

## Crotalidae Polyvalent Immune FAB (Ovine) (CroFab®)

The vast majority of poisonous snakes in the United States are the pit vipers (crotalids), of which the Copperhead and Timber Rattlesnake are the only native venomous snakes in Maryland. The venom of pit vipers is complex, producing tissue destruction, vasculature changes and clotting defects. The severity of symptoms can be species and patient specific.

**Mechanism/Indications:** CroFab® consists of polyvalent antibody fragments created by injecting sheep with the following North American snake venoms: *Crotalus atrox* (Western Diamondback rattlesnake), *Crotalus adamanteus* (Eastern Diamondback rattlesnake), *Crotalus scutulatus* (Mojave rattlesnake), and *Agkistrodon piscivorus* (Cottonmouth or Water Moccasin). Cottonmouth, copperhead and rattlesnake species are closely related so that CroFab® has good cross sensitivity to all North American pit vipers species. The antibody works by binding to and neutralizing the snake toxin(s), redistributing it away from target tissues and aiding in elimination so that it cannot exert its effects.

**Dosing:** Administration of antivenin should be initiated as soon as possible in patients who develop signs of progressive envenomation (*e.g.*, worsening local injury, coagulation abnormality, or systemic signs of envenomation). Each vial of CroFab® is reconstituted with 10 mL of Sterile Water for Injection USP by gentle swirling. The contents of the reconstituted vials are further diluted in 250 mL of 0.9% Sodium Chloride USP and used within 4 hours. The recommended initial dose is 4 to 6 vials infused over 60 minutes. The rate for the first 10 minutes is 25-50 mL/hour, and afterwards it can be increased to 250 mL/hour as long as the patient does not experience any allergic reaction. Reassess the patient for up to one hour later, and if control (*e.g.*, local injury has not worsened, systemic signs have stabilized and coagulation ability is normal) is not achieved after the initial dosing, an additional 4-6 vials should be given. Once control is achieved, administer 2 additional vials every 6 hours for up to 18 hours. Patients should be monitored for recurrent coagulopathy for 1-2 weeks after antivenin administration.

**Adverse Effects:** The only contraindication to administration is a known hypersensitivity to papain or papaya. The most common adverse events reported in clinical studies were urticaria and rash. Although uncommon, especially compared to the older, defunct antivenin product, patients should be monitored for more serious signs and symptoms of anaphylaxis or anaphylactoid reactions such as shortness of breath, wheezing, edema and hypotension. Also rare, delayed serum sickness has been reported 7-21 days after administration.

Ashley Burns  
Student Pharmacist  
University of Maryland School of Pharmacy

*For more on Crotalidae Polyvalent Immune FAB (Ovine) (CroFab®):*

- Pizon AF, Riley BD, Ruha A et al. Antidotes in Depth: Antivenom (Crotaline and Elapid). In: Flomenbaum NE, Goldfrank LR, Hoffman RS et al, eds: *Goldfrank's Toxicologic Emergencies*. New York NY, 2006; 1657-1662.
- Cannon R, Ruha AM, & Kashani J: Acute hypersensitivity reactions associated with administration of crotalidae polyvalent immune Fab antivenom. *Ann Emerg Med* 2008; 51(4): 407-411.
- Lavonas EJ, Gerardo CJ, O'Malley G, et al. Initial experience with Crotalidae polyvalent immune Fab (ovine) antivenom in the treatment of copperhead snakebite. *Ann Emerg Med* 2004; 43: 200-206.