Alteplase (tPA)Thrombolysis for Acute Stroke Dosing Chart

Concentration: 1 mg/mL

Admixture:
Reconstitute 100 mg vial with 100 mL sterile water provided, see package insert for detailed instructions.
Withdraw bolus dose from vial. Infuse remainder of dose over 60 minutes.

	First Over 1 minute	Next 60 minutes	
Weight kg	**Loading dose** mg	**DOSE** mg	**RATE** mL/hr
40	4	32	32
42	4	34	34
44	4	36	36
46	4	37	37
48	4	39	39
50	5	40	40
52	5	42	42
54	5	44	44
56	5	45	45
58	5	47	47
60	5	49	49
62	6	50	50
64	6	52	52
66	6	53	53
68	6	55	55
70	6	57	57

	First Over 1 minute	Next 60 minutes	
Weight kg	**Loading dose** mg	**DOSE** mg	**RATE** mL/hr
72	6	59	59
74	7	60	60
76	7	61	61
78	7	63	63
80	7	65	65
82	7	67	67
84	8	68	68
86	8	69	69
88	8	71	71
90	8	73	73
92	8	75	75
94	8	77	77
96	9	77	77
98	9	79	79
100 & up	9	81	81

Values have been rounded off

ALTEPLASE

OTHER NAMES	CLASSIFICATION	*ELDER ALERT
Tissue-type Plasminogen Activator (Recombinant) rt-PA, t-PA, ACTIVASE rt-PA, Cathflo®	Thrombolytic	See Cautions

INDICATIONS FOR IV USE

HEALTH CANADA APPROVED:[1]

- Treatment of acute MI. **In SHR alteplase has been replaced with tenecteplase for this indication.**
- Treatment of acute ischemic stroke within 3 (to 4.5) hours from symptom onset.* (see non-approved indications below)
- For the restoration of function to central venous access devices[15]

NON-APPROVED HEALTH CANADA INDICATIONS BUT SUBSTANTIATED IN THE LITERATURE:

- Treatment of acute ischemic stroke within 4.5 hours from symptom onset.[16]
- Treatment of pulmonary embolism with severe hemodynamic compromise and/or severe hypoxemia. [2]
- Catheter-directed thrombolysis after angiographic placement of catheter tip. [2-4]
- Lysis of hemodialysis catheter-associated fibrin sheaths. [5-6]

CONTRAINDICATIONS to use in ACUTE ISCHEMIC STROKE (*per Activase® rt-PA product monograph*)[13,14]

- **Refer to appendix A in SHR Acute Stroke Thrombolytic (tPA) Administration Order Set for SHR inclusion/exclusion criteria**[17]
- ➢ *Hypersensitivity to alteplase*
- Time of onset of stroke greater than 3 hours. Do **not** administer alteplase in a minor, or rapidly resolving stroke.
- Evidence of an intracranial hemorrhage **or** suspicion of a subarachnoid hemorrhage; intracranial neoplasm, AV malformation or aneurysm
- Recent (within 3 months) stroke or serious head trauma; intracranial or intraspinal surgery
- Myocardial infarction in the previous 3 months and/or clinical presentation associated with post-MI pericarditis.
- Gastrointestinal or urinary tract hemorrhage in previous 21 days
- Major surgery in previous 14 days
- History of intracranial hemorrhage
- BP elevated (SBP >185 mm Hg and DBP > 110 mm Hg). Aggressive treatment required to reduce BP to specified limits.
- Seizure at the onset of stroke
- Active internal bleeding
- Known bleeding risk: current use of an oral anticoagulant (e.g. warfarin) **or** an INR greater than 1.7 or a PT greater than 15 secs; heparin in the previous 48 hours and an elevated aPTT on presentation; platelet count less than 100,000 mm^3
- Blood glucose less than 3 or greater than 22 mmol/L
- Arterial puncture at a noncompressible site within the previous 7 days

CAUTIONS[1]

- * Elderly: may have pre-existing conditions that may increase risk of intracranial bleeding.
- Avoid conditions in which bleeding constitutes a substantial hazard or would be difficult to control because of its location.
- Avoid any excessive or rough handling of patient; avoid invasive procedures (e.g. arterial puncture, venipuncture, IM injection). If these procedures are absolutely necessary, use extreme precautionary methods (use radial artery instead of femoral; use small-gauge catheters and needles, and sites that are easily observed and compressible where bleeding can be controlled; avoid handling catheter sites and use extended pressure application of up to 30 minutes).

DRUG INTERACTIONS: Oral anticoagulant or heparin may increase risk of hemorrhage.

- Drugs that affect platelet function, such as ASA, NSAID's, may increase risk of hemorrhage.

