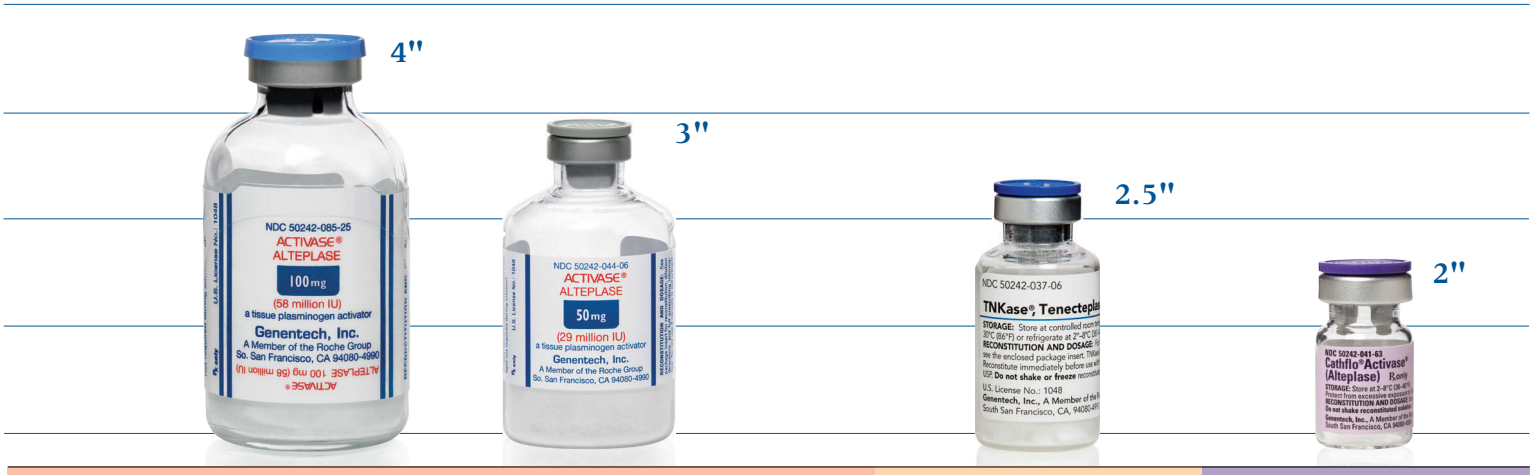
Pioneering Thrombolytic Therapy for Over 3 Decades[1]

Genentech's ThrombolyticExperience™



Over 1.7 million acute myocardial infarction (AMI) patients treated with Activase

ACTIVASE® ALTEPLASE
A RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR

1987:
First FDA-approved thrombolytic in AMI

ACTIVASE® ALTEPLASE
A RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR

1990:
Only FDA-approved thrombolytic in AMPE

Over 616,000 acute ischemic stroke (AIS) patients treated with Activase

ACTIVASE® ALTEPLASE
A RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR

1996:
Only FDA-approved thrombolytic in AIS

Over 390,000 AMI patients treated with TNKase

TNKase® Tenecteplase

2000:
Only FDA-approved single-bolus dose for AMI

Over 12 million patients with thrombotically occluded central venous access device (CVAD) treated with Cathflo

cathflo® ACTIVASE® (ALTEPLASE)

2001:
Only FDA-approved thrombolytic for CVAD restoration in adult and pediatric patients

Activase® (alteplase)

Activase (alteplase) is indicated for the treatment of acute ischemic stroke. Exclude intracranial hemorrhage as the primary cause of stroke signs and symptoms prior to initiation of treatment. Initiate treatment as soon as possible but within 3 hours after symptom onset.

Activase is indicated for use in acute myocardial infarction (AMI) for the reduction of mortality and reduction of the incidence of heart failure.

Limitation of Use: The risk of stroke may outweigh the benefit produced by thrombolytic therapy in patients whose AMI puts them at low risk for death or heart failure.

Activase is indicated for the lysis of acute massive pulmonary embolism (PE), defined as:

- Acute pulmonary emboli obstructing blood flow to a lobe or multiple lung segments.
- Acute pulmonary emboli accompanied by unstable hemodynamics, e.g., failure to maintain blood pressure without supportive measures.

