Alteplase Injection for Acute Ischemic Stroke

Alteplase (tissue plasminogen activator, recombinant; tPA) is approved by the U.S. FDA for intravenous thrombolysis in acute ischemic stroke within 3 hours of the onset of stroke symptoms. Use the following drug information to increase your understanding of this agent and provide safe patient care.

Inclusion criteria (Powers, et al., 2018)

• Diagnosis of ischemic stroke causing measurable neurological deficit
• 18 years of age or older
• Onset of symptoms < 3 hours
  o Includes patients with severe stroke and patients with mild but disabling stroke symptoms
  o Equally effective in patients < 80 and > 80 years of age
• For select patients with symptom onset 3- to 4.5- hours:
  o 80 years of age or less
  o No history of diabetes mellitus and prior stroke, no current oral anticoagulant use, NIHSS score ≤ 25, no anticoagulants, cerebral imaging showing ischemia involving less than one third of middle cerebral artery (MCA) territory
• Blood pressure (BP) that can be lowered safely (< 185/110 mm Hg) with antihypertensive agents.
• Initial glucose > 50 mg/dL
• Non-contrast computed tomography (NCCT) showing early mild-moderate ischemic changes.
• Patients taking mono-antiplatelet therapy or combination therapy (i.e. aspirin and clopidogrel) and patients with end-stage renal disease on hemodialysis and normal aPTT are eligible for therapy.

Contraindications (Powers, et al., 2018)

• Unclear time and/or unwitnessed symptom onset and last known baseline state > 3 or 4.5 hours
• Current or history of intracranial hemorrhage
• CT scan showing hypoattenuation or hypoperfusion representing irreversible injury
• Recent (within 3 months) ischemic stroke, severe head trauma, or intracranial/intraspinal surgery
• Subarachnoid hemorrhage
• Gastrointestinal (GI) malignancy or GI bleed within 21 days of stroke event
• Intracranial conditions that may increase the risk of bleeding such as intracranial neoplasm, arteriovenous malformation, or aneurysm
• Coagulopathy: Platelet count < 100,000/mm$^3$, INR > 1.7, aPTT > 40 seconds, or PT > 15 seconds
• Low molecular weight heparin (LMWH) treatment doses within the previous 24 hours
• Current use of anticoagulant with INR > 1.7 or PT > 15 seconds
• Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated laboratory tests
• Concurrent use of glycoprotein IIb/IIIa receptor inhibitors
• Infective endocarditis
• Aortic arch dissection
• Intra-axial intracranial neoplasm – lesions located within the brain tissue

Note: See current clinical practice guidelines for complete list of recommendations for treatment with parenteral alteplase and relative indications.

Pregnancy Risk Category: C

Dosage and Administration

Available forms: 50-mg vial, 100-mg vial

Dosage: Dose is calculated based on patient weight (0.9 mg/kg) with a maximum total of 90 mg over 60 minutes. Ten percent of total dose given as an IV bolus over 1 minute, followed by an IV infusion of the remainder of the dose over 1 hour.

Administration:
• May be administered IV or intra-arterially (intra-arterial administration is an off-label route).
• May be given to eligible patients even if endovascular therapies (EVTs) are being considered.
• Consult package insert for complete instructions on medication preparation, reconstitution and administration.

Nursing Considerations

• BEFORE administration:
  o Carefully lower blood pressure (BP) to maintain systolic BP < 185 mmHg and diastolic BP < 110 mmHg before initiating fibrinolytic therapy (Powers, et al., 2018).
  o Due to an increased risk of intracranial bleeding, check INR, PTT and blood glucose prior to administration.
• Assess for exclusion criteria/contraindications.
• Explain use and administration of the drug to the patient and the family; tell them to report adverse reactions immediately.
• Admit to the intensive care unit (ICU) for monitoring.

**DURING** administration:
• Maintain strict bedrest during treatment.
• Measure BP and perform neurological assessment every 15 minutes during infusion for 2 hours, then every 30 minutes for 6 hours, then hourly until 24 hours after treatment.
  ▪ Increase frequency of BP measurements if SBP > 180 mm Hg or if DPB > 105 mm Hg; administer antihypertensive as needed to maintain these levels.
• If any change in neurological status or symptoms occurs, such as severe headache, acute hypertension, nausea or vomiting, or worsening neurological examination, the alteplase administration should be stopped and a CT scan obtained.
• Avoid invasive procedures and I.M. injections, and perform venipunctures carefully and only as required, avoiding internal jugular and subclavian venous punctures.
• Closely monitor the patient for internal bleeding and frequently assess all puncture sites.
  ▪ If serious bleeding occurs, stop the alteplase infusion immediately.

**AFTER** administration:
• Monitor BP and perform neurologic assessment every 15 minutes during infusion for 2 hours, then every 30 minutes for 6 hours, then hourly until 24 hours after treatment. After the initial 24 hours, monitor vital signs, control blood pressure, and perform neurological assessments frequently per your facility’s policy.
• Maintain BP < 180/105 mmHg for at least 24 hours after treatment.
• Hold antiplatelet or anticoagulation therapy and invasive procedures for 24 hours following administration.
• Monitor for serious adverse events, such as bleeding and angioedema.
  ▪ Concomitant use of angiotensin-converting enzyme (ACE) inhibitors may increase the risk of orolingual angioedema.
  ▪ Concomitant use of anticoagulants and drugs that inhibit platelet function increase the risk of bleeding.
• Delay insertion of nasogastric tubes, indwelling bladder catheters, or intra-arterial pressure catheters if patient can be managed without them.
Obtain follow-up CT or MRI scan 24 hours after treatment before starting anticoagulants or antiplatelet agents.

Adverse reactions

- Bleeding (most common)
- Orolingual angioedema
- Arrhythmias
- Hypotension
- Edema
- Cholesterol embolization
- Venous thrombosis
- Re-embolization of deep venous thrombi (DVT) in patients with pulmonary embolism
- Nausea
- Vomiting
- Hypersensitivity reactions

Management of Symptomatic Bleeding Within 24 Hours After Administration of IV Alteplase (Powers, et al., 2018)

- Stop alteplase infusion.
- Obtain CBC, PT (INR), aPTT, fibrinogen level, and type and cross-match.
- Obtain emergent nonenhanced head CT.
- Per order, administer cryoprecipitate (includes factor VIII): 10 U infused over 10-30 minutes (onset in 1 hour, peaks in 12 hour); administer additional dose for fibrinogen level < 200 mg/dL.
- Per order, administer tranexamic acid 1000 mg IV infused over 10 min OR E-aminocaproic acid 4-5 g over 1 hour, followed by 1 g IV until bleeding is controlled.
- Obtain hematology and neurosurgery consult.
- Manage BP, intracranial pressure (ICP), cerebral perfusion pressure (CPP), mean arterial pressure (MAP), temperature, and glucose.

Management of Orolingual Angioedema Associated with IV Alteplase (Powers, et al., 2018)

- Maintain airway.
  - Intubation may not be needed if edema is limited to anterior tongue and lips.
  - Edema involving larynx, palate, floor of mouth, oropharynx with rapid progression (within 30 minutes) poses higher risk of respiratory compromise requiring intubation.
  - Awake fiberoptic intubation is preferred.
As ordered, perform the following:

- Discontinue IV alteplase infusion and hold ACE-inhibitors.
- Administer IV methylprednisolone 125 mg.
- Administer IV diphenhydramine 50 mg.
- Administer ranitidine 50 mg IV or famotidine 20 mg IV.
- If there is an increase in angioedema, administer epinephrine (0.1%) 0.3 mL subcutaneously or by nebulizer 0.5 mL.
- Administer icatibant (selective bradykinin B₂ receptor antagonist), 3 mL (30 mg) subcutaneously in abdomen.

References:


