Hold ourselves accountable to the standard of care

Use evidence-based guidelines to deliver quality care to patients with central lines
Central Venous Access Devices (CVADs) deliver life-sustaining therapies

An evidence-based list of indications for CVAD use include, but are not limited to:
1. Clinical instability of the patient and/or complexity of infusion regimen (multiple infusates)
2. Episodic chemotherapy treatment anticipated for more than 3 months
3. Prescribed continuous infusion therapy (e.g., parenteral nutrition, fluid and electrolytes, medications, blood or blood products)
4. Invasive hemodynamic monitoring
5. Long-term intermittent infusion therapy (e.g., any medication including anti-infectives in patients with a known or suspected infection)
6. History of failed or difficult peripheral venous access, if use of ultrasound guidance has failed

Catheters can be used either short or long term for the infusion of:
- Antibiotics
- Parenteral nutrition
- Medication/solutions in patients with limited peripheral access
- Chemotherapy or other vesicant or irritating solutions
- Blood and blood products
- Therapy that is ongoing or continued at home

Why is it important to ensure central line patency?

An occluded line may complicate patient care by:
- Disrupting therapies or delaying procedures
- Interrupting administration of medications and solutions
- Delays in discharge
- Additional procedures, such as catheter replacement

“Foster a just culture and individual accountability through a focus on improving systems and processes by clinicians and leaders.”
INS Infusion Therapy Standards of Practice, 2016, page S21, standard 6A

“Catheter salvage is preferred over catheter removal for management of CVAD occlusions.”
INS Infusion Therapy Standards of Practice, 2016, page S104, standard 48.3

INS=Infusion Nurses Society.
CVADs provide access to central venous circulation

Central venous access devices are:
- Also known as central venous catheters (CVC) or central lines
- A mainstay for patients requiring intravenous (IV) administration of medications and other fluids
- Tip of a CVAD generally placed in the lower third of the superior vena cava (SVC), near its junction with the right atrium
- Blood flow rate in SVC is approximately 2 liters per minute
- In SVC, infusates are rapidly hemodiluted and distributed in the central venous system

CVAD insertion and tip sites

Types of CVADs

Peripheraly inserted central catheters (PICCs)
- Can be used for a variety of IV therapies
- May be used for blood sampling with proper technique
- Can be used in a variety of care settings across diverse patient populations
- May be placed bedside or in an outpatient setting

Nontunneled catheters
- Also called subclavian, percutaneous, or short-term catheters
- Typically used for days or weeks for all types of IV therapy, to draw blood, and to monitor central venous pressure
- May be placed bedside or, if necessary, in an emergency setting, without sedation

Tunneled catheters
- Designed for long-term use and frequent venous access
- Provide reliable IV access for extended courses of antibiotics, chemotherapy, and parenteral nutrition
- Surgically inserted

Implanted ports
- Consist of 2 attached parts: the catheter and portal body with reservoir
- Long-term dwell capacity, requiring little maintenance when not in use
- Useful for cyclically infused therapies, such as chemotherapy
- Blood draws may also be done through the port
- Surgically inserted
Catheter occlusion is the most common noninfectious complication in the long-term use of CVADs.

- Oclusions may occur in up to 25% of CVADs.
- May occur soon after insertion of a device or develop at any time.

One in 4 catheters may become occluded.

“Catheter occlusions are categorized as thrombotic or nonthrombotic, and an accurate diagnosis of the type of occlusion is essential for appropriate treatment.”

Causes of catheter occlusions

- About 58% of catheter occlusions are thrombotic.
- Thrombotic occlusions result from the formation of a thrombus within, surrounding, or at the tip of the catheter.
- About 42% of catheter occlusions are due to nonthrombotic causes, including precipitates, malpositioning, mechanical obstructions, and other factors.

Mechanical occlusions

- Mechanical occlusions may result from malposition during insertion and use, or catheter migration.
- Factors influencing the incidence of malposition include an increase in intrathoracic pressure from coughing, sneezing, or vomiting; arm movements; forceful flushing of the catheter; and thrombus formation.

Precipitates

- Precipitates can form as a result of drug crystallization, drug-drug incompatibilities, or drug-solution incompatibilities.
- Drug precipitates in the catheter may occur in conjunction with thrombus formation and should always be considered during assessment of an occlusion, since this may have implications for how the occlusion should be managed.

Lipid residue

- Lipid residue can accumulate in central venous catheters, often following the administration of lipid-containing, three-in-one total parenteral nutrition admixtures or drugs with oleaginous vehicles.

