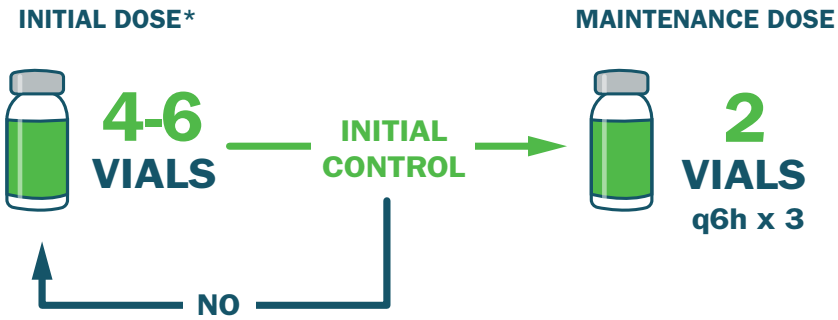
Appropriate Dosing of CroFab

Dose to Achieve Initial and Sustained Control of Envenomation[1]

CroFab should be administered as soon as possible in patients with any signs of envenomation (e.g., local, systemic, or hematologic effects) to prevent clinical deterioration.[1]

- Administer an initial dose of 4-6 vials* and monitor for signs of progression
  - Administer an additional 4-6 vials if initial control is not achieved ~1 hour after initial dose
- Once initial control is achieved, administer an additional 2 vials every 6 hours for up to 18 hours (total of 3 doses)
  - Scheduled maintenance dosing reduced the incidence of coagulation abnormalities due to residual venom[1]

In pre- and postmarketing studies, 67-88% of patients achieved initial control with an initial dose of 4-6 vials when given according to recommended dosing.[2,3]



*Based on clinical experience with CroFab, the recommended initial dose is 4-6 vials; however, the starting dose may vary from a minimum of 4 vials to a maximum of 12 vials based on clinical judgment and severity of envenomation[1]

Indication

CroFab® Crotalidae Polyvalent Immune Fab (Ovine) is a sheep-derived antivenin indicated for the management of adult and pediatric patients with North American crotalid envenomation. The term crotalid is used to describe the Crotalinae subfamily (formerly known as Crotalidae) of venomous snakes which includes rattlesnakes, copperheads and cottonmouths/water moccasins.

Important Safety Information

Contraindications

Do not administer CroFab® to patients with a known history of hypersensitivity to any of its components, or to papaya or papain unless the benefits outweigh the risks and appropriate management for anaphylactic reactions is readily available.

Warnings and Precautions

Coagulopathy: In clinical trials, recurrent coagulopathy (the return of a coagulation abnormality after it has been successfully treated with antivenin), characterized by decreased fibrinogen, decreased platelets, and elevated prothrombin time, occurred in approximately half of the patients studied; one patient required re-hospitalization and additional antivenin administration. Recurrent coagulopathy may persist for 1 to 2 weeks or more. Patients who experience coagulopathy due to snakebite should be monitored for recurrent coagulopathy for up to 1 week or longer. During this period, the physician should carefully assess the need for re-treatment with CroFab® and use of any type of anticoagulant or anti-platelet drug.

Hypersensitivity Reactions: Severe hypersensitivity reactions may occur with CroFab®. In case of acute hypersensitivity reactions, including anaphylaxis and anaphylactoid reactions, discontinue infusion and institute appropriate emergency treatment. Patients allergic to papain, chymopapain,other papaya extracts, or the pineapple enzyme bromelain may also have an allergic reaction to CroFab®. Follow-up all patients for signs and symptoms of delayed allergic reactions or serum sickness (e.g., rash, fever, myalgia, arthralgia).

CroFab®
crotalidae polyvalent immune fab (ovine)

Please see additional Important Safety Information and scan the QR code on reverse for full Prescribing Information.

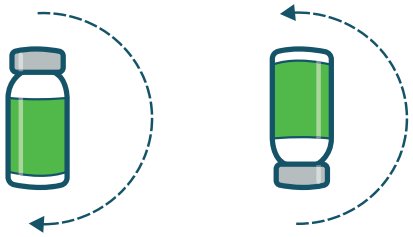
Reconstitution & Administration

5-YEAR SHELF LIFE
Expired Product Replacement Policy

Reconstitute CroFab in 3 Simple Steps[1]

1 Select and fill syringe with 18 mL of 0.9% sterile saline

2 Inject sterile saline solution ***slowly*** into CroFab vial



3 Rotate vial 180 degrees and manually invert up to twice per second until no solid material remains in the vial. The entire dose should then be further diluted in 250 mL of 0.9% sterile saline

- **Each batch of CroFab is tested for reconstitution time and must reconstitute in <7 minutes.[4]**
  - **Based on data from 72 batches of CroFab, the median time to reconstitute CroFab is 3 minutes.**
- **The reconstituted product will appear colorless to pale yellow, and opalescent (not clear).[1]**

Scan to watch an informational step-by-step guide on reconstituting and administering CroFab.

Administer CroFab by Intravenous Infusion Over 60 Minutes[1]

- The infusion should proceed slowly over the first 10 minutes at a rate of 25-50 mL/hour, with careful observation for any allergic reaction
- If no such reaction occurs, the infusion rate may be increased to the full rate of 250 mL/hour until completion

Important Safety Information (continued)

Adverse Reactions

The most common adverse reactions (incidence ≥5% of subjects) reported in the clinical studies were urticaria, rash, nausea, pruritus and back pain. Adverse reactions involving the skin and appendages (primarily rash, urticaria, and pruritus) were reported in 12 of the 42 patients. Two patients had a severe allergic reaction (severe hives and a severe rash and pruritus) following treatment and one patient discontinued CroFab® due to an allergic reaction. Recurrent coagulopathy due to envenomation and requiring additional treatment may occur.

References:
1. CroFab® [prescribing information]. BTG International Inc; August 2018. **2.** Dart RC et al. *Arch Intern Med*. 2001;161(16):2030-2036. **3.** Lavonas EJ et al. *Ann Emerg Med*. 2004;43(2):200-206. **4.** Data on file. Conshohocken, PA; BTG International Inc. 2019.

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BTG Specialty Solutions Center™: 1-844-293-0007 (Voice), 1-215-392-5470 (Fax)
www.crofab.com

Full Prescribing Information

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