PREGNANCY/BREAST FEEDING: Contact Pharmacy for most recent information

ADMINISTRATION

MODE	DIRECT INTO IV TUBING	INTERMITTENT INFUSION	CONTINUOUS INFUSION
	YES	YES	YES
ADULT	**Ischemic stroke:** **Bolus dose** over 1 minute administered by **physician**[12]	Further dilution not required. **Ischemic stroke**: Infuse over 1 hour[12] **Pulmonary embolism:** Infuse over 2 hours.[2]	**Catheter-directed thrombolysis:** Add 50 mg to 500 – 1000 mL NS for 0.1 – 0.05 mg/mL [4,8]
REQUIREMENTS	IV infusion device and a vented administration set if infusing directly from glass bottle		

MONITORING * To be administered (except Bolus dose) and monitored by Critical Care Personnel

REQUIRED

Intermittent infusion of doses 10 mg or greater (e.g. ischemic stroke or pulmonary embolism):

- **Acute ischemic stroke**: continuous cardiac monitoring (see **Appendix A**) for a minimum of 2 hours.
- Baseline T, BP, HR and neurological assessment, then q 15 minutes for the first 2 hours after drug initiated; then q 30 minutes and PRN for 2 hours; then q4h and PRN.
- Visual assessment for signs and symptoms of bleeding q 30 min during infusion, then q1 h x 6, then q4 h x 48 hours.
- Assess for frank or occult blood in stool, emesis, sputum and urine for at least 72 hours after initiation of therapy.

Continuous infusion: refer to p. 2 **CONTINUED…**

MONITORING REQUIRED (continued)….

Continuous infusion:

- Visual assessment for signs and symptoms of bleeding q 30 min during infusion, then q1h x 6. If on concomitant heparin continue q 2h x 3 then stop i.e. monitor for 12 hours after infusion stops if on concomitant heparin.
- Baseline BP, HR and neurological assessment, then q1 h during infusion and for 6 hours after. If on concomitant heparin continue q2h x 3 then stop.
- Assess for frank or occult blood in stool, emesis, sputum and urine for at least 72 hours after initiation of therapy.

MONITORING

RECOMMENDED:

- Baseline PT-INR, PTT, CBC with platelet count, fibrinogen, hematocrit, thrombin time and repeat daily during infusion.
- Observe for neurological changes, e.g. headache, visual changes.

RECONSTITUTION

- See package insert for reconstitution instructions. **Do not shake the vial. Swirl and/or invert gently to mix.**
- Available as alteplase 50 and 100 mg vial, plus 50 or 100 mL sterile water for injection for reconstitution.

COMPATIBILITY/STABILITY

- Reconstituted vials are stable up to 24 hours at room temperature and in fridge. [9]
- Incompatible with bacteriostatic water for injection as preservatives can interact with alteplase. [1]
- Limited stability information available, concentrations of 0.1 and 0.05 mg/mL in NS have been used successfully [8,10] and stability for 24 hours at room temperature is assumed.
- For drug-drug compatibility contact Pharmacy.

ADVERSE EFFECTS[1]

HEMATOLOGICAL

- Superficial or surface bleeding at puncture sites. Apply local pressure.
- Serious internal bleeding, e.g. retroperitoneal, intracerebral: Discontinue infusion and, if necessary, administer cryoprecipitate and packed red blood cells. Tranexamic acid may be considered in an emergency. Do **not** use dextran.

ALLERGIC REACTIONS

- Anaphylactoid reaction, laryngeal edema, rash, urticaria (rare).

MISCELLANEOUS

- Reperfusion arrhythmias, hypotension; when used for acute MI.
- Cerebral edema, cerebral herniation, seizure, new ischemic stroke; when used for ischemic stroke.

DOSE

ADULT

- **Ischemic stroke:**[1] 0.9 mg/kg (max 90 mg) over 60 minutes, with 10% of total dose as a bolus at the start of the infusion.
- **Pulmonary embolism:**[2] 100 mg over 2 hours.
- **Acute MI:** Initial dose 15 mg, then 0.75 mg/kg body weight over 30 minutes, not to exceed 50 mg, then 0.5 mg/kg over 60 minutes, not to exceed 35 mg. In SHR alteplase has been replaced with tenecteplase for this indication.

Catheter-directed thrombolysis of large vessel occlusion after angiographic placement of catheter tip:[4]

- There is no generally accepted dosing regimen, preferred method of infusion or consensus regarding the use of concomitant anticoagulation.
- Continuous infusion: starting dose of 0.25 - 1 mg/hour is recommended. Suggest 2 mg/hour x 4 hours then 0.5 mg/hour.[11] Doses of up to 10 mg/hour and 0.1 mg/kg/hour have been studied and are associated with an increased risk of bleeding.
- Intra-thrombus bolus or lacing: may decrease the duration of treatment and may be of advantage in acutely ischemic limbs. Must be weighed against the possible increased risk of hemorrhage.
  One study used 5 mg boluses at 10 minute intervals to a maximum of 15 mg followed by an infusion as above.

