

Alteplase: Catheter Directed Thrombolysis for Limb Deep Vein Thrombosis

Who can administer

- Administration RESTRICTED - see [Appendix 1](#)

Important information

- Patients are **under the care of a Consultant Interventional Radiologist (IR)** who is available 24/7 to answer questions related to the catheters, drugs etc
- See also - [Attached protocols](#) from Gerard O'Sullivan, Consultant Interventional Radiologist
- **Purpose**
 - Thrombolytic agent- tissue plasminogen activator (tPa) Actilyse Alteplase (unlicensed indication)
 - To chemically dissolve thrombus by attacking the fibrin within the thrombus, thereby clearing the affected region of deep venous thrombus
- For use in thrombolysis (**acute MI**), **acute massive PE**, **acute ischaemic stroke**-see [separate monograph](#)
- For use in PE (low dose for intermediate/high risk)- unlicensed-see [separate monograph](#)

Available preparations

- Actilyse **20mg** vial (with 20ml Water for Injection provided)
 - (can use other strengths if 20mg is not available- ie use 2x 10mg instead)

Reconstitution

- Use 20ml Water for Injection provided

Infusion fluids

- Use Sodium Chloride 0.9% **only**

Â	Dilution	Concentration produced
Preferred concentration	20mg added to 480ml infusion fluid	0.04mg per ml

- **Replace bag and giving set every 24 hours** ^(ref 5)
- Occasionally an alternative dilution may be used (when a larger volume/lower concentration is required)- see under Further Information

Dose in adults

- Possible starting doses are indicated in the tables below and are based on patient weight
- The dose may vary according to the number of catheters, CLAUSS fibrinogen levels and other patient factors
- Consequently, the Interventional radiologist must document the following in the patient notes
 - Infusion concentration in mg/ml

- Dose in mg/hour of alteplase **per catheter**
- Infusion rate in mL/hour **per catheter**
- The table below indicates the rate in ml/hour when a dose of 0.01mg/kