose = 6 vials
- 4. Additional dosing:** Additional doses of 2 vials POLYSERP-P may be given at hours 2, 4, 6, 12, and 24 if needed.
- 5. Preparation and administration:** Reconstitute every 2 vials of POLYSERP-P in the same 10 mL syringe by mixing the first vial, drawing it back up into syringe, and injecting it into the second vial to yield 2 vials/1 syringe (6 vial dose = 3 syringes)

total). Administer sequentially via slow, continuous direct IV or IO push over approximately 2 minutes each. If a reaction occurs stop the push, treat the reaction, reassess response to treatment criteria. Dilute remaining dose in a 100 mL bag of isotonic fluids and administer via slow IV or IO infusion over 30 minutes if needed.

- a. Direct push** is recommended for convenience, but POLYSERP-P may also be administered via IV or IO infusion. Mix in a 50 mL or 100 mL bag of isotonic fluids and administer the entire bag over 5–10 minutes.

AFRICOM – NORTH AFRICA FREEZE-DRIED/UNREFRIGERATED

POLYSERP/Inosan, Spain: POLYSERP MENA Polyvalent (POLYSERP-M)

First line (AFRICOM–NORTH AFRICA): BROAD-SPECTRUM treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in North Africa (Algeria, Egypt, Libya, Morocco, Tunisia, Western Sahara) when the causative species is either unknown or among the 27 snakes for which this product is directly indicated. Directly or indirectly covers all of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.

Feasibility of use in austere environments: RECOMMENDED for use in operational settings and specifically designed to fill the capability gap for ground medics operating in these areas. Updated version of Inoserp MENA made specifically for the austere and operational medicine environment. Freeze-dried, unrefrigerated, stable at temperatures > 100° F for at least 180 days without loss of efficacy. Broad coverage and simple dosing enable administration in the field for any symptomatic snakebite by unknown species in this region. Special operations and conventional units deploying to austere operational environments and areas with critical threat venomous species should carry 8 vials per medic. It is recommended that a reserve quantity is stocked in all role 2 and role 3 facilities in AFRICOM in case additional antivenom is needed upon arrival, and also to restock field medics that have used their supply.

Adverse reactions: High efficacy against all major syndromes and low incidence of serious adverse reactions of approximately 1% based on current publications.^{165–172}

- 1. Indications:** Broad spectrum polyvalent directly indicated for the treatment of neurotoxic, hemotoxic, and cytotoxic envenomation syndromes caused by 27 different species of Middle Eastern, North African, and Central Asian snakes from the families *Elapidae* and *Viperidae*. First line for snake envenomations in this region when the causative species is unknown or among those for which the product is directly indicated.
 - a. NEUROTOXIC:** *Naja haje*, *N. oxiana*; *Walterinnesia aegyptia*
 - b. CYTOTOXIC and/or HEMOTOXIC:** *Bitis arietans*; *Cerastes cerastes*, *C. vipera*, *C. gasperettii*; *Daboia palestinae*, *D. mauritanica*, *D. deserti*; *Echis carinatus sochureki*, *E. coloratus*, *E. khosatskii*, *E. leucogaster*, *E. megalcephalus*, *E. omanensis*, *E. pyramidum*; *Macrovipera lebetina obtusa*, *M. l. transmediterranea*, *M. l. turanica*; *Montivipera bornmuelleri*, *M. raddei kurdistanica*; *Naja nubiae*, *N. pallida*; *Pseudocerastes persicus persicus*, *P. fieldi*; *Vipera latastei*
- 2. Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
- 3. Initial dosing by syndrome:**
 - a. NEUROTOXIC** initial dose = 6 vials
 - b. HEMOTOXIC** initial dose = 6 vials
 - c. CYTOTOXIC** initial dose = 6 vials

4. **Additional dosing:** Additional doses of 2 vials POLYSERP-M may be given at hours 2, 4, 6, 12, and 24 if needed.
5. **Preparation and administration:** Reconstitute every 2 vials of POLYSERP-M in the same 10 mL syringe by mixing the first vial, drawing it back up into syringe, and injecting it into the second vial to yield 2 vials/1 syringe (6 vial dose = 3 syringes total). Administer sequentially via slow, continuous direct IV or IO push over approximately 2 minutes each. If a reaction occurs stop the push, treat the reaction, reassess response to treatment criteria. Dilute remaining dose in a 100 mL bag of isotonic fluids and administer via slow IV or IO infusion over 30 minutes if needed.
 - a. Direct push is recommended for convenience, but POLYSERP-M may also be administered via IV or IO infusion. Mix in a 50 mL or 100 mL bag of isotonic fluids and administer the entire bag over 5–10 minutes.

AFRICOM – SUB-SAHARAN AFRICA LIQUID/REFRIGERATED

South African Vaccine Producers, South Africa: **SAVP SAIMR Boomslang Monovalent (SAIMR-B)**

Second line, boomslang only (AFRICOM–SUB-SAHARAN AFRICA): Confirmed or suspected boomslang bite with no indications of improvement after 10 vials of POLYSERP-P. Monovalent that can only be used to treat the WHO category 2 boomslang. Does not provide coverage against any other WHO category 1 or category 2 species.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Requires cold chain refrigeration. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities in sub-Saharan Africa.

Adverse reactions: No clinical trials but effective anecdotally and in case reports.¹⁷³ Moderate to high rates of anaphylaxis are anticipated based data from related SAIMR-P polyvalent.^{174–180}

1. **Indications:** This monovalent is only effective for the boomslang.
 - a. **HEMOTOXIC:** *Dispholidus typus*
2. **Initial dosing by syndrome:**
 - a. NOT INDICATED FOR NEUROTOXIC
 - b. HEMOTOXIC with CONFIRMED OR SUSPECTED BOOMSLANG BITE (typical onset coagulopathy and bleeding 1–3 days after the bite; no significant pain, swelling, or tissue destruction)
 - i. Initial dose = 2 vials SAIMR-B
 1. POLYSERP-P should be the first line treatment for this species if available due to lower risk of allergic reactions.
 - c. NOT INDICATED FOR HEMOTOXIC envenomation by snakes other than the boomslang
 - d. NOT INDICATED FOR CYTOTOXIC
3. **Additional dosing:** Additional doses of 1 vial SAIMR-B may be repeated, if needed, at hours 2, 4, 6, 12, and 24 until cessation of all active bleeding or at 6, 12, and 24 for coagulopathy without bleeding.
4. **Pretreatment:** RECOMMENDED for this antivenom. Administer 0.25 mg epinephrine injected SQ prior to beginning antivenom infusion to reduce the risk of a serious reaction. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to 0.25 mg.
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 100 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.

- b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

AFRICOM – SUB-SAHARAN AFRICA LIQUID/REFRIGERATED

South African Vaccine Producers, South Africa: **SAVP SAIMR Polyvalent Snake Antivenom (SAIMR-P)**

Second line (AFRICOM–SUB-SAHARAN AFRICA): Unknown neurotoxic and/or cytotoxic envenomation in sub-Saharan Africa or with no indications of improvement after 10 vials of POLYSERP-P. Will not treat hemotoxic envenomations. SOUTHERN AFRICA: Directly or indirectly covers all WHO category 1 and category 2 species for which an antivenom currently exists. EAST/CENTRAL/WEST AFRICA: Covers many cytotoxic and neurotoxic snakes in West, Central, and East Africa but has major coverage gaps with no efficacy against all WHO category 1 or category 2 hemotoxic snake species.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Requires cold chain refrigeration. Recommend storing small quantities at strategically located Role 2 & 3 facilities in AFRICOM AOR.

Adverse reactions: High efficacy but very high rates of anaphylaxis ranging from 25%–75% have been documented in multiple publications.^{50,174–180}

1. **Indications:** This polyvalent can be used to treat neurotoxic and cytotoxic envenomations by 10 different species of African snakes. The product has been used successfully to treat additional species of African snakes through paraspecific neutralization, but research in this area is limited and most experiences are anecdotal. The 10 species listed below are the official treatment indications recommended by the manufacturer:
 - a. **NEUROTOXIC SNAKES:** *Dendroaspis polylepis*, *D. angusticeps*, *D. jamesoni*, *Naja melanoleuca*, *N. nivea*, *N. annulifera*
 - b. **CYTOTOXIC SNAKES:** *Bitis arietans*, *B. gabonica*, *Naja mossambica*, *Hemachatus haemachatus*
2. **Initial dosing by syndrome:**

NEUROTOXIC initial dose = 10 vials

 - a. NOT INDICATED FOR HEMOTOXIC
 - b. CYTOTOXIC initial dose = 10 vials
3. **Additional dosing:** Additional doses of 5 vials SAIMR-P may be given at hours 2, 4, 6, 12, and 24 if needed.
4. **Pretreatment:** RECOMMENDED for this antivenom. Administer 0.25 mg epinephrine injected SQ prior to beginning antivenom infusion to reduce the risk of a serious reaction. Pediatric epinephrine dose is weight based (0.01 mg/kg).
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 250–500 mL bag of isotonic solution and administer by intravenous infusion over 10–30 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

AFRICOM – NORTH AFRICA LIQUID/REFRIGERATED

National Antivenom & Vaccine Production Center, Saudi

Arabia: **Polyvalent Snake Antivenom (NAVPC-P)**

Second line (AFRICOM–NORTH AFRICA): Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 10 vials of POLYSERP-M. Directly or indirectly covers some of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.

Second line (CENTCOM–ARABIAN PENINSULA): Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 10 vials of POLYSERP-M. Only for Arabian Peninsula, very limited utility further East. Directly or indirectly covers most of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Requires refrigeration, moderate to high rates of adverse reactions are anticipated. Better alternatives exist. If purchased it should be kept at Role 2 & 3 facilities in the Arabian Peninsula.

Adverse reactions: Insufficient evidence to determine risk of adverse reactions at this time.

1. **Indications:** This polyvalent can be used to treat neurotoxic and cytotoxic envenomations by 6 different species of Middle Eastern, North African, and Central Asian snakes. It may be able to neutralize venom from additional species through paraspecific neutralization but this has not been researched.^{181–186} The 6 species listed below are the official treatment indications recommended by the manufacturer:

- NEUROTOXIC:** *Walterinnesia aegyptia*, *Naja haje*
- HEMOTOXIC and/or CYTOTOXIC:** *Bitis arietans*, *Echis coloratus*, *Echis carinatus*, *Cerastes cerastes*

2. **Initial dosing by syndrome:**

- NEUROTOXIC** initial dose = 10 vials
- HEMOTOXIC** initial dose = 5 vials
- CYTOTOXIC** initial dose = 5 vials

3. **Additional dosing:** Additional doses of 5 vials NAVPC-C may be given at hours 2, 4, 6, 12, and 24 if needed.

4. **Pretreatment:** RECOMMENDED for this antivenom due to insufficient evidence for determining risk of EARs. Administer 0.25 mg epinephrine injected SQ prior to beginning antivenom infusion to reduce the risk of a serious reaction. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to 0.25 mg.

5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 250–500 mL bag of isotonic solution and administer by intravenous infusion over 10–30 minutes.

- If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
- If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

CENTCOM – ANTIVENOM RECOMMENDATIONS

CENTCOM – MIDDLE EAST/CENTRAL ASIA/ARABIAN PENINSULA FREEZE-DRIED/UNREFRIGERATED

POLYSERP/Inosan, Spain: POLYSERP MENA Polyvalent (POLYSERP-M)

First line (CENTCOM–ARABIAN PENINSULA/MIDDLE EAST/CENTRAL ASIA): BROAD-SPECTRUM treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in the Arabian Peninsula, the Middle East, and Central Asia when the

causative species is either unknown or among the 27 snakes for which this product is directly indicated. Directly or indirectly covers all WHO category 1 species in the region. Directly or indirectly covers all category 2 snakes in this region for which an antivenom currently exists except for *Gloydius halys*, which is covered by Shanghai SIOBP-G or Iranian RAZI-P. Paraspecific neutralization against *Gloydius* unknown but not anticipated.

Feasibility of use in austere environments: RECOMMENDED for use in operational settings and specifically designed to fill the capability gap for ground medics operating in these areas. Updated version of Inoserp MENA made specifically for the austere and operational medicine environment. Freeze-dried, unrefrigerated, stable at temperatures > 100° F for at least 180 days without loss of efficacy. Broad coverage and simple dosing enable administration in the field for any symptomatic snakebite by unknown species in this region. Special operations and conventional units deploying to austere operational environments and areas with critical threat venomous species should carry 8 vials per medic. It is recommended that a reserve quantity is stocked in all role 2 and role 3 facilities in AFRICOM in case additional antivenom is needed upon arrival, and also to restock field medics that have used their supply.