TNKase® (tenecteplase)

TNKase is indicated for use in the reduction of mortality associated with acute myocardial infarction (AMI). Treatment should be initiated as soon as possible after the onset of AMI symptoms.

Cathflo® Activase® (alteplase)

Cathflo is indicated for the restoration of function to central venous access devices as assessed by the ability to withdraw blood.

Each product has a distinct vial size specific to its indication. Activase is alteplase packaged in 50- and 100-mg vials; TNKase is tenecteplase, a modified tPA molecule that is administered in one 5-second, single-bolus injection. Cathflo is alteplase packaged in a single-use, 2-mg vial.

tPA=tissue plasminogen activator.

The most frequent adverse reaction associated with all thrombolytics in all approved indications is bleeding. Please see select Important Safety Information throughout and the accompanying full Prescribing Information.

Genentech's ThrombolyticExperience™

Activase® (alteplase)

Indications

Activase (alteplase) is indicated for the treatment of acute ischemic stroke. Exclude intracranial hemorrhage as the primary cause of stroke signs and symptoms prior to initiation of treatment. Initiate treatment as soon as possible but within 3 hours after symptom onset.

Activase is indicated for use in acute myocardial infarction (AMI) for the reduction of mortality and reduction of the incidence of heart failure.

Limitation of Use: The risk of stroke may outweigh the benefit produced by thrombolytic therapy in patients whose AMI puts them at low risk for death or heart failure.

Activase is indicated for the lysis of acute massive pulmonary embolism (PE), defined as:

- Acute pulmonary emboli obstructing blood flow to a lobe or multiple lung segments.
- Acute pulmonary emboli accompanied by unstable hemodynamics, e.g., failure to maintain blood pressure without supportive measures.

Important Safety Information

Contraindications

Do not administer Activase to treat acute ischemic stroke in the following situations in which the risk of bleeding is greater than the potential benefit: current intracranial hemorrhage (ICH); subarachnoid hemorrhage; active internal bleeding; recent (within 3 months) intracranial or intraspinal surgery or serious head trauma; presence of intracranial conditions that may increase the risk of bleeding (e.g., some neoplasms, arteriovenous malformations, or aneurysms); bleeding diathesis; and current severe uncontrolled hypertension.

Do not administer Activase to treat acute myocardial infarction or pulmonary embolism in the following situations in which the risk of bleeding is greater than the potential benefit: active internal bleeding; history of recent stroke; recent (within 3 months) intracranial or intraspinal surgery or serious head trauma; presence of intracranial conditions that may increase the risk of bleeding; bleeding diathesis; and current severe uncontrolled hypertension.

Warnings and Precautions

Bleeding

Activase can cause significant, sometimes fatal internal or external bleeding, especially at arterial and venous puncture sites. Avoid intramuscular injections and trauma to the patient. Perform venipunctures carefully and only as required. Fatal cases of hemorrhage associated with traumatic intubation in patients administered Activase have been reported. Aspirin and heparin have been administered concomitantly with and following infusion with Activase in the management of acute myocardial infarction and pulmonary embolism. The concomitant administration of heparin and aspirin with and following infusions of Activase for the treatment of acute ischemic stroke during the first 24 hours after symptom onset has not been investigated. Because heparin, aspirin, or Activase may cause bleeding complications, carefully monitor for bleeding, especially at arterial puncture sites. Hemorrhage can occur 1 or more days after administration of Activase, while patients are still receiving anticoagulant therapy. If serious bleeding occurs, terminate the Activase infusion, and treat appropriately.

In the following conditions, the risks of bleeding with Activase are increased and should be weighed against the anticipated benefits: recent major surgery or procedure; cerebrovascular disease; recent intracranial hemorrhage; recent gastrointestinal or genitourinary bleeding; recent trauma; hypertension; acute pericarditis; subacute bacterial endocarditis; hemostatic defects including those secondary to severe hepatic or renal disease; significant hepatic dysfunction; pregnancy; diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions; septic thrombophlebitis or occluded AV cannula at seriously infected site; advanced age; and patients currently receiving oral anticoagulants, or any other condition in which bleeding constitutes a significant hazard or would be particularly difficult to manage because of its location.

