

# Alteplase for the Management of Occluded Central Venous Access Devices: Safety Considerations

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Central venous access device (CVAD) dysfunction, with loss of patency because of thrombotic occlusion, has been reported to be the most common complication in central lines, even more common than catheter-related infection (Moureau, Poole, Murdock, Gray, & Semba, 2002). Occlusion of CVADs can cause life-threatening treatment delays, patient discomfort, infection, and the need for catheter removal and replacement.

Alteplase (Cathflo® Activase®, Genentech, Inc.) is the only thrombolytic approved by the U.S. Food and Drug Administration (FDA) to restore catheter function as assessed by the ability to draw blood. Numerous studies have demonstrated the efficacy of alteplase for catheter clearance, along with a low incidence of complications (Semba et al., 2002; Shen et al., 2003). Although the incidence of complications is low, knowledge of safety precautions and considerations for special populations can help healthcare professionals to prevent unnecessary problems.

## Alteplase for Central Venous Catheter Clearance

The FDA approved alteplase for catheter clearance in adults in 2001 and for pediatric use in 2005. Alteplase is tissue plasminogen activator (t-PA) made by recombinant DNA technology. t-PA is an enzyme that occurs naturally in the body; it binds to fibrin in a clot, converting plasminogen to plasmin, thus initiating fibrinolysis (breakdown of the clot).

The standard dose of alteplase used for catheter clearance in adults is much smaller than the dose commonly used for myocardial infarction: 2 mg/2 ml versus 100 mg (Genentech, Inc., 2007). In addition to the smaller dose, systemic exposure to alteplase used for catheter clearance is minimal because the alteplase dwells in the catheter, with direct exposure to the clot (Middleton & Ruzevick, 2004). Further enhancing its safety profile: Any alteplase circulating systemically is very unlikely to reach pharmacologic concentrations because the drug's half-life is less than five minutes (Middleton & Ruzevick).

## Dosage and Administration

The dose of alteplase for patients weighing 30 kg (66 pounds) or more is 2 mg/2 ml, regardless of the priming volume of the CVAD (Genentech, Inc., 2007). For patients weighing less than 30 kg, the recommended dose is 110% of the priming volume of the CVAD, not exceeding 2 mg/2 ml (Genentech, Inc.). Alteplase contains no preservatives and, if not used immediately, must be stored at 2°C–30°C (36°F–86°F) and used within eight hours. After reconstitution, 2 mg/2 ml should be withdrawn from the vial

and instilled into the CVAD. After 30 minutes of dwell time, catheter patency can be assessed by pulling back on a syringe to aspirate blood. If a blood return is positive, 4–5 ml of blood should be aspirated for patients weighing 10 kg or more, or 3 ml for patients weighing less than 10 kg. The catheter then can be irrigated with normal saline per hospital procedure. If a blood return is not obtained after 30 minutes of dwell time, alteplase should be left to dwell another 90 minutes (for a total of 120 minutes). A second dose can be repeated if a blood return is not obtained after 120 minutes. For more detailed instructions, refer to the package insert (Genentech, Inc.).

## Adverse Reactions

Few adverse reactions were reported in clinical trials that investigated alteplase for catheter clearance. Two hallmark studies were the Cardiovascular Thrombolytic to Open Occluded Lines (COOL) trial and the COOL-2 trial. The first was a phase III, double-blind, randomized prospective trial comparing alteplase (2 mg/2 ml) to placebo (N = 149) (Ponec et al., 2001). The COOL-2 trial was an open-label, single-arm study investigating alteplase for catheter clearance in 995 patients (Deitcher et al.,

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