Genentech
A Member of the Roche Group

December 19, 2014

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

Dear Pharmacist:

Subject: Cathflo® Activase® (alteplase) with new rubber stoppers is now available and does not require filter needles

In March 2013, some vials of Cathflo Activase were found to contain rubber stopper particulates after reconstitution. At that time, Genentech informed pharmacists and recommended using a 5-micron filter needle for withdrawing the reconstituted solution from the vial of Cathflo Activase as a precautionary measure to remove any potential particulate matter. We are pleased to announce that Genentech has changed the rubber stopper on vials of Cathflo Activase. These vials do **not** require use of filter needles to withdraw the reconstituted solution from the vial. Testing has been performed on these new Cathflo vials and no detectable particulate matter has been observed. These new vials of Cathflo Activase are now available and are currently being shipped. To help distinguish between the new vials and the previous vials potentially affected by rubber stopper particulates, the new vials have a purple-colored label on the vial and are packaged in a purple carton while the previous vials have a white-colored label on the vial and are packaged in a white carton:

White carton and white label on vial
Should be filtered with 5-micron filter needle

Purple carton and purple label on vial
Does not require filter needle

If you are using your existing supply of white-labeled Cathflo Activase, please continue to use a 5-micron filter to withdraw the reconstituted solution from the vial.

Regardless of which vials are used, always follow all recommended steps for reconstitution of Cathflo Activase, which include careful inspection after reconstitution for foreign matter or discoloration. Do not administer Cathflo Activase if particulate matter is discovered**.** 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.

Cathflo Activase is indicated for the restoration of function to central venous access devices (catheters) as assessed by the ability to withdraw blood. It should be administered according to the Instructions for Administration in the full Prescribing Information (PI).

Please ensure that your staff and any provider in your institution who may be involved in the reconstitution and administration of Cathflo Activase receive a copy of this letter, take inventory of which vials of Cathflo Activase are available for use, and specifically review 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 Genentech Medical Communications at (800) 821-8590 (5:30 a.m.-4 p.m. PST, M-F). The lot number of the product used is important information to provide with any report of adverse events or quality complaints.

Adverse events or quality problems experienced with the use of Cathflo Activase 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

For ongoing updates on Cathflo Activase, please visit www.cathflo.com.

Sincerely,

Sandra Horning, 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 (i.e., 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.

Instructions for Administration of **new** or purple-labeled Cathflo Activase

Preparation of Solution

Reconstitute Cathflo Activase to a final concentration of 2 mg/2 mL:

1. Aseptically withdraw 2.2 mL of Sterile Water for Injection, USP (diluent is not provided). Do not use Bacteriostatic Water for Injection, USP.

2. Inject the 2.2 mL of Sterile Water for Injection, USP, into the Cathflo 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.

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°C –30°C (36°F –86°F).

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

Instillation of Solution into the Catheter

4. Inspect the product prior to administration for foreign matter and discoloration. Solution should be inspected immediately before use.

5. Withdraw 2 mL (2 mg) of reconstituted solution from the vial

6. Instill the appropriate dose of Cathflo (see DOSAGE AND ADMINISTRATION) into the occluded catheter using an appropriately sized syringe.

7. 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 8.

8. Assess catheter function after a total of 120 minutes of dwell time by attempting to aspirate blood. If catheter is functional, go to step 9. If catheter is still occluded, a second dose of equal amount may be instilled. Repeat steps 1 through 7.

9. If catheter function has been restored, aspirate 4 mL to 5 mL of blood in patients ≥10kg or 3 mL in patients <10 kg to remove Cathflo and residual clot. Then gently irrigate the catheter with 0.9% Sodium Chloride, USP.

Any unused solution should be discarded.

Instructions for Administration of **previous** or white-labeled Cathflo Activase

Preparation of Solution

Reconstitute Cathflo Activase to a final concentration of 2 mg/2 mL:

1. Aseptically withdraw 2.2 mL of Sterile Water for Injection, USP (diluent is not provided). Do not use Bacteriostatic Water for Injection, USP.

2. Inject the 2.2 mL of Sterile Water for Injection, USP, into the Cathflo 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.

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°C –30°C (36°F –86°F).

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

Instillation of Solution into the Catheter

4. Inspect the reconstituted product prior to withdrawal for foreign matter and discoloration. Solution should be inspected immediately before use. Do not administer Cathflo if particulate matter is discovered.

5. Filter the reconstituted solution using the following protocol:

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

6. Instill the appropriate dose of Cathflo (see DOSAGE AND ADMINISTRATION) into the occluded catheter using an appropriately sized syringe.

7. 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 8.

8. Assess catheter function after a total of 120 minutes of dwell time by attempting to aspirate blood. If catheter is functional, go to step 9. If catheter is still occluded, a second dose of equal amount may be instilled. Repeat steps 1 through 7.

9. If catheter function has been restored, aspirate 4 mL to 5 mL of blood in patients ≥10kg or 3 mL in patients <10 kg to remove Cathflo and residual clot. Then gently irrigate the catheter with 0.9% Sodium Chloride, USP.

Any unused solution should be discarded.