Hypersensitivity

Hypersensitivity, including urticarial / anaphylactic reactions, have been reported after administration of Activase. Rare fatal outcome for hypersensitivity was reported. Angioedema has been observed during and up to 2 hours after Activase infusion in patients treated for acute ischemic stroke and acute myocardial infarction. In many cases, patients received concomitant angiotensin-converting enzyme inhibitors. Monitor patients treated with Activase during and for several hours after infusion for hypersensitivity. If signs of hypersensitivity occur, e.g. anaphylactoid reaction or angioedema develops, discontinue the Activase infusion and promptly institute appropriate therapy (e.g., antihistamines, intravenous corticosteroids, epinephrine).

Thromboembolism

The use of thrombolytics can increase the risk of thrombo-embolic events in patients with high likelihood of left heart thrombus, such as patients with mitral stenosis or atrial fibrillation. Activase has not been shown to treat adequately underlying deep vein thrombosis in patients with PE. Consider the possible risk of re-embolization due to the lysis of underlying deep venous thrombi in this setting.

Cholesterol Embolization

Cholesterol embolism, sometimes fatal, has been reported rarely in patients treated with thrombolytic agents; the true incidence is unknown. It is associated with invasive vascular procedures (e.g., cardiac catheterization, angiography, vascular surgery) and/or anticoagulant therapy.

Coagulation Tests May be Unreliable during Activase Therapy

Coagulation tests and/or measures of fibrinolytic activity may be unreliable during Activase therapy unless specific precautions are taken to prevent *in vitro* artifacts. When present in blood at pharmacologic concentrations, Activase remains active under *in vitro* conditions, which can result in degradation of fibrinogen in blood samples removed for analysis.

Adverse Reactions

The most frequent adverse reaction associated with Activase therapy is bleeding.

TNKase® (tenecteplase)

Indication

TNKase® (tenecteplase) is indicated for use in the reduction of mortality associated with acute myocardial infarction (AMI). Treatment should be initiated as soon as possible after the onset of AMI symptoms.

Important Safety Information

Contraindications

TNKase therapy in patients with AMI is contraindicated in the following situations because of an increased risk of bleeding: active internal bleeding; history of cerebrovascular accident; intracranial or intraspinal surgery, or trauma within 2 months; intracranial neoplasm, arteriovenous malformation, or aneurysm; known bleeding diathesis; and severe uncontrolled hypertension.

Warnings

Bleeding

The most common complication encountered during TNKase therapy is bleeding. Should serious bleeding (not controlled by local pressure) occur, any concomitant heparin or antiplatelet agents should be discontinued immediately and treated appropriately.

In clinical studies of TNKase, patients were treated with both aspirin and heparin. Heparin may contribute to the bleeding risks associated with TNKase. The safety of the use of TNKase with other antiplatelet agents has

not been adequately studied. Intramuscular injections and nonessential handling of the patient should be avoided for the first few hours following treatment with TNKase.

The risk of bleeding may be increased in the following conditions and should be weighed against the anticipated benefits: recent major surgery, cerebrovascular disease, recent gastrointestinal or genitourinary bleeding, recent trauma, hypertension, acute pericarditis, subacute bacterial endocarditis, hemostatic defects, severe hepatic dysfunction, pregnancy, diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions, septic thrombophlebitis or occluded AV cannula at seriously infected site, advanced age, patients currently receiving oral anticoagulants, recent administration of GP IIb/IIIa inhibitors, and any other condition in which bleeding constitutes a significant hazard or would be particularly difficult to manage because of its location.

Thromboembolism

The use of thrombolytics can increase the risk of thrombo-embolic events in patients with high likelihood of left heart thrombus, such as patients with mitral stenosis or atrial fibrillation.

Cholesterol Embolization

Cholesterol embolism has been reported rarely in patients treated with all types of thrombolytic agents; the true incidence is unknown. This serious condition, which can be lethal, is also associated with invasive vascular procedures (e.g., cardiac catheterization, angiography, vascular surgery) and/or anticoagulant therapy.

Arrhythmias

Coronary thrombolysis may result in arrhythmias associated with reperfusion. It is recommended that anti-arrhythmic therapy for bradycardia and/or ventricular irritability be available when TNKase is administered.