Adverse reactions: High efficacy against all major syndromes and low incidence of serious adverse reactions of approximately 1% based on current publications.^{165–172}

1. **Indications:** Broad spectrum polyvalent directly indicated for the treatment of neurotoxic, hemotoxic, and cytotoxic envenomation syndromes caused by 27 different species of Middle Eastern, North African, and Central Asian snakes from the families *Elapidae* and *Viperidae*. First line for snake envenomations in this region when the causative species is unknown or among the species for which the product is directly indicated.

- NEUROTOXIC:** *Naja haje*, *N. oxiana*; *Walterinnesia aegyptia*
- CYTOTOXIC and/or HEMOTOXIC:** *Bitis arietans*; *Cerastes cerastes*, *C. vipera*, *C. gasperettii*; *Daboia palestinae*, *D. mauritanica*, *D. deserti*; *Echis carinatus sochureki*, *E. coloratus*, *E. khosatskii*, *E. leucogaster*, *E. megalcephalus*, *E. omanensis*, *E. pyramidum*; *Macrovipera lebetina obtusa*, *M. l. transmediterranea*, *M. l. turanica*; *Montivipera bornmuelleri*, *M. raddei kurdistanica*; *Naja nubiae*, *N. pallida*; *Pseudocerastes persicus persicus*, *P. fieldi*; *Vipera latastei*

2. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

3. **Initial dosing by syndrome:**

- NEUROTOXIC** initial dose = 6 vials
- HEMOTOXIC** initial dose = 6 vials
- CYTOTOXIC** initial dose = 6 vials

4. **Additional dosing:** Additional doses of 2 vials POLYSERP-M may be given at hours 2, 4, 6, 12, and 24 if needed.

5. **Preparation and administration:** Reconstitute every 2 vials of POLYSERP-M in the same 10 mL syringe by mixing the first vial, drawing it back up into syringe, and injecting it into the second vial to yield 2 vials/1 syringe (6 vial dose = 3 syringes total). Administer sequentially via slow, continuous direct IV or IO push over approximately 2 minutes each. If a reaction occurs stop the push, treat the reaction, reassess response to treatment criteria. Dilute remaining dose in a 100 mL bag of isotonic fluids and administer via slow IV or IO infusion over 30 minutes if needed.

- Direct push is recommended for convenience, but POLYSERP-M may also be administered via IV or IO infusion. Mix in a 50 mL or 100 mL bag of isotonic fluids and administer the entire bag over 5–10 minutes.

CENTCOM – MIDDLE EAST/CENTRAL ASIA
LIQUID/REFRIGERATED

Shanghai Institute of Biological Products, China: *Agkistrodon (Gloydius) halys Monovalent Antivenom (SIOBP-G)*:

Note that this product is listed as *Agkistrodon halys* on the SIOBP website and product packaging but the taxonomy for this species has changed. *Agkistrodon halys* was moved to the genus *Gloydius* and should be listed as *Gloydius halys* as it is listed elsewhere. The product is abbreviated as SIOBP-G in the CPGs to account for this correction.

First line (CENTCOM–MIDDLE EAST/CENTRAL ASIA): Monovalent for the WHO category 2 species *Gloydius halys*. Indicated only for confirmed envenomation by *Gloydius halys* or related *Gloydius* species. Does not provide coverage against any other WHO category 1 or category 2 species.

Second line (CENTCOM–MIDDLE EAST/CENTRAL ASIA): Indicated for unknown cytotoxic and/or hemotoxic envenomation in Middle East or Central Asia with no signs of improvement after 10 vials of POLYSERP-M.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Requires cold chain refrigeration. Recommend storing small quantities at strategically located Role 2 & 3 facilities in CENTCOM AOR.

Incidence of adverse reactions: Low to moderate rates of EARs and serum sickness are anticipated but clinical evidence is limited.^{187–189}

- 1. Indications:** This monovalent can be used to treat cytotoxic and hemotoxic envenomations by *Gloydius halys*, a pit viper native to the Middle East and Central Asia. It will most likely neutralize venom from related species in the genus *Gloydius* through paraspecificity, but this has not been tested in detail. There are several publications indicating that it may also have paraspecificity against some of the Southeast Asian green pit vipers from the genera *Cryptelytrops* and *Trimeresurus*.^{190,191} However, it is not currently indicated by the manufacturer for these species.
 - a. HEMOTOXIC AND/OR CYTOTOXIC:** *Gloydius halys*
- 2. Initial dosing by syndrome:**
 - a. NOT INDICATED FOR NEUROTOXIC**
 - b. HEMOTOXIC initial dose = 2 vials**
 - c. CYTOTOXIC initial dose = 2 vials**
- 3. Additional dosing:** Additional doses of 2 vials SIOBP-G may be given at hours 2, 4, 6, 12, and 24 if needed.
- 4. Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met.
- 5. Preparation and administration:** Dilute the entire dose of antivenom in a single 100 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs,** slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs,** stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

CENTCOM – MIDDLE EAST/CENTRAL ASIA
LIQUID/REFRIGERATED

Razi Serum and Vaccine Research Institute, Islamic Republic of Iran: *Polyvalent Snake Antivenom (RAZI-P)*

Second line (CENTCOM–MIDDLE EAST/CENTRAL ASIA): Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 10 vials of POLYSERP-M.

Directly or indirectly covers all WHO category 1 species in the region. Directly or indirectly covers some of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Requires cold chain refrigeration. Recommend storing small quantities at strategically located Role 2 & 3 facilities in CENTCOM AOR or selecting alternative second line from this CPG.

