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Alteplase (Cathflo™ Activase®)

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Drug name: Alteplase, marketed as Cathflo™ Activase® (Genentech, Inc., South San Francisco, CA), is a human tissue plasminogen activator (t-PA) produced by recombinant DNA technology.

Classification: Thrombolytic

Action: As with native t-PA, alteplase is highly fibrin specific and thus acts specifically on fibrin-rich clots in catheter occlusion. Alteplase works by targeting fibrin (the substance that causes blood to clot), dissolving the thrombus (blood clot) and restoring function to the central venous access device (CVAD).

Indications: Alteplase is indicated for the restoration of function to CVADs as assessed by the ability to withdraw blood (Genentech, Inc., 2002).

Efficacy: U.S. Food and Drug Administration approval for alteplase is based on two phase III clinical trials designed to assess safety and efficacy. A placebo-controlled, double-blind, randomized trial (Cardiovascular Thrombolytic to Open Occluded Lines [COOL]) Efficacy Trial and a larger, open-label trial (COOL-2) investigated the use of alteplase in patients who had an indwelling CVAD for administration of chemotherapy, total parenteral nutrition, or long-term administration of antibiotics or other medications (Genentech, Inc., 2002).

Both studies enrolled patients whose catheters were not functioning (defined as the inability to withdraw at least 3 cc of blood from the device) but with the ability to instill the necessary volume of study drug. Restoration of function was assessed by successful withdrawal of 3 cc of blood and infusion of 5 cc of saline through the catheter. Patients with known mechanical occlusion as well as patients who were younger than two years old or weighed less than 10 kg were excluded from both studies (Deitcher et al., 2002; Ponec et al., 2001). Alteplase restored function in 67% of catheters with one 2 mg/2 ml dose and in 88% of catheters with up to 2 mg/2 ml doses (Deitcher et al.; Genentech, Inc., 2002; Ponec et al.).

Metabolism: Alteplase limits systemic exposure because it dwells in the catheter in direct exposure to the clot. Although a small amount may enter the bloodstream, circulating plasma levels are not expected to reach pharmacologic concentrations because of the drug's short half-life.

If a 2 mg dose (recommended for patients weighing 30 kg or more) of alteplase was administered by bolus injection directly into the systemic circulation (rather than instilled into the catheter), the concentration of circulating alteplase would be expected to return to endogenous circulation levels of 5–10 ng/ml within 30 minutes. Clearance is mediated primarily by the liver (Genentech, Inc., 2002).

Half-life: The initial half-life of alteplase is less than five minutes when in circulation.

Adverse events: Few serious adverse events were reported in the COOL-2 trial, the largest published study of the use of thrombolytics for restoring function to occluded CVADs (N = 995). Patients received a 2–4 mg cumulative dose of alteplase. The most serious adverse events reported in clinical trials were sepsis, gastrointestinal bleeding, and venous thrombosis (Genentech, Inc., 2002). Adverse events in the COOL-2 trial included sepsis (0.4%), major hemorrhage (defined as a severe blood loss, blood loss requiring transfusion, or blood loss causing hypotension) (0.4%), gastrointestinal bleeding (0.3%), and venous thrombosis (0.3%). Intracranial hemorrhages or embolic events were not reported (Deitcher et al., 2002; Genentech, Inc.).

Dosage: Alteplase is instilled into the catheter at a concentration of 1 mg/ml. The recommended dosage for patients weighing 30 kg or more is 2 mg/2 ml; for patients weighing 10 kg or more but less than 30 kg, the dosage is 110% of the internal lumen volume of the catheter, not to exceed 2 mg/2 ml. If catheter function is not restored at 120 minutes after one dose of alteplase, a second dose may be instilled. Information on the efficacy or safety of dosing in excess of 2 mg per dose for this indication is not available (Genentech, Inc., 2002).

Dilution and reconstitution: Alteplase is a sterile, white to pale yellow lyophilized powder and should be reconstituted immediately before use.

Administration: Reconstitute alteplase to a final concentration of 1 mg/ml.

Preparation of solution

1. Withdraw 2.2 ml of sterile water for injection, USP. Diluent is not included. Do not use bacteriostatic water for injection, USP.
2. Inject the 2.2 ml of sterile water for injection, USP, into the alteplase vial, directing the stream into the powder. If slight foaming occurs, let the vial stand undisturbed to allow large bubbles to dissipate.

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