Use with Percutaneous Coronary Intervention (PCI)

In patients with large ST-segment elevation myocardial infarction, physicians should choose either thrombolysis or PCI as the primary treatment strategy for reperfusion.

Precautions

Standard management of myocardial infarction should be implemented concomitantly with TNKase treatment. In the event of serious bleeding, heparin and antiplatelet agents should be discontinued immediately.

Hypersensitivity

Anaphylactoid reactions associated with the administration of TNKase are rare and can be caused by hypersensitivity to the active substance tenecteplase or to any of the excipients. If symptoms of hypersensitivity occur, appropriate therapy should be initiated.

Drug and Drug/Laboratory Test Interactions

Formal interaction studies of TNKase with other drugs have not been performed. Patients studied in clinical trials of TNKase were routinely treated with heparin and aspirin.

During TNKase therapy, results of coagulation tests and/or measures of fibrinolytic activity may be unreliable unless specific precautions are taken to prevent *in vitro* artifacts. Tenecteplase is an enzyme that, when present in blood in pharmacologic concentrations, remains active under *in vitro* conditions. This can lead to degradation of fibrinogen in blood samples removed for analysis.

Adverse Reactions

The most frequent adverse reaction associated with TNKase is bleeding.

Should serious bleeding occur, concomitant heparin and antiplatelet therapy should be discontinued. Death or permanent disability can occur in patients who experience stroke or serious bleeding episodes. For TNKase-treated patients in ASSENT-2, the incidence of intracranial hemorrhage was 0.9% and incidence of any stroke was 1.8%. The incidence of all strokes, including intracranial bleeding, increases with advancing age.

Cathflo® Activase® (alteplase)

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.

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.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate the carcinogenic potential or the effect on fertility.

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.

Genentech's Thrombolytic Dosing and Administration

3 products, 4 indications, 1 ongoing commitment

Activase® (alteplase)—AIS[2]

Please see full Prescribing Information for reconstitution instructions.

The recommended treatment dose of Activase is 0.9 mg/kg (not to exceed 90 mg total treatment dose) infused over 60 minutes, with 10% of the total treatment dose administered as an initial bolus over 1 minute. The remaining treatment dose should be infused intravenously over 60 minutes.

Step 1: **INSPECT** the solution for particulate matter and discoloration prior to administration.

Step 2: To ensure proper dosing, **DISCARD** excess by removing any quantity of drug in excess of that specified for the patient's treatment. Be sure to **INSERT** the needle into the keyhole port of the vial top, away from the puncture site made by the transfer device, and do not prime the syringe.

Step 3: The bolus treatment dose is 10% of the 0.9 mg/kg treatment dose. **PREPARE** it in one of the following ways, using a syringe and needle:

Prepare Bolus

Remove From Y-Site

Remove the treatment dose from the Y-site injection port on the infusion line after the infusion set is primed.

Or Remove From Vial

Remove the treatment dose before the vial is attached to the infusion set. Be sure to insert the needle away from the puncture site made by the transfer device.

Do not prime the syringe.

Step 4: 100-mg vials—**INSERT** the spike end of an infusion set through the center of the stopper of the vial of reconstituted Activase, using the same puncture site made by the transfer device. Peel the clear plastic hanger from the vial label. Hang the Activase vial from the resulting loop. 50-mg vials—**ADMINISTER** using either a polyvinyl chloride bag or glass vial and infusion set.

Step 5: **PRIME** infusion set tubing with Activase solution and administer initial IV bolus over 1 minute.

Step 6: Administer remainder—**INFUSE** the remaining 90% of the 0.9 mg/kg treatment dose over 60 minutes. The infusion should begin immediately following the bolus treatment dose. Activase (bolus and the remainder of the treatment dose) can also be administered using an infusion pump. Make sure to prime the pump tubing with Activase solution so that the infusion begins immediately following the bolus treatment dose.

Step 7: **CLEAR** IV tubing: Spike a small bag (eg, 50 mL) of 0.9% Sodium Chloride, U.S. Pharmacopeia (USP), with the end of the Activase infusion set when the Activase vial is empty. The infusion should continue at the same rate.