Adverse reactions: Limited evidence but appears to be low based on current publications.^{192–199}

- 1. Indications:** This polyvalent can be used to treat neurotoxic and cytotoxic envenomations by 6 different species of Middle Eastern, North African, and Central Asian snakes. It may be able to neutralize venom from additional species through paraspecific neutralization but this has not been researched. The 6 species listed below are the official treatment indications recommended by the manufacturer:
 - a. NEUROTOXIC:** *Naja oxiana*
 - b. HEMOTOXIC and/or CYTOTOXIC:** *Pseudocerastes persicus fieldi*, *Echis carinatus*, *Vipera albicornuta*, *Vipera lebetina obtusa*, *Agkistrodon (Gloydius) halys*
- 2. Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met.
- 3. Initial dosing by syndrome:**
 - a. NEUROTOXIC initial dose = 10 vials**
 - b. HEMOTOXIC initial dose = 5 vials**
 - c. CYTOTOXIC initial dose = 5 vials**
- 4. Additional dosing:** Additional doses of 5 vials RAZI-P may be given at hours 2, 4, 6, 12, and 24 if needed.
- 5. Preparation and administration:** Dilute the entire dose of antivenom in a single 250–500 mL bag of isotonic solution and administer by intravenous infusion over 10–30 minutes.
 - a. If a mild or moderate reaction occurs,** slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs,** stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

CENTCOM – ARABIAN PENINSULA
LIQUID/REFRIGERATED

National Antivenom & Vaccine Production Center, Saudi

Arabia: *Polyvalent Snake Antivenom (NAVPC-P)*

Second line (CENTCOM–ARABIAN PENINSULA): Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 10 vials of POLYSERP-M. Only for Arabian Peninsula, very limited utility further East. Directly or indirectly covers most of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Requires refrigeration, moderate to high rates of adverse reactions are anticipated. Better alternatives exist. If purchased it should be kept at Role 2 & 3 facilities in the Arabian Peninsula.

Adverse reactions: Insufficient evidence to determine risk of adverse reactions at this time.

- 1. Indications:** This polyvalent can be used to treat neurotoxic and cytotoxic envenomations by 6 different species of Middle Eastern, North African, and Central Asian snakes. It may be able to neutralize venom from additional species through paraspecific

neutralization but this has not been researched.¹⁸¹⁻¹⁸⁶ The 6 species listed below are the official treatment indications recommended by the manufacturer:

- a. **NEUROTOXIC:** *Walterinnesia aegyptia*, *Naja haje*
 - b. **HEMOTOXIC and/or CYTOTOXIC:** *Bitis arietans*, *Echis coloratus*, *Echis carinatus*, *Cerastes cerastes*
2. **Initial dosing by syndrome:**
- a. NEUROTOXIC initial dose = 10 vials
 - b. HEMOTOXIC initial dose = 5 vials
 - c. CYTOTOXIC initial dose = 5 vials
3. **Additional dosing:** Additional doses of 5 vials NAVPC-C may be given at hours 2, 4, 6, 12, and 24 if needed.
4. **Pretreatment:** RECOMMENDED for this antivenom due to insufficient evidence for determining risk of EARs. Administer 0.25 mg epinephrine injected SQ prior to beginning antivenom infusion to reduce the risk of a serious reaction. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to 0.25 mg.
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 250–500 mL bag of isotonic solution and administer by intravenous infusion over 10–30 minutes.
- a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

EUCOM – ANTIVENOM RECOMMENDATIONS

EUCOM – OUTSIDE UK/SCANDINAVIA FREEZE-DRIED/REFRIGERATED

Sanofi-Pasteur, France: **Viperfav (VIPERFAV)**²⁰⁰⁻²⁰⁶

First line (EUCOM–EUCOM OUTSIDE UK/SCANDINAVIA): Single-source treatment option for neurotoxic, hemotoxic, and cytotoxic snake envenomations by the most medically and epidemiologically significant species in Europe (*Vipera berus*, *V. aspis*, *V. ammodytes*) with paraspecific coverage against other European *Vipera* species. Can be used in the EUCOM AOR when the causative species is unknown or species for which this product is directly indicated.

Second line (EUCOM–UK/SCANDINAVIA): Second line treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations within the UK and Scandinavia if first line (VIPERATAB) is not available.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Requires cold chain refrigeration between 2–8° C (35.6–46.4° F). Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities. Likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

Adverse reactions: High efficacy against all major syndromes and low incidence of serious adverse reactions based on current publications.

1. **Indications:** Polyvalent antivenom directly indicated for the treatment of neurotoxic, hemotoxic, and cytotoxic envenomation syndromes caused by *Vipera berus*, *V. aspis*, *V. ammodytes* but has demonstrated efficacy against other species of European vipers (genus *Vipera*) as well.
2. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
3. **Initial dosing by syndrome:**

- a. NEUROTOXIC initial dose = 2 vials
 - b. HEMOTOXIC initial dose = 1–2 vials
 - c. CYTOTOXIC initial dose = 1–2 vials
4. **Additional dosing:** Additional doses of 1 vial VIPERFAV may be given at hours 2, 4, 6, 12, and 24 if needed.
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 100 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
- a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

EUCOM – UK/SCANDINAVIA FREEZE-DRIED/REFRIGERATED

Micropharm, UK: **ViperaTab (VIPERATAB)**^{200,204,207–209}

First line (EUCOM–UK/SCANDINAVIA): Single-source treatment option for neurotoxic, hemotoxic, and cytotoxic snake envenomations by the most medically and epidemiologically significant species in the UK and Scandinavia (*Vipera berus*) with paraspecific coverage against some other European *Vipera* species.

Second line (EUCOM–OUTSIDE OF UK/SCANDINAVIA): Second line treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in the EUCOM AOR outside of the UK and Scandinavia if first line (VIPERFAV) is not available.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Requires cold chain refrigeration between 2–8° C (35.6–46.4° F). Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities. Likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

Adverse reactions: High efficacy against UK/Scandinavian European viper (*Vipera berus*) envenomations and low incidence of serious adverse reactions based on current publications.

1. **Indications:** Polyvalent antivenom directly indicated for the treatment of neurotoxic, hemotoxic, and cytotoxic envenomation syndromes caused by *Vipera berus*. Has demonstrated efficacy against other species of European vipers (*V. aspis*, *V. ammodytes*) as well but is not directly indicated for these species.
2. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
3. **Initial dosing by syndrome:**
 - a. NEUROTOXIC initial dose = 2 vials
 - b. HEMOTOXIC initial dose = 2 vials
 - c. CYTOTOXIC initial dose = 2 vials
4. **Additional dosing:** Additional 2 vials VIPERATAB may be given at hours 2, 4, 6, 12, and 24 if needed.
5. **Preparation and administration:** Each box of VIPERATAB comes with two 4 mL vials of antivenom (one box = one dose). Dilute the entire dose of antivenom in a single 100 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed

elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

INDOPACOM – ANTIVENOM RECOMMENDATIONS

INDOPACOM – SOUTHEAST ASIA (BROAD-SPECTRUM HEMO/CYTOTOXIC) FREEZE-DRIED/UNREFRIGERATED Thai Red Cross, Thailand: **Hemato Polyvalent Antivenom (TRC-HPAV)**^{61,190,191,210-212}

First line (INDOPACOM–SOUTHEAST ASIA): Broad-spectrum treatment option for all hemotoxic and cytotoxic snake envenomations by known or unknown species in Southeast Asia. Best regional polyvalent.

