

March 22, 2013

Important Drug Information
Cathflo[®] Activase[®] (alteplase): NDC 50242-041-64

Dear Pharmacist:

Subject: Cathflo[®] Activase[®] (alteplase) should be filtered with a 5 micron filter needle during withdrawal of the reconstituted solution to remove potential rubber stopper particulates.

Some vials of Cathflo Activase have been found to contain rubber stopper particulates after reconstitution. Studies have indicated that filtration through a 5 micron filter needle is sufficient to remove these particles. Cathflo Activase vials should be carefully inspected after reconstitution for foreign matter or discoloration. Do not administer Cathflo Activase if particulate matter is discovered. There is a potential risk that particulate matter may cause embolic events if introduced into the bloodstream.

Cathflo Activase is indicated to restore function to central venous access devices (catheters). It should be administered according to the Instructions for Administration in the full Prescribing Information (FPI). Specifically, health care providers should follow these instructions for use:

- **Follow all recommended steps for reconstitution of Cathflo Activase**
- **Carefully inspect the reconstituted product prior to withdrawal for foreign matter and discoloration. Reconstituted product is a colorless to pale yellow transparent solution.**
- **Do not administer Cathflo Activase if particulate matter is discovered.**

After inspecting for particulates, Cathflo Activase should be filtered during withdrawal of the reconstituted solution from the vial using the following protocol:

- **Attach a 5 micron filter needle to an appropriately sized syringe**
- **Withdraw 2 mL (2 mg) of solution from the reconstituted vial.**
- **Remove the filter needle from syringe**

Please see the attached Instructions for Administration for a complete guide to preparation and instillation of Cathflo Activase

Based on a recent review of the company's adverse event surveillance systems, there have been no reports of adverse events that could be attributed definitively to the particulate matter.

In the event you discover particulate matter upon reconstitution, do not administer Cathflo Activase to the patient. Instead, please contact Genentech Product Support at (800) 334-0290. You will be asked to return the affected vial to Genentech and you will receive a replacement vial.

Please ensure your staff and any provider in your institution who may be involved in the reconstitution and administration of Cathflo Activase receives a copy of this letter and specifically reviews the instructions for use.

Genentech encourages the reporting of adverse events expeditiously. To report adverse events, product quality complaints, or to request medical information related to Cathflo Activase please contact

CAT0001727602

Genentech Medical Communications at (800) 821-8590 (5:30 a.m.-4 p.m. PST, M-F).

Adverse events or quality problems experienced with the use of this product may also be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail, telephone, or fax.

- Online: www.fda.gov/medwatch/report.htm
- Regular Mail: use postage-paid, pre-addressed Form FDA 3500 available at: www.fda.gov/MedWatch/getforms.htm. Mail to: MedWatch, 5600 Fishers Lane, Rockville, MD 20857
- Telephone: 1-800-332-1088
- Fax: 1-800-FDA-0178

We will continue to work diligently to provide a consistent supply of Cathflo Activase. For ongoing updates on Cathflo Activase supply, please visit www.cathflo.com. We appreciate your assistance in this matter and apologize for any inconvenience.

Sincerely,



Hal Barron, MD
Chief Medical Officer
Genentech USA

Please see Important Safety Information below.

Indication

Cathflo Activase (Alteplase) is indicated for the restoration of function to central venous access devices (CVADs) as assessed by the ability to withdraw blood.

Important Safety Information

Cathflo Activase should not be administered to patients with known hypersensitivity to Alteplase or any component of the formulation.

In clinical trials, the most serious adverse events reported after treatment were sepsis, gastrointestinal bleeding, and venous thrombosis.

Certain causes of catheter dysfunction should be considered before treatment with Cathflo Activase (ie, catheter malposition, mechanical failure, constriction by a suture and lipid deposits or drug precipitates within the catheter lumen).

The most frequent adverse reaction associated with all thrombolytics in all approved indications is bleeding. Caution should be exercised with patients who have any condition for which bleeding constitutes a significant hazard.

Cathflo Activase should be used with caution in the presence of known or suspected infection in the catheter.

Please see accompanying Prescribing Information for additional Important Safety Information

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Instructions for Administration
(additions to current full Prescribing Information in *bold+italics*)

Preparation of Solution

Reconstitute Cathflo Activase to a final concentration of 1 mg/mL:

1. Aseptically withdraw 2.2 mL of Sterile Water for Injection, USP (diluent is not provided). Do not use Bacteriostatic Water for Injection.
2. Inject the 2.2 mL of Sterile Water for Injection, USP, into the Cathflo Activase vial, directing the diluent stream into the powder. Slight foaming is not unusual; let the vial stand undisturbed to allow large bubbles to dissipate.
3. Mix by gently swirling until the contents are completely dissolved. Complete dissolution should occur within 3 minutes. **DO NOT SHAKE**. The reconstituted preparation results in a colorless to pale yellow transparent solution containing 1 mg/mL Cathflo Activase at a pH of approximately 7.3.
4. Cathflo Activase contains no antibacterial preservatives and should be reconstituted immediately before use. The solution may be used for intracatheter instillation within 8 hours following reconstitution when stored at 2–30°C (36–86°F).

No other medication should be added to solutions containing Cathflo Activase.

Instillation of Solution into the Catheter

1. Inspect the product prior to administration for foreign matter and discoloration.
2. ***Attach a 5 micron filter needle to an appropriately sized syringe***
3. Withdraw 2 mL (2 mg) of solution from the reconstituted vial
4. ***Remove the filter needle from syringe***
5. Instill the appropriate dose of Cathflo Activase (see DOSAGE AND ADMINISTRATION) into the occluded catheter.
6. After 30 minutes of dwell time, assess catheter function by attempting to aspirate blood. If the catheter is functional, go to Step 9. If the catheter is not functional, go to Step 7.
7. After 120 minutes of dwell time, assess catheter function by attempting to aspirate blood and catheter contents. If the catheter is functional, go to Step 9. If the catheter is not functional, go to Step 8.
8. If catheter function is not restored after one dose of Cathflo Activase, a second dose of equal amount may be instilled. Repeat the procedure beginning with Step 1 under Preparation of Solution.
9. If catheter function has been restored, aspirate 4–5 mL of blood in patients ≥ 10 kg or 3 mL in patients < 10 kg to remove Cathflo Activase and residual clot, and gently irrigate the catheter with 0.9% Sodium Chloride, USP.

Any unused solution should be discarded.