Indication

Activase is indicated for the treatment of acute ischemic stroke (AIS). Exclude intracranial hemorrhage as the primary cause of stroke signs and symptoms prior to initiation of treatment. Initiate treatment as soon as possible but within 3 hours after symptom onset.

Important Safety Information

Contraindications

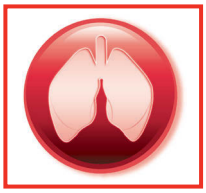
Do not administer Activase to treat acute ischemic stroke in the following situations in which the risk of bleeding is greater than the potential benefit: current intracranial hemorrhage (ICH); subarachnoid hemorrhage; active internal bleeding; recent (within 3 months) intracranial or intraspinal surgery or serious head trauma; presence of intracranial conditions that may increase the risk of bleeding (e.g., some neoplasms, arteriovenous malformations, or aneurysms); bleeding diathesis; and current severe uncontrolled hypertension.

ACTIVASE® ALTEPLASE
A RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR

www.activase.com

Please see continued Important Safety Information on page 2.

Activase® (alteplase)—AMPE[2]



Please see full Prescribing Information for reconstitution and administration instructions.

100 mg administered as a controlled infusion over 2 hours via an IV line.

Institute or reinstate heparin near the end of or immediately following the Activase infusion when the partial thromboplastin time or thrombin time returns to twice normal or less.

Indication

Activase is indicated for the lysis of acute massive pulmonary embolism (PE), defined as:

- Acute pulmonary emboli obstructing blood flow to a lobe or multiple lung segments.
- Acute pulmonary emboli accompanied by unstable hemodynamics, e.g., failure to maintain blood pressure without supportive measures.

Important Safety Information

Contraindications

Do not administer Activase to treat acute myocardial infarction or pulmonary embolism in the following situations in which the risk of bleeding is greater than the potential benefit: active internal bleeding; history of recent stroke; recent (within 3 months) intracranial or intraspinal surgery or serious head trauma; presence of intracranial conditions that may increase the risk of bleeding (e.g., some neoplasms, arteriovenous malformations, or aneurysms); bleeding diathesis; and current severe uncontrolled hypertension.

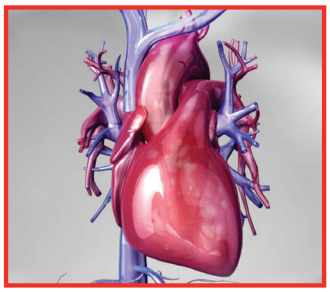
ACTIVASE® ALTEPLASE
A RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR

www.activase.com

Please see continued Important Safety Information on page 2.

Genentech's ThrombolyticExperience™

Activase® (alteplase)—AMI[2]



Please see full Prescribing Information for reconstitution and administration instructions.

Dose is based upon patient weight, not to exceed 100 mg.

Accelerated Infusion

Patient weight	Initial IV bolus	Infusion over the next 30 minutes	Infusion over the next 60 minutes
>67 kg	15 mg	50 mg	35 mg
≤67 kg	15 mg	0.75 mg/kg	0.50 mg/kg

3-hour Infusion

Patient weight	Bolus	Rest of 1st hour	Rest of 2nd hour	Rest of 3rd hour
≥65 kg	6–10 mg	50–54 mg	20 mg	20 mg
<65 kg	0.075 mg/kg	0.675 mg/kg	0.25 mg/kg	0.25 mg/kg

Indication

Activase (alteplase) is indicated for use in acute myocardial infarction (AMI) for the reduction of mortality and reduction of the incidence of heart failure.

Limitation of Use: The risk of stroke may outweigh the benefit produced by thrombolytic therapy in patients whose AMI puts them at low risk for death or heart failure.

Important Safety Information

Contraindications

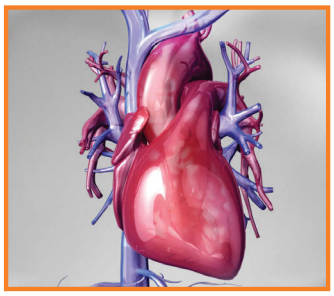
Do not administer Activase to treat acute myocardial infarction in the following situations in which the risk of bleeding is greater than the potential benefit: active internal bleeding; history of recent stroke; recent (within 3 months) intracranial or intraspinal surgery or serious head trauma; presence of intracranial conditions that may increase the risk of bleeding (e.g. some neoplasms, arteriovenous malformations, or aneurysms); bleeding diathesis; and current severe uncontrolled hypertension.