Feasibility of use in austere environments: RECOMMENDED for operational settings. Unrefrigerated storage at ambient tropical temperatures of $\leq 25^{\circ}\text{C}/77^{\circ}\text{F}$. Lyophilized product that likely retains stability at higher temperatures for short excursions (likely up to several months). Recommend carrying full dose into field on extended operations in austere environments and storing larger quantities at strategically located Role 2 & 3 facilities in INDOPACOM AOR.

Adverse reactions: High efficacy against and low incidence of serious adverse reactions based on current publications.

- 1. Indications:** Polyvalent antivenom directly indicated for the treatment of hemotoxic and cytotoxic envenomation syndromes caused by *Calloselasma rhodostoma*, *Trimerurus albolabris*, and *Daboia russelli siamensis*. Has demonstrated efficacy against other related species of Asian vipers within the same genera (*Cryptelytrops*, *Popeia*, *Daboia*, etc.); is not directly indicated for these species but is the best hemotoxic/cytotoxic polyvalent in the region and should be tried as first line in most cases.
- 2. Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
- 3. Initial dosing by syndrome:**
 - a. NOT INDICATED FOR NEUROTOXIC
 - b. HEMOTOXIC initial dose = 10 vials
 - c. CYTOTOXIC initial dose = 10 vials
- 4. Additional dosing:** Additional 2 vials TRC-HPAV may be given at hours 2, 4, 6, 12, and 24 if needed.
- 5. Preparation and administration:** Dilute the entire dose of antivenom in a single 250–500 mL bag of isotonic solution and administer by intravenous infusion over 10–30 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

INDOPACOM – SOUTHEAST ASIA (BROAD-SPECTRUM NEUROTOXIC) FREEZE-DRIED/UNREFRIGERATED Thai Red Cross, Thailand: **Neuro Polyvalent Antivenom (TRC-NPAV)**^{61,190,211,213-215}

First line (INDOPACOM–SOUTHEAST ASIA): Broad-spectrum treatment option for all neurotoxic snake envenomations by known or unknown species in Southeast Asia. Best regional polyvalent.

Feasibility of use in austere environments: RECOMMENDED for operational settings. Unrefrigerated storage at ambient tropical

temperatures of $\leq 25^{\circ}\text{C}/77^{\circ}\text{F}$. Lyophilized product that likely retains stability at higher temperatures for field excursions (likely stable for several months at higher temps based on data from similar products). Recommend carrying full dose into field on extended operations in austere environments and storing larger quantities at strategically located Role 2 & 3 facilities in INDOPACOM AOR.

Adverse reactions: High efficacy and low incidence of serious adverse reactions based on current publications.

- 1. Indications:** Polyvalent antivenom directly indicated for the treatment of hemotoxic and cytotoxic envenomation syndromes caused by *Ophiophagus hannah*, *Naja kaouthia*, *Bungarus candidus*, and *B. fasciatus candidus*. Has demonstrated efficacy against other related species of Asian cobras and kraits; is not directly indicated for these species but is the best hemotoxic/cytotoxic polyvalent in the region and should be tried as the first line in most cases.
- 2. Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
- 3. Initial dosing by syndrome:**
 - a. NEUROTOXIC initial dose = 10 vials
 - i. *King cobra (O. hannah) bites likely to require much higher doses of antivenom due to massive venom yield; it is not unusual to require dozens of vials in these cases.*
 - b. NOT INDICATED FOR HEMOTOXIC
 - c. NOT INDICATED FOR CYTOTOXIC
- 4. Additional dosing:** Additional 5 vials TRC-NPAV may be given at hours 2, 4, 6, 12, and 24 if needed. Bites from large king cobras may require several dozen vials or more due to massive venom yield.
- 5. Preparation and administration:** Dilute the entire dose of antivenom in a single 250–500 mL bag of isotonic solution and administer by intravenous infusion over 10–30 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

INDOPACOM – SOUTHEAST CHINA/NORTH LAOS/ NORTH VIETNAM FREEZE-DRIED/REFRIGERATED National Institute Preventative Medicine, Taiwan: **Naja atra/ Bungarus multicinctus Bivalent (NIPM-NBB)**²¹⁶⁻²²⁴

**First line (INDOPACOM–TAIWAN/SOUTHEAST CHINA/
NORTH LAOS/NORTH VIETNAM):** Bivalent treatment option for neurotoxic cobra and krait envenomations in East Asia.

Feasibility of use in austere environments: CONDITIONALLY RECOMMENDED for operational settings during short excursions. Lyophilized but requires cold chain refrigeration below 10°C (50°F); however, testing by Taiwanese CDC showed no loss of potency after 30 days of incubation at $35^{\circ}\text{C}/95^{\circ}\text{F}$ and also after it was returned to refrigerated storage for 4 months thereafter. Recommend carrying full dose into field on extended operations in austere environments and storing larger quantities at regional Role 2 & 3 facilities.

Adverse reactions: High efficacy and low incidence of serious adverse reactions based on current publications.

- 1. Indications:** Polyvalent antivenom directly indicated for the treatment of hemotoxic and cytotoxic envenomation syndromes

caused by *Naja atra* and *Bungarus multicinctus*. Has demonstrated efficacy against other related species of Asian cobras and kraits but is not directly indicated for these species.

2. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
3. **Initial dosing by syndrome:**
 - a. NEUROTOXIC initial dose = 5 vials
 - b. NOT INDICATED FOR HEMOTOXIC
 - c. NOT INDICATED FOR CYTOTOXIC
4. **Additional dosing:** Additional 5 vials NIPM-NBB may be given at hours 2, 4, 6, 12, and 24 if needed.
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 100–500 mL bag of isotonic solution and administer by intravenous infusion over 10–30 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

INDOPACOM – JAPAN FREEZE-DRIED/REFRIGERATED Chemo-Sero Therapeutic Research Institute, Japan: Kaketsuken Habu Antivenom (CSTRI-HABU)^{225–229}

First line (INDOPACOM–JAPAN): First line treatment option for Habu envenomation (*Protobothrops* spp.).

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Lyophilized but requires cold chain refrigeration below 10° C (50° F); likely to retain efficacy for short excursions lasting several weeks in the field but should be disposed of and replaced after extended time outside refrigeration. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities.