ELDERLY No specific changes are necessary.

PEDIATRIC/NEONATE Limited information available at this time.

RENAL/HEPATIC IMPAIRMENT ADJUSTMENTS No information available at this time.

MISCELLANEOUS

- **Correction of catheter occlusion:** alteplase 2mg (Cathflo®) is indicated for correction of catheter occlusion.
- **Intra-pleural use: Adults** - instill 10 mg (5 x 2 mg vials) into chest tube. **Pediatrics (age greater than 2 years)** – instill 2 mg into chest tube. Contact Pharmacy for further instructions (see SHR Pharmacy Department Clinical Policy and Procedure manual 25:30.08 re: Alteplase (tPA) for Intrapleural Use).
- Manufacturers have an extensive return policy. **Please return any unused alteplase to the pharmacy for credit.**
- Subcutaneous/IM administration: not applicable

References available SHR Pharmacy Department **December 2014**

ALTEPLASE intravenous- REFERENCES

1. Repchinsky C, editor. Compendium of Pharmaceuticals and Specialties. 39th ed. Ottawa: Canadian Pharmaceutical Association; 2004.

2. Wagstaff AJ, Gillis JC, Goa KL. Alteplase. A reappraisal of its pharmacology and therapeutic use in vascular disorders other than acute myocardial infarction. Drugs. 1995; 289-316.

3. Kandarpa K. Catheter-directed thrombolysis of peripheral arterial occlusions and deep vein thrombosis. Thombosis and Haemostasis. 1999; 82:987-96.

4. Semba CP, Murphy TP, Bakal CW, Calis KA, Matalon TA. Thrombolytic therapy with use of alteplase (rt-PA) in peripheral arterial occlusive disease: review of the clinical literature. J Vasc Interv Radiol. 2000; 11:149-61.

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7. Suggested Guidelines for Thrombolytic Treatment of Acute Myocardial Infarction. Committee on Thrombolysis of the B.C. Cardiac Society, Co-chairmen: Thomas Ashton, Mark Henderson, Richard Mildenberger, John Webb. 1994.

8. Swischuk JL, Fox PF, Young K, Hussain S, Smouse B, Castaneda F, et al. Transcatheter intraarterial infusion of rt-PA for acute lower limb ischemia: results and complications. J Vasc Interv Radiol. 2001; 12:423-30.

9. Data on file. Hoffmann-La Roche Ltd. Mississauga, ON. 13 Oct 1999.

10. Stanford Protocol. Catheter-directed thrombolysis using alteplase (rt-PA). Semba CP, Razavi MK, Dake MD. Interventional Radiology, Stanford University Medical Center, Stanford CA. Aug 1999.

11. Personal communication. Dr I. H. Weir. Section Head; Angiography and Interventional Radiology, Department of Medical Imaging. VIHA (South Island) Nov 8, 2002.

12. SHR Approved Clinical Health Record Form # 101779 (06/02) – "Activase® - rt – PA (Alteplase) for Acute Ischemic Stroke Patients".

13. Activase® rt-PA (Acute Ischemic Stroke) product monograph. Roche Canada. eCPS 2014. Accessed November 27, 2014.

14. Jauch EC et al. Guidelines for the Early Management of Patients with Acute Ischemic Stroke - 2013 Guidelines. *Stroke* 2013;44:870-947.

15. Cathflo® product monograph. Roche Canada. eCPS 2009. Accessed July 28, 2009.

16. DynaMed - http://web.b.ebscohost.com.cyber.usask.ca/dynamed - accessed Aug 15/14.
    - t-PA can be started within 3 - 4.5 hours of symptom onset
        - recommended within 3 hours (ACCP Grade 1A, AHA/ASA Class I, Level A)
        - suggested if 3 - 4.5 hours after symptom onset (ACCP Grade 2C, AHA/ASA Class I, Level B)

17. SHR Acute Stroke Thrombolytic (tPA) Administration Order Set 2014

Dec. 2014 – made a few changes re: contraindications on p. 1 (including referral to Appendix A of SHR Acute Care Stroke PPOs for inclusion/exclusion criteria) and added in ability of Critical Care Personnel **and assigned/certified Stroke or Neuroscience RN (RUH)** (this is the wording requested by Ruth Whelan and Ann Saulnier 6300) to administer and monitor alteplase infusions (after bolus dose administered by physician).