Salvaging catheters with nonthrombotic occlusions

- In many instances, mechanical problems, such as kinked tubing or clogged in-line filters, can be identified and corrected.
- Possible interventions to reposition catheters include patient positioning, rapid flushing of the catheter guidewire, catheter exchange, fluoroscopic catheter guidance, or partial catheter withdrawal.
- Catheters occluded by calcium-phosphate precipitates can be treated with 0.1 N hydrochloric acid.
- Sodium bicarbonate (1 mEq/mL) is used for substances known to dissolve in an alkaline environment.
- Lipid occlusions have been treated with ethanol (70%) or sodium hydroxide (0.1 mmol/mL).
- The use of incompatible drugs or solutions should be avoided.

Data in this section derived from a study of 200 dysfunctional catheters in 172 adult patients.
When introduced into the body, all catheters begin to accumulate fibrin. This is the body’s natural attempt to protect itself against a foreign body. The fibrin starts to form a layer around the outside of the catheter within minutes of insertion, beginning at either the line entry site or where the tip contacts the vein.4,13

Fibrin tail, or flap4
- Extends from the catheter tip but is drawn inward, blocking the opening of the catheter lumen on aspiration attempts
- Results in an ability to infuse fluids but an inability to withdraw blood

Intraluminal thrombus5
- Occurs when blood refluxes inside the catheter lumen
- Common causes of reflux include coughing, inadequate flushing after blood draws or after checking for blood return, or improper use of flush syringes

Mural thrombus3-5
- Forms where the catheter touches or “rub” the vein wall
- Common sites are the entry site, anywhere along the catheter path, and the catheter tip

Fibrin sheath4,5
- Forms when fibrin adheres to the external catheter surface, which may include the entry site, and may encase all or part of the catheter like a sock
- May completely cover the opening of the catheter tip

Catheter occlusions can be partial or complete9
- Partial occlusion: ability to infuse but not withdraw fluids, or the presence of sluggish flow*
- Complete occlusion: inability to infuse or aspirate

Aspirating for a positive blood return may reveal a partial occlusion
- Fibrin tail allowing infusion
- Beginning to flap back with start of withdrawal
- Blocking aspiration of the catheter

Flushing the line is not enough—you must be able to withdraw blood to rule out a partial occlusion before administering critical therapies.1

*One quantitative measure for sluggish flow is a blood return of less than 3 mL in 3 seconds, as recommended by the Oncology Nursing Advisory Board.11
Recognizing signs of CVAD occlusion

With a blood flow through the SVC of approximately 2 liters per minute, A free-flowing blood return should be readily achievable. Lack of blood return or a sluggish flow may indicate a catheter occlusion or a malpositioned tip, and further assessment of the line will be necessary.3

Signs of a CVAD occlusion include:
- Inability to withdraw blood or sluggish blood return
- Sluggish flow
- Inability to flush or infuse through the CVAD
- Frequent occlusion alarms on electronic infusion device
- Infiltration/extravasation or swelling/leaking at the infusion site

CVAD occlusions should not be left untreated because another lumen is patent.1

Recommended routine assessment of catheter patency

"Ensure brisk blood return. Ensure consistent verification of blood return prior to, during, and after infusion."7

Prior to the administration of any medications or solutions, the nurse should always:
- Aspirate for a positive blood return that is the color and consistency of whole blood
- Check for other indications of an occlusion
- Attempt to flush to determine resistance, flushing with an adequate volume of saline or appropriate solution
- Palpate the insertion site to determine tenderness
- Assess the patient for any pain or discomfort

Documentation of CVAD patency is a clinical practice standard and should include:
- Device patency
- Absence of signs and symptoms of complications
- Lack of resistance when flushing
- Presence of a blood return upon aspiration

ONS=Oncology Nursing Society.
**Recommended algorithm for assessing and treating occluded catheters**

**Indication**
Cathflo® Activase® (alteplase) is indicated for the restoration of function to central venous access devices as assessed by the ability to withdraw blood.

**Important Safety Information**

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

**Precautions**

**General**
Certain causes of catheter dysfunction should be considered before treatment with Cathflo Activase (e.g., catheter malposition, mechanical failure, constriction by a suture and lipid deposits or drug precipitates within the catheter lumen). These types of conditions should be considered before treatment with Cathflo Activase. Excessive pressure should be avoided when Cathflo Activase is instilled into the catheter. Such force could cause rupture of the catheter or expulsion of the clot into the circulation.

