ALTEPLASE:

Class: Thrombolytic Agent (Fibrinolytic Agent).

Indications:

- Management of acute myocardial infarction for the lysis of thrombi in coronary arteries; management of acute ischemic stroke

-Acute myocardial infarction (AMI): Chest pain ≥20 minutes, ≤12-24 hours; S-T elevation ≥0.1 mV in at least two ECG leads

-Acute pulmonary embolism (APE): Age ≤75 years: Documented massive pulmonary embolism by pulmonary angiography or echocardiography or high probability lung scan with clinical shock .

-Restoration of central venous catheter function

***Unlabeled/Investigational :** Acute peripheral arterial occlusive disease.

Dosage:

-Coronary artery thrombi: Front loading dose (weight-based):

-Patients >67 kg: Total dose: 100 mg over 1.5 hours; infuse 15 mg over 1-2 minutes. Infuse 50 mg over 30 minutes. Infuse remaining 35 mg of alteplase over the next hour. Maximum total dose: 100 mg

-Patients ≤67 kg: Infuse 15 mg I.V. bolus over 1-2 minutes, then infuse 0.75 mg/kg (not to exceed 50 mg) over next 30 minutes, followed by 0.5 mg/kg over next 60 minutes (not to exceed 35 mg) Maximum total dose: 100 mg. See "Notes."

Note: Concurrently, begin heparin 60 units/kg bolus (maximum: 4000 units) followed by continuous infusion of 12 units/kg/hour (maximum: 1000 units/hour) and adjust to aPTT target of 1.5-2 times the upper limit of control.

Note: Thrombolytic should be administered within 30 minutes of hospital arrival. Administer concurrent aspirin, clopidogrel, and anticoagulant therapy (ie, unfractionated heparin, enoxaparin, or fondaparinux) with alteplase (O'Gara, 2013).

-Acute massive or submassive pulmonary embolism: I.V. (Activase®): 100 mg over 2 hours; may be administered as a 10 mg bolus followed by 90 mg over 2 hours as was done in patients with submassive PE (Konstantinides, 2002). **Note:** Not recommended for submassive PE with minor RV dysfunction, minor myocardial necrosis, and no clinical worsening or low-risk PE (ie, normotensive, no RV dysfunction, normal biomarkers) (Jaff, 2011).

-Acute ischemic stroke: I.V. (Activase®): Within 3 hours of the onset of symptom onset (labeled use) **or** within 3-4.5 hours of symptom onset (unlabeled use; Hacke, 2008; Jauch, 2013): **Note:** Perform noncontrast-enhanced CT or MRI prior to administration. Initiation of anticoagulants (eg, heparin) or antiplatelet agents (eg, aspirin) within 24 hours after starting alteplase is not recommended; however, initiation of aspirin within 24-48 hours after stroke onset is recommended (Jauch, 2013). Initiation of SubQ heparin (≤10,000 units) or equivalent doses of low molecular weight heparin for prevention of DVT during the first 24 hours of the 3-4.5 hour window trial did not increase incidence of intracerebral hemorrhage (Hacke, 2008).

Recommended total dose: 0.9 mg/kg (maximum total dose: 90 mg)

Patients ≤100 kg: Load with 0.09 mg/kg (10% of 0.9 mg/kg dose) as an I.V. bolus over 1 minute, followed by 0.81 mg/kg (90% of 0.9 mg/kg dose) as a continuous infusion over 60 minutes.

Patients >100 kg: Load with 9 mg (10% of 90 mg) as an I.V. bolus over 1 minute, followed by 81 mg (90% of 90 mg) as a continuous infusion over 60 minutes.

-Intracatheter: Central venous catheter clearance: Cathflo® Activase® 1 mg/mL:

-Patients <30 kg: 110% of the internal lumen volume of the catheter, not to exceed 2 mg/2 mL; retain in catheter for 0.5-2 hours; may instill a second dose if catheter remains occluded

-Patients ≥30 kg: 2 mg (2 mL); retain in catheter for 0.5-2 hours; may instill a second dose if catheter remains occluded

-Intra-arterial: Acute peripheral arterial occlusive disease (unlabeled use): 0.02-0.1 mg/kg/hour for up to 36 hours .Advisory Panel to the Society for Cardiovascular and Interventional Radiology on Thrombolytic Therapy recommendation: ≤2 mg/hour and subtherapeutic heparin (aPTT <1.5 times baseline)

Complicated parapneumonic effusion (unlabeled use): Intrapleural: 10 mg in 30 mL NS administered twice daily with a 1 hour dwell time for a total of 3 days; each dose followed in >2 hours by intrapleural dornase alfa (Rahman, 2011). Some clinicians suggest consideration of fibrinolytic use when patients have failed at least 24 hours of chest tube drainage and are poor surgical candidates (Hamblin, 2010).

Prosthetic valve thrombosis, right-sided (any size thrombus) or left-sided (thrombus area <0.8 cm^2), or left-sided (thrombus area ≥0.8 cm^2) when contraindications to surgery exist (unlabeled use) (Alpert, 2003; Guyatt, 2012; Roudaut, 2003): I.V.:

High-dose regimen: Load with 10 mg, followed by 90 mg over 90-180 minutes (without heparin during infusion)

Low-dose regimen (preferred for very small adults): Load with 20 mg, followed by 10 mg/hour for 3 hours (without heparin during infusion)

Note: After successful administration of alteplase, heparin infusion should be introduced until warfarin achieves therapeutic INR (aortic: 3.0-4.0; mitral: 3.5-4.5) (Bonow, 2008). The 2012 ACCP guidelines for antithrombotic therapy make no recommendation regarding INR range after prosthetic valve thrombosis .

Available dosage form in the hospital: VIAL

Common side effect: Arrhythmias: Coronary thrombolysis may result in reperfusion arrhythmias. Bleeding: Doses >150 mg are associated with increased risk of intracranial hemorrhage; monitor all potential bleeding sites. If serious bleeding occurs, the infusion of alteplase and heparin should be stopped.

Pregnancy Risk Factor: C