CroFab LexiComp Drug Information

Therapeutic Category

• Antivenin – treats rattlesnakes (*Crotalus, Sistrurus*), copperheads, and cottonmouth/water moccasins envenomation

Dosing: Pediatric

**Crotalid envenomation:** Children and Adolescents: Clinical trials included patients as young as 11 years of age. Use has *been reported to be both safe and effective in children as young as 1 year of age* (Johnson 2008; Schmidt 2005; Seifert 2009).

*Note: Antivenom dosage is based on venom load and severity of symptoms and not on patient size; therefore, a reduced, weight-based antivenom dose in pediatric patients is not recommended* (Behm 2003; Lavonas 2011a; Offerman 2002).

Clinicians are encouraged to contact their local poison control center or clinical toxicologist for consultation when treating any envenomed patient, but especially pediatric patients.

*Initial dose: IV: 4 to 6 vials as soon as possible and preferably within 6 hours of snakebite; monitor for 1 hour following infusion to determine if initial control has been achieved as evidenced by arrest of local signs of envenomation* (eg, leading edge of local injury is not progressing).

*Some clinicians recommend an initial dose of 8 to 12 vials in patients presenting with immediately life-threatening effects* (eg, shock, respiratory distress, cardiovascular collapse, significant hemorrhage, or severe neurologic toxicity) (Goto 2009; Lavonas 2011a).

*If control is not achieved: repeat with additional dose of 4 to 6 vials until initial control is achieved and local manifestations, coagulation tests and systemic signs are normal.*

**Maximum initial dose:** 12 vials.

**Maintenance dose** (begin once control of envenomation achieved): *IV: 2 vials every 6 hours for up to 18 hours.* Optimal dosing beyond 18 hours has not been established; however, treatment may be continued if deemed necessary based on patient condition.
Administration

**IV infusion:** Administer at *an initial rate of 25 to 50 mL/hour for the first 10 minutes; if tolerated and no allergic reaction observed, then increase rate so that total dose infuses over 60 minutes, usually to 250 mL/hour.* Continue to monitor closely.

*Immediate treatment for anaphylactoid and/or hypersensitivity reactions should be available during the infusion.*

*Decreasing the rate of infusion may help control some infusion-related adverse effects, such as fever, nausea, low back pain, and wheezing.*

Adverse Reactions

- Cardiovascular: Hypotension
- Central nervous system: Chills
- Dermatologic: Pruritus, skin rash, urticaria
- Gastrointestinal: Anorexia, nausea
- Hypersensitivity: Anaphylactoid reaction, anaphylaxis, hypersensitivity reaction, serum sickness
- Respiratory: Asthma, cough, dyspnea, wheezing
- Miscellaneous: Fever

Rare but important or life-threatening: Angioedema, blood coagulation disorder (delayed, recurrent), chest discomfort, delayed hypersensitivity, dizziness, erythema, headache, hemorrhage, hyperhidrosis, laryngeal edema, musculoskeletal chest pain, swelling of lips, swelling (recurrent and refractory to treatment), swollen tongue, tachycardia, tachypnea, thrombocytopenia (refractory to treatment), tremor

Contraindications

Hypersensitivity to any component of the formulation (including *papaya or papain*), unless the benefits outweigh the risks and appropriate management for anaphylaxis is readily available

Warnings/Precautions

*Concern related to adverse effects:*

- Hypersensitivity reactions: Derived from sheep plasma; anaphylaxis and anaphylactoid reactions are possible, especially in patients with known allergies to sheep protein. Immediate treatment (including epinephrine 1 mg/mL) for anaphylactoid and/or hypersensitivity reactions should be available prior to administration. *In case of acute hypersensitivity reactions, including anaphylaxis and anaphylactoid reactions, discontinue infusion and institute appropriate emergency treatment.* Incidence of acute hypersensitivity reactions may be lower than previously thought (Buchanan 2009;
Cannon 2008; Lavonas 2011). This product lacks the immunogenic Fc fragments and proteins found in the older equine-derived product. Sensitization may occur with repeated doses.

- Processed with papain and may cause hypersensitivity reactions in patients allergic to papaya, other papaya extracts, papain, chymopapain, or the pineapple-enzyme bromelain. There may also be cross allergenicity with dust mite and latex allergens.

**Disease-related concerns:**

- Crotalid envenomation: *Should be used within 4 to 6 hours* of the envenomation to prevent clinical deterioration and the development of coagulation abnormalities; however, the administration of antivenom may be beneficial even if treatment has been delayed (Bush 2013).

Coagulation abnormalities are due directly to snake venom interference with the coagulation cascade. *Recurrent coagulopathy occurs in approximately 50% of patients and may persist for 1 to 2 weeks or more;* patients who have evidence of coagulopathy *during the first 12 hours postantivenom treatment have an ~66% chance of recurrence, which typically occurs 2 to 14 days after completion of antivenom administration* (Boyer 2001). *Repeat dosing may be indicated* (Miller 2010; Ruha 2011).

Patients should *be monitored for at least 1 week and evaluated for other preexisting conditions associated with bleeding disorders.* In severe envenomations, a decrease in platelets may occur, lasting hours to several days. *Blood products are generally ineffective* as they are rapidly consumed by circulating venom.

**Warnings: Additional Pediatric Considerations**

Accumulation of thimerosal has been associated with neurological and renal toxicity; developing fetuses and young infants and children are most susceptible; the presence of thimerosal should not deter use as the risks of untreated crotalid envenomations far outweigh the risk of thimerosal exposure.

**Pregnancy Implications**

Information related to the use of crotalidae polyvalent immune FAB (ovine) in pregnancy is limited (Brown 2013; Ghosh 2018; LaMonica 2010; Langley 2010).

In general, the health and prognosis of the mother should be taken into consideration when using medications as antidotes; *they should be administered to pregnant women if there is a clear indication for use and should not be withheld because of fears of teratogenicity* (Bailey 2003).
Treatment with antivenom should be considered in snake envenomations in which it is usually required as definitive management or in envenomations refractory to supportive care (Brown 2013).

*Extended monitoring of the mother and fetus is recommended* (Brown 2013; Ghosh 2018).

**Monitoring Parameters**

Vital signs; CBC, platelet count, prothrombin time, aPTT, fibrinogen levels, fibrin split products, clot retraction, bleeding and coagulation times, BUN, electrolytes, bilirubin; size of bite area (repeat every 15 to 30 minutes); intake and output; signs and symptoms of anaphylaxis/allergy; signs and symptoms of delayed allergic reaction or serum sickness (rash, fever, myalgia, arthralgia).

CBC, platelet counts, and clotting studies should be evaluated at 6-hour intervals until patient is stable.