**Bleeding**
The most frequent adverse reaction associated with all thrombolytics in all approved indications is bleeding. Cathflo Activase has not been studied in patients known to be at risk for bleeding events that may be associated with the use of thrombolytics. Caution should be exercised with patients who have any condition for which bleeding constitutes a significant hazard.

Should serious bleeding in a critical location (e.g., intracranial, gastrointestinal, retroperitoneal, pericardial) occur, treatment with Cathflo Activase should be stopped and the drug should be withdrawn from the catheter.

**Infections**
Cathflo Activase should be used with caution in the presence of known or suspected infection in the catheter. Using Cathflo Activase in patients with infected catheters may release a localized infection into the systemic circulation. As with all catheterization procedures, care should be used to maintain aseptic technique.

Please see select Important Safety Information throughout and the accompanying full Prescribing Information.

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**Cathflo 2 mg is the standard of care for treatment of thrombotically occluded catheters**

**Cathflo is the only FDA-approved thrombolytic agent for the restoration of function to CVADs as assessed by the ability to withdraw blood**

**Cathflo is the only thrombolytic recommended by clinical practice standards**

- Infusion Nurses Society (INS)
- Association for Vascular Access (AVA)
- American Association of Critical Care Nurses (AACN)
- Oncology Nursing Society (ONS)

**Cathflo—a fibrin-specific MOA**

- The fibrin-specific mechanism of action (MOA) addresses the root cause of thrombotic occlusions
- Cathflo binds to fibrin in the thrombus, converting entrapped plasminogen to plasmin, initiating local fibrinolysis

**Cathflo pharmacokinetics**

- When Cathflo 2 mg is administered according to the instructions for dosing and administration, circulating plasma levels of alteplase are not expected to reach pharmacologic concentrations.

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*The clinical significance of fibrin specificity is unknown.*
**Cathflo Activase (alteplase) 2 mg is integral to evidence-based practices for treating thrombotically occluded catheters**

- In the pivotal trials COOL-1 and COOL-2, the efficacy of Cathflo was evaluated in 1122 primarily adult patients.

**Cumulative efficacy**

In COOL-1, Cathflo restored function to 88% (112/127) of central lines after up to 2 doses using a 120-minute dwell time for each in catheters with occlusions present for up to 24 hours.

In COOL-1 and COOL-2, Cathflo restored function to 68% (796/1043) of central lines after 1 dose and 88% (902/1043) of central lines after 2 doses in catheters with occlusions present for less than 14 days.

**First-dose efficacy**

In COOL-2, Cathflo restored function after 1 dose in 75% (747/995) of central lines after up to 120 minutes of dwell time in catheters with occlusions present for any duration.

**Occlusions >14 days efficacy**

In COOL-2, Cathflo restored function to 57% (30/53) of central lines after 1 dose and 72% (38/53) of central lines after up to 2 doses in catheters with occlusions present for longer than 14 days.

**Maintained patency**

In a subset of patients (n=346) who had a successful treatment outcome, 74% (256/346) of central lines maintained patency up to 30 days after treatment with Cathflo.

**Use 2 mg alteplase (Cathflo Activase) to restore patency and maintain catheter function.**

**Important Safety Information (cont’d)**

**Hypersensitivity**

Hypersensitivity, including urticaria, angioedema and anaphylaxis, has been reported in association with use of Cathflo Activase. Monitor patients treated with Cathflo Activase for signs of hypersensitivity and treat appropriately if necessary.

**Drug Interactions and Drug/Laboratory Test Interactions**

The interaction of Cathflo Activase with other drugs has not been formally studied. Concomitant use of drugs affecting coagulation and/or platelet function has not been studied. Potential interactions between Cathflo Activase and laboratory tests have not been studied.

Please see select Important Safety Information throughout and the accompanying full Prescribing Information.

**Cathflo safety profile in adult and pediatric patients**

Cathflo has a safety profile studied in both adult and pediatric patients.

- In the pivotal trials COOL-1 and COOL-2, the safety profile of Cathflo was evaluated in 1122 primarily adult patients.
- CAPS evaluated the safety profile of Cathflo in 310 pediatric patients. Patient ages ranged from 2 weeks to 17 years.