Please see continued Important Safety Information on page 2.

ACTIVASE®
ALTEPLASE
A RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR

www.activase.com

TNKase® (tenecteplase)—AMI[3]



Please see full Prescribing Information for reconstitution instructions.

Step 1: Determine the correct dose of TNKase based on patient weight. TNKase is for IV administration only.

Step 2: **WITHDRAW** the appropriate volume of solution based on patient weight. **The recommended total dose should not exceed 50 mg.**

Step 3: **FLUSH** a dextrose-containing line with a saline-containing solution prior to and following administration (precipitation may occur when TNKase is administered in an IV line containing dextrose). **ADMINISTER** as an IV bolus over 5 seconds.

Patient weight (kg)	TNKase (mg)	Reconstituted TNKase (mL)
<60	30	6
≥60 to <70	35	7
≥70 to <80	40	8
≥80 to <90	45	9
≥90	50	10

Indication

TNKase® is indicated for use in the reduction of mortality associated with acute myocardial infarction (AMI). Treatment should be initiated as soon as possible after the onset of AMI symptoms.

Important Safety Information

Contraindications

TNKase therapy in patients with AMI is contraindicated in the following situations because of an increased risk of bleeding: active internal bleeding; history of cerebrovascular accident; intracranial or intraspinal surgery, or trauma within 2 months; intracranial neoplasm, arteriovenous malformation, or aneurysm; known bleeding diathesis; and severe uncontrolled hypertension.

Please see continued Important Safety Information on page 2.

TNKase® Tenecteplase

www.tnkase.com

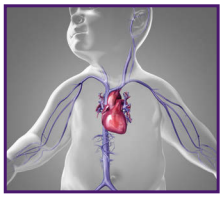
Cathflo® Activase® (alteplase) 2 mg—CVAD in Adult and Pediatric Patients[4]

Please see full Prescribing Information for reconstitution instructions.

Adult

Patient weight	FDA-approved Cathflo dose
≥30 kg (66 lb)	2 mg in 2 mL
<30 kg (66 lb)	110% of the internal lumen volume of CVAD, not to exceed 2 mg in 2 mL

Pediatric



Patient weight	FDA-approved Cathflo dose
<30 kg (66 lb)	110% of the internal lumen volume of CVAD, not to exceed 2 mg in 2 mL
≥30 kg (66 lb)	2 mg in 2 mL

Measure the internal lumen volume to determine the Cathflo dose for pediatric patients*[5]

Device	Device ranges
Peripherally inserted central catheter (PICC)	Device priming volume ranges from 0.06 to 0.6 mL. Check manufacturer guidelines.
Tunneled and nontunneled	Device priming volume ranges from 0.12 to 1.3 mL. Check manufacturer guidelines.
Implanted port	Device priming volume ranges from 0.8 to 2 mL. Check manufacturer guidelines.

†Dependent on the CVAD manufacturer, size, number of lumens, add-on device, patient weight, and final length of the catheter, the priming volume will vary.

Step 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.

Step 2: **INSTILL** the appropriate dose of Cathflo into the occluded catheter using a 10-mL syringe (see dosing chart above).

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

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

Step 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**.

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.

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.

Please see continued Important Safety Information on page 3.

cathflo ACTIVASE (ALTEPLASE)

www.cathflo.com

Genentech's Commitment to Patient Care:

1. Ask your Genentech clinical specialist about available resources

2. Organize in-person or virtual education with a clinical practice expert

- Speakers Bureau Program
- Cathflo Nurse Trainer (CNT) Program

HealthStream®

3. Sustain education with interactive learning modules that can be incorporated into your learning management system (LMS)

- Genentech stroke modules (AIS)*
- Cathflo modules (CVAD)*

Please call Genentech Customer Service at 1-800-551-2231 to locate your Genentech clinical specialist.

*Interactive learning modules also available online through HealthStream.

References: 1. Data on file, Genentech USA, Inc. **2.** Activase [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2018. **3.** TNKase [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2018. **4.** Cathflo Activase Prescribing Information. Genentech USA, Inc.; 2018. **5.** AVA Pediatric Special Interest Group. *Best Practice Guidelines in the Care and Maintenance of Pediatric Central Venous Catheters.* 2nd ed. Association for Vascular Access; 2015:1-70. **6.** Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2018;49: e46-e110. **7.** Infusion Nurses Society. Infusion therapy standards of practice. *J Infus Nurs.* 2016;39(suppl1):S1-S159. **8.** Camp-Sorrell D, ed. *Access Device Standards of Practice for Oncology Nursing.* 4th ed. Pittsburgh, PA: Oncology Nursing Society; 2017. **9.** McKnight S. Nurse's guide to understanding and treating thrombotic occlusion of central venous access devices. *Medsurg Nurs.* 2004;13:377-382. **10.** Haire WD, Herbst SF. Consensus conference on the use of alteplase (t-PA) for the management of thrombotic catheter dysfunction. *J Vasc Access Devices.* Summer 2000:1-8. **11.** Criddle LM. Ask the experts. *Crit Care Nurse.* 2007;27:78-81. **12.** Cummings-Winfield C, Mushani-Kanji T. Restoring patency to central venous access devices. *Clin J Oncol Nurs.* 2008;12:925-934.

For any questions related to thrombolytic dosing and administration, contact Genentech Customer Service at 1-800-551-2231.

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

Genentech's ThrombolyticExperience™

Highest Level of Evidence in Select Stroke and CVAD Guidelines

Activase® (alteplase) is the standard of care for treating eligible patients with AIS within 3 hours of symptom onset

AHA/ASA practice guidelines recommend intravenous Activase (a recombinant tissue plasminogen activator) use for management of AIS.[6]

AHA/ASA
American Heart Association and American Stroke Association

IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is recommended for selected patients who may be treated within 3 hours of ischemic stroke symptom onset or patient last known well or at baseline state.[6]

—Class I; Level of Evidence A, 2018 AHA/ASA Guideline

In patients eligible for IV alteplase, benefit of therapy is time-dependent, and treatment should be initiated as quickly as possible.[6]

—Class I; Level of Evidence A, 2018 AHA/ASA Guideline

Single-use vial

Cathflo® Activase® (alteplase) 2 mg is the standard of care for the treatment of thrombotically occluded catheters

Cathflo is the only thrombolytic recommended by clinical practice standards, including the Infusion Nurses Society (INS), Association for Vascular Access (AVA), American Association of Critical Care Nurses (AACN), and Oncology Nursing Society (ONS).[7-12]

INS
Infusion Nurses Society

Instillation of tPA based on manufacturers' directions for use is recommended in current guidelines. There is limited research available to support the efficacy of thrombolytic drugs for alternative dosing.[7]

—Class I; Level of Evidence A, INS Infusion Therapy Standards of Practice, 2016, page S105, standard 48, practice criterion G-2

ONS
Oncology Nursing Society

Use 2 mg alteplase (Cathflo Activase) to restore patency and maintain catheter function.[8]

—Practice Standard, ONS Access Device Standards of Practice, 2017, page 10, section VI, practice standard B

Single-use vial

Activase® (alteplase)

Activase (alteplase) is indicated for the treatment of acute ischemic stroke. Exclude intracranial hemorrhage as the primary cause of stroke signs and symptoms prior to initiation of treatment. Initiate treatment as soon as possible but within 3 hours after symptom onset.

Activase is indicated for use in acute myocardial infarction (AMI) for the reduction of mortality and reduction of the incidence of heart failure.

Limitation of Use: The risk of stroke may outweigh the benefit produced by thrombolytic therapy in patients whose AMI puts them at low risk for death or heart failure.

Activase is indicated for the lysis of acute massive pulmonary embolism (PE), defined as:

- Acute pulmonary emboli obstructing blood flow to a lobe or multiple lung segments.
- Acute pulmonary emboli accompanied by unstable hemodynamics, e.g., failure to maintain blood pressure without supportive measures.

Cathflo® Activase® (alteplase)

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

The most frequent adverse reaction associated with all thrombolytics in all approved indications is bleeding.

rtPA=recombinant tissue plasminogen activator.

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Genentech's ThrombolyticExperience™