Adverse reactions: High efficacy and low incidence of serious adverse reactions based on current publications.

1. **Indications:** Directly indicated for the treatment of hemotoxic and cytotoxic envenomation syndromes caused by the Japanese Habu (*Protobothrops [Trimeresurus] flavoviridis*)
2. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met; however, total reactions (~11% overall; ~25% serum sickness) higher than other regional products. Consider pretreatment on an individual basis.
3. **Initial dosing by syndrome:**
 - a. NOT INDICATED FOR NEUROTOXIC
 - b. HEMOTOXIC = 1–2 vials
 - c. CYTOTOXIC = 1–2 vials
4. **Additional dosing:** Additional 1 vial CSTRI-HABU may be given at hours 2, 4, 6, 12, and 24 if needed.
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 100 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

INDOPACOM – JAPAN FREEZE-DRIED/REFRIGERATED Chemo-Sero Therapeutic Research Institute, Japan: Kaketsuken Mamushi Antivenom (CSTRI-MAMU)^{225–229}

First line (INDOPACOM–JAPAN): First line treatment option for Mamushi envenomation (*Gloydius blomhoffii*) in Japan.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Lyophilized but requires cold chain refrigeration below 10° C (50° F); likely to retain efficacy for short excursions lasting several weeks in the field but should be disposed of and replaced after extended time outside refrigeration. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities.

Adverse reactions: High efficacy and low incidence of serious adverse reactions based on current publications.

1. **Indications:** Directly indicated for the treatment of hemotoxic and cytotoxic envenomation syndromes caused by the Japanese Mamushi, *Gloydius blomhoffii*.
2. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
3. **Initial dosing by syndrome:**
 - a. NOT INDICATED FOR NEUROTOXIC
 - b. HEMOTOXIC = 1–2 vials
 - c. CYTOTOXIC = 1–2 vials
4. **Additional dosing:** Additional 1 vial CSTRI-MAMU may be given at hours 2, 4, 6, 12, and 24 if needed.
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 100 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

INDOPACOM – NORTH & SOUTH KOREA/VIETNAM/EAST RUSSIA FREEZE-DRIED/REFRIGERATED Japan Snake Institute, Japan: Anti-Yamakagashi Antivenom (JSI-AYA)^{225–227}

First line (INDOPACOM–JAPAN/CHINA/NORTH KOREA/SOUTH KOREA/VIETNAM/EASTERN RUSSIA): First line treatment option for Keelback envenomation (*Rhabdophis tigrinus*).

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Lyophilized but requires cold chain refrigeration below 10° C (50° F); likely to retain efficacy for short excursions lasting several weeks in the field but should be disposed of and replaced after extended time outside refrigeration. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities.

Adverse reactions: High efficacy and low incidence of serious adverse reactions based on current publications.

1. **Indications:** Directly indicated for the treatment of hemotoxic and cytotoxic envenomation syndromes caused by the Tiger Keelback (*Rhabdophis tigrinus*) and other East Asian keelbacks.
2. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
3. **Initial dosing by syndrome:**
 - a. NOT INDICATED FOR NEUROTOXIC

- b. HEMOTOXIC = 1–2 vials
- c. CYTOTOXIC = 1–2 vials
- 4. **Additional dosing:** Additional 1 vial JSI-AYA may be given at hours 2, 4, 6, 12, and 24 if needed.
- 5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 100 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

INDOPACOM – EAST CHINA FREEZE-DRIED/REFRIGERATED

Korea Vaccine, Korea: **Agkistrodon Mamushi Antivenom (KOVAX-AKA)**^{229–234}

First line (INDOPACOM–NORTH KOREA/SOUTH KOREA): First line treatment option for Mamushi envenomations in North and South Korea.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Lyophilized but requires cold chain refrigeration below 10° C (50° F); likely to retain efficacy for short excursions lasting several weeks in the field but should be disposed of and replaced after extended time outside refrigeration. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities.

Adverse reactions: High efficacy and low incidence of serious adverse reactions based on current publications.

1. **Indications:** Directly indicated for the treatment of hemotoxic and cytotoxic envenomation syndromes caused by the major species of Mamushi in the Korean Peninsula (*Gloydius brevicaudus*, *G. ussuriensis*, *G. intermedius*). May neutralize other related species.
2. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
3. **Initial dosing by syndrome:**
 - a. NOT INDICATED FOR NEUROTOXIC
 - b. HEMOTOXIC = 1–2 vials
 - c. CYTOTOXIC = 1–2 vials
4. **Additional dosing:** Additional 1 vial KOVAX-AMA may be given at hours 2, 4, 6, 12, and 24 if needed.
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 100 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

INDOPACOM – SOUTHEAST CHINA/NORTH VIETNAM/
LAOS FREEZE-DRIED/REFRIGERATED
National Institute Preventative Medicine, Taiwan: **Sharp-nosed Viper Monovalent (NIPM-SNV)**^{229–234}

First line (INDOPACOM–TAIWAN/SOUTHEAST CHINA/NORTH VIETNAM/LAOS): First line treatment option for Sharp-nosed viper envenomations (*Deinagkistrodon acutus*).

Feasibility of use in austere environments: CONDITIONALLY RECOMMENDED for operational settings during short excursions. Lyophilized but requires cold chain refrigeration below 10° C (50° F); however, testing by Taiwanese CDC showed no loss of potency after 30 days of incubation at 35° C/95° F and also after it was returned to refrigerated storage for 4 months thereafter. Recommend carrying full dose into field on extended operations in austere environments and storing larger quantities at regional Role 2 & 3 facilities.

Adverse reactions: High efficacy and low incidence of serious adverse reactions based on current publications.

1. **Indications:** Monovalent antivenom directly indicated for the treatment of hemotoxic and cytotoxic envenomation syndromes caused by *Deinagkistrodon acutus*.
2. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
3. **Initial dosing by syndrome:**
 - a. NOT INDICATED FOR NEUROTOXIC
 - b. HEMOTOXIC initial dose = 2 vials
 - c. CYTOTOXIC initial dose = 2 vials
4. **Additional dosing:** Additional 1 vials NIPM-SNV may be given at hours 2, 4, 6, 12, and 24 if needed.
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 100 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

INDOPACOM – SEA SNAKE BITES/
MARINE ENVIRONMENTS LIQUID/REFRIGERATED
Commonwealth Serum Laboratories, Australia: **Sea Snake (CSL-SS)**
First Line (INDOPACOM–MARINE ENVIRONMENTS ONLY): Neurotoxic envenomation in INDOPACOM by sea snakes or unknown species occurring in a strictly marine environment.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Requires cold chain refrigeration between 2–8° C (35.6–46.4° F). Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities. Likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

Adverse reactions: High-quality product with low rates of reactions anticipated.