**COOL-1 and COOL-2 (N=1122)**

<table>
<thead>
<tr>
<th>Serious adverse events</th>
<th>0.4%</th>
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<tbody>
<tr>
<td>Sepsis</td>
<td></td>
</tr>
<tr>
<td>Major hemorrhage</td>
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<tr>
<td>Gastrointestinal bleeding</td>
<td>0.3%</td>
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<tr>
<td>Venous thrombosis</td>
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<tr>
<td>Intracranial hemorrhage</td>
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<tr>
<td>Embolic event</td>
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**CAPS (N=310)**

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<tr>
<th>Serious adverse events</th>
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<tr>
<td>Catheter-related complications</td>
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<tr>
<td>Sepsis</td>
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<tr>
<td>Major hemorrhage</td>
<td>0.0%</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
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</tr>
<tr>
<td>Embolic event</td>
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</tbody>
</table>

**Adapted from Blaney M, et al.**

**CAPS** = Cathflo Activase Pediatric Study.

CAPS was an open-label, single-arm trial that evaluated the safety of Cathflo in 310 patients between the ages of 2 weeks and 17 years. Cathflo was evaluated in a maximum of 2 doses at ≤2 mg per dose. The primary objective was to evaluate safety, as measured by the incidence of intracranial hemorrhage (ICH). Secondary objectives included assessing restoration rates at 30 minutes and 120 minutes, and serious adverse events within 48 hours.

**Use 2 mg alteplase (Cathflo Activase) to restore patency and maintain catheter function.**

**Important Safety Information (cont’d)**

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

Long-term studies in animals have not been performed to evaluate the carcinogenic potential or the effect on fertility.
Dosing and administration of Cathflo Activase (alteplase) 2 mg

Administration

After WASHING hands and applying gloves:

1. After reconstitution using 2.2 mL sterile water for injection and aseptic technique, performing hand hygiene, and donning gloves, INSPECT solution for foreign matter and discoloration.

2. INSTILL the appropriate dose of Cathflo into the occluded catheter using a 10-mL syringe (see dosing chart on the following page).

3. After 30 minutes of DWELL time, assess catheter function by attempting to aspirate blood. If the catheter is functional, go to step 5; if not functional, go to step 4.

4. ASSESS catheter function after a total of 120 minutes of dwell time by attempting to aspirate blood. If the catheter is functional, go to step 5. If the catheter is still occluded, a second dose of equal amount may be instilled. Repeat steps 1 through 3.

5. If catheter function has been restored, ASPIRATE 4 mL to 5 mL of blood in patients ≥10 kg or 3 mL in patients <10 kg to remove Cathflo and residual clot. Then discard aspirate, and flush the catheter with 0.9% Sodium Chloride, USP. Any unused solution should be discarded.

Important Safety Information (cont’d)

Pregnancy

There are no adequate and well-controlled studies in pregnant women. Cathflo Activase should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Adverse Reactions

In clinical trials, the most serious adverse events reported after treatment were sepsis, gastrointestinal bleeding, and venous thrombosis. You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

Please see select Important Safety Information throughout and the accompanying full Prescribing Information.

FDA-approved dosing with Cathflo 2 mg

- Cathflo is available in a single-use, 2-mg vial and it is not recommended that it be compounded, frozen, or thawed
- If catheter function is not restored at 120 minutes after 1 dose of Cathflo, a second dose may be instilled*

*Studies only evaluated up to two 2-mg doses.

Cathflo Dosing Chart

<table>
<thead>
<tr>
<th>PATIENT WEIGHT</th>
<th>CATHFLO DOSE</th>
</tr>
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<tbody>
<tr>
<td>≥30 kg (66 lb)</td>
<td>2 mg in 2 mL</td>
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<tr>
<td>&lt;30 kg (66 lb)</td>
<td>110% of the internal lumen volume of CVAD, not to exceed 2 mg in 2 mL</td>
</tr>
</tbody>
</table>

Single-use vial

Note: Store lyophilized Cathflo at refrigerated temperature (2°C–8°C/36°F–46°F). Cathflo should be reconstituted immediately before use. The solution may be used within 8 hours if stored at 2°C to 30°C (36°F–86°F). No other medication should be added to solutions containing Cathflo.


The instillation of alteplase 2 mg (Cathflo Activase) is effective in restoring catheter patency in patients.

INS Infusion Therapy Standards of Practice, 2016, page S105, standard 48, practice criterion G.

Visit Cathflo.com to order and download additional tools and educational resources.
Is your hospital delivering the standard of care for patients with central lines?

- Utilize the highest level of evidence available for central line care and maintenance
- Include patency checks in central line care protocols and maintenance bundle
- Develop a culture of accountability using CVAD quality metrics and EHR documentation

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Please see accompanying full Prescribing Information for additional Important Safety Information.

To learn more about the management of thrombotically occluded catheters, please visit www.cathflo.com or call Genentech Customer Service at 1-800-551-2231 to locate your local Genentech clinical specialist.

www.cathflo.com

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