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).

**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).

**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.).