1. **Indications:** This polyvalent can be used to treat neurotoxic envenomations by most major species of sea snakes in Australasia.
2. **Initial dosing by syndrome:**
 - a. Neurotoxic syndrome initial dose = 3 vials
 - b. NOT INDICATED for hemotoxic envenomations
 - c. NOT INDICATED for cytotoxic envenomations
3. **Additional dosing:** Additional doses of 1 vials CSL-SS may be given at hours 2, 4, 6, 12, and 24 if needed.
4. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other

pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 100 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

INDOPACOM – MALUKU ISLANDS/ WEST PAPUA ISLANDS LIQUID/REFRIGERATED

Commonwealth Serum Laboratories, Australia: **Polyvalent (CSL-P) First Line (INDOPACOM–MALUKU/WEST PAPUA ISLANDS ONLY):** Neurotoxic envenomation in INDOPACOM by Australasian elapids or unknown species occurring East of Wallace's line.

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Requires cold chain refrigeration between 2–8° C (35.6–46.4° F). Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities. Likely to retain efficacy during short excursion at higher temperatures for several weeks in the field but should be disposed of and replaced afterwards.

Adverse reactions: High-quality product with low rates of reactions anticipated.

1. **Indications:** This polyvalent can be used to treat neurotoxic envenomations by the most medically significant species of Australasian elapid snakes found East of Wallace's line.
2. **Initial dosing by syndrome:**
 - a. NEUROTOXIC syndrome initial dose = 3 vials
 - b. HEMOTOXIC syndrome initial dose = 3 vials
 - c. NOT INDICATED for cytotoxic envenomations
3. **Additional dosing:** Additional doses of 1 vial CSL-P may be given at hours 2, 4, 6, 12, and 24 if needed.
4. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 100 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

NORTHCOM – ANTIVENOM RECOMMENDATIONS

NORTHCOM – UNITED STATES/CANADA
FOR ALL NORTHCOM ANTIVENOMS, REFER TO THE PACKAGE INSERT IN THE ANTIVENOM BOX FOR SPECIFIC USAGE INSTRUCTIONS AS PER FDA REGULATIONS FOR DOMESTICALLY APPROVED PRODUCTS.

Also see *Unified treatment algorithm for the management of crotaline snakebite in the United States* (Lavonas et al. 2011) for specific dosing and management guidelines on pit viper bites.^{101,235}

BTG Therapeutics, United States: **CroFab (CROFAB)**^{94,95,101,236,237}

- a. FREEZE-DRIED/REFRIGERATED
- b. **Indications:** Envenomation by all Pit Viper species (rattlesnakes, copperheads, cottonmouths) in North America. Freeze-dried; requires refrigeration but one study has demonstrated that it will maintain efficacy under field conditions for ≥ 90 days if needed.
- c. **Initial dosing:** 4–6 vials

RDT/Instituto Bioclon, United States/Mexico: **ANAVIP (ANAVIP)**⁹²

- a. FREEZE-DRIED/UNREFRIGERATED
- b. **Indications:** Currently only indicated by FDA for rattlesnake envenomations. Not currently indicated for copperhead or cottonmouth envenomations, although this may change in the near future depending on results of upcoming studies. Freeze dried and field-stable at room temperature of 25° C/77° F.
- c. **Initial dosing:** 10 vials

Pfizer, United States: **North American Coral Snake Antivenom (NACSA)**²³⁸

- a. FREEZE-DRIED/REFRIGERATED
- b. **Indications:** Indicated for envenomations by North American coral snake species in the United States including Eastern coral snake (*Micrurus fulvius*) and Texas coral snake (*Micrurus tener*). Store between 2–8° C/35.6–46.4° F; however, likely retains stability for short excursions in the field.
- c. **Initial dosing:** 5 vials

SOUTHCOM – ANTIVENOM RECOMMENDATIONS

SOUTHCOM – ENTIRE AOR
FREEZE-DRIED/UNREFRIGERATED
Instituto Bioclon, Mexico: **ANTIVIPMYN-TRI (BIOCL-AVT)**^{239–243}

First Line (SOUTHCOM–ENTIRE SOUTHCOM AOR): BROAD-SPECTRUM treatment option for all hemotoxic and cytotoxic snake envenomations anywhere in the SOUTHCOM AOR when the causative species is either unknown or among the ≥ 14 snakes for which this product is directly indicated. Directly or indirectly covers most of the WHO category 1 and category 2 snakes in this region.

Feasibility of use in austere environments: RECOMMENDED for operational settings. Unrefrigerated storage at ambient tropical temperatures of ≤ 37° C/98.6° F. Lyophilized product that likely retains stability at higher temperatures for short excursions. Recommend carrying full dose or loading dose (≥ 5 vials) into field on extended operations in austere environments and storing larger quantities at strategically located Role 2 & 3 facilities in SOUTHCOM AOR.

Adverse reactions: High-quality product with low rates of reactions anticipated.

1. **Indications:** This broad-spectrum polyvalent can be used to treat hemotoxic and cytotoxic envenomations by more than 14 different species of Central and South American snakes. It may be able to neutralize venom from additional species through paraspecific neutralization but this has not been officially determined. The species listed below are the official treatment indications recommended by the manufacturer:
 - a. **HEMOTOXIC and/or CYTOTOXIC:** *Crotalus durissis terrificus*; *Bothrops asper*, *B. atrox*, *B. neuwiedii*, *B. alternatus*, *B. jararacussu*, *B. venezulensis*, *B. pictus*, *B. brazili*; *Lachesis muta muta*, *L. m. stenophrys*; *Sistrurus spp.*; *Agkistrodon spp.*
2. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met.

3. **Initial dosing by syndrome:**
 - a. NOT INDICATED FOR NEUROTOXIC
 - b. HEMOTOXIC initial dose = 10 vials
 - c. CYTOTOXIC initial dose = 10 vials
4. **Additional dosing:** Additional doses of 5 vials BIOCL-AVT may be given at hours 2, 4, 6, 12, and 24 if needed.
5. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
6. **Preparation and administration:** Dilute the entire dose of antivenom in a single 250–500 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

SOUTHCOM – ENTIRE AOR FREEZE-DRIED/UNREFRIGERATED

Instituto Bioclon, Mexico: **ANTIVIPMYN-TRI (BIOCL-AVT)**^{88–92}

First Line (SOUTHCOM–ENTIRE SOUTHCOM AOR): BROAD-SPECTRUM treatment option for all hemotoxic and cytotoxic snake envenomations anywhere in the SOUTHCOM AOR when the causative species is either unknown or among the ≥ 14 snakes for which this product is directly indicated. Directly or indirectly covers most of the WHO category 1 and category 2 snakes in this region.

Feasibility of use in austere environments: RECOMMENDED for operational settings. Unrefrigerated storage at ambient tropical temperatures of ≤ 37° C/98.6° F. Lyophilized product that likely retains stability at higher temperatures for short excursions. Recommend carrying full dose or loading dose (≥ 5 vials) into field on extended operations in austere environments and storing larger quantities at strategically located Role 2 & 3 facilities in SOUTHCOM AOR.

Adverse reactions: High-quality product with low rates of reactions anticipated.

1. **Indications:** This broad-spectrum polyvalent can be used to treat hemotoxic and cytotoxic envenomations by more than 14 different species of Central and South American snakes. It may be able to neutralize venom from additional species through paraspecific neutralization but this has not been officially determined. The species listed below are the official treatment indications recommended by the manufacturer:
 - a. **HEMOTOXIC and/or CYTOTOXIC:** *Crotalus durissis terrificus*; *Bothrops asper*, *B. atrox*, *B. neuwiedii*, *B. alternatus*, *B. jararacussu*, *B. venezulensis*, *B. pictus*, *B. brazili*; *Lachesis muta muta*, *L. m. stenophrys*; *Sistrurus spp.*; *Agkistrodon spp.*
2. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met.
3. **Initial dosing by syndrome:**
 - a. NOT INDICATED FOR NEUROTOXIC
 - b. HEMOTOXIC initial dose = 10 vials
 - c. CYTOTOXIC initial dose = 10 vials
4. **Additional dosing:** Additional doses of 5 vials BIOCL-AVT may be given at hours 2, 4, 6, 12, and 24 if needed.

5. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
6. **Preparation and administration:** Dilute the entire dose of antivenom in a single 250–500 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

SOUTHCOM – CENTRAL AMERICA/SOUTH AMERICA LIQUID/REFRIGERATED

Instituto Bioclon, Mexico: **CORALMYN (BIOCL-COR)**^{244–248}

First Line (SOUTHCOM–CENTRAL AMERICA): Neurotoxic envenomation in Central America by coral snakes or unknown species (coral snakes are only strictly neurotoxic snakes in SOUTHCOM AOR).

Second Line (SOUTHCOM–SOUTH AMERICA): May treat some coral snakes in South America but major coverage gaps in that region compared to the first line for South America (INS-AAP).

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Requires cold chain refrigeration between 2–8° C (35.6–46.4° F). Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities in South America. Likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

Adverse reactions: High-quality product with low rates of reactions anticipated.

1. **Indications:** This polyvalent can be used to treat neurotoxic envenomations by most major species of Central American coral snakes from the genus *Micrurus*.
 - a. **NEUROTOXIC:** Central American coral snakes (*Micrurus spp.*)
2. **Initial dosing by syndrome:**
 - a. NEUROTOXIC syndrome initial dose = 10 vials
 - b. NOT INDICATED for hemotoxic envenomations
 - c. NOT INDICATED for cytotoxic envenomations
3. **Additional dosing:** Additional doses of 5 vials BIOCL-COR may be given at hours 2, 4, 6, 12, and 24 if needed.
4. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 250–500 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

SOUTHCOM – SOUTH AMERICA/CENTRAL AMERICA LIQUID/REFRIGERATED

Instituto Nacional de Salud, Colombia: **Antiveneno Anticoral Polivalente (INS-AAP)**²⁴⁸

First Line (SOUTHCOM–SOUTH AMERICA): Broadest efficacy against neurotoxic snake bites by coral snakes or unknown species in South America. Coral snakes are the only strictly neurotoxic species in SOUTHCOM.

Second Line (SOUTHCOM–CENTRAL AMERICA): Should treat most coral snake species in Central America but will have some coverage gaps compared to the first line for Central America (BIOCL-COR).

Feasibility of use in austere environments: NOT RECOMMENDED for operational settings. Liquid product that requires cold chain refrigeration between 4–8° C/39.2–46.4° F. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities in South America. Likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

Adverse reactions: High-quality product with low rates of reactions anticipated.

1. **Indications:** This polyvalent can be used to treat neurotoxic envenomations by most major species of South American coral snakes from the genus *Micrurus* as well as some Central American species.
 - a. **NEUROTOXIC:** South American coral snakes (*Micrurus spp.*) including *Micrurus dumerilii*, *M. mipartitus*, *M. surinamensis*, *M. isozonus*, *M. lemniscatus*, *M. spixi*, *M. Medemi*
2. **Initial dosing by syndrome:**
 - a. NEUROTOXIC syndrome initial dose = 10 vials
 - b. NOT INDICATED for hemotoxic envenomations
 - c. NOT INDICATED for cytotoxic envenomations

3. **Additional dosing:** Additional doses of 5 vials INS-AAP may be given at hours 2, 4, 6, 12, and 24 if needed.
4. **Pretreatment:** NOT ROUTINELY INDICATED unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.
5. **Preparation and administration:** Dilute the entire dose of antivenom in a single 250–500 mL bag of isotonic solution and administer by intravenous infusion over 10 minutes.
 - a. If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
 - b. If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

Acknowledgments

Joint Trauma System Clinical Practice Guidelines are developed by subject matter experts and peer reviewed by members serving on the Defense Committee on Trauma: The Committee on Tactical Combat Casualty Care; the Committee on Surgical Combat Casualty Care; and the Committee on EnRoute Combat Casualty Care. Special thanks to those who devote their time, expertise, and experience to aid the JTS in publishing evidence-driven CPGs, providing the optimum chance for survival and maximum potential for functional recovery.

Joint Trauma System Clinical Practice Guideline
References can be found online at
<https://jsom.us/2U7MhtP>



For a glimpse into the work done by the Asclepius Snakebite Foundation, please see the photo gallery on pages 160–161.