

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 binds to and neutralizes the snake toxin(s), redistributing it away from target tissues and aiding in its elimination. Indications include severe or progressing swelling beyond a major joint and/or coagulopathy and/or hypotension from snakebite.

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). The Maryland Poison Center recommends 4 vials as a loading dose for copperheads, 4-6 vials for timber rattlesnakes. Each vial of CroFab® is reconstituted with 18 mL of 0.9% normal saline by gentle swirling and/or manually inverting until no solid material is visible. DO NOT SHAKE. The entire dose should be further diluted into 250 mL of 0.9% saline, starting the infusion @ 10 mL/hr, tripling the rate every 3 minutes. Goal rate is 300 mL/hr, which will be reached in less than 12 minutes if there are no adverse effects. Infuse the entire 250 mL. Reassess the patient one hour later, and if control (*i.e.* 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 X 3 doses. Copperhead snakebites with minimal envenomation may not need CroFab® beyond the initial loading dose. Patients should be monitored for recurrent symptoms and coagulopathy for 1-2 weeks after antivenin. (Note: Guidelines for treating upper and lower extremity bites have been developed by the Maryland Poison Center and can be made available to those managing a snakebite patient).

Adverse Effects: The only contraindication to administration is a known hypersensitivity to pineapple, papain, papaya, chymopapain or latex. The most common adverse events reported in clinical studies were urticaria and rash. Although uncommon, especially compared to the older, no longer available 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.

(cont. on pg. 2)

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

- CroFab® Crotalidae Polyvalent Immune Fab (Ovine) [package insert]. West Conshohocken, PA: BTG International Inc; March 2012
- Pizon AF, Ruha A. Antidotes in Depth: Antivenom:Snakes (Native [U.S.] venomous [crotaline and elapid]). In: Hoffman RS, Howland MA, Lewin N, et al, eds: Goldfrank's Toxicologic Emergencies. 10th ed. New York NY, 2015;1547-1551.
- 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.
- Lavonas EJ, Ruha AM, Banner W, Bebarta V et al. Unified treatment algorithm for the management of crotaline snakebite in the United States: results of an evidence-informed consensus workshop. *BMC Emergency Medicine* 2011; 11:2. <http://www.biomedcentral.com/1471-227X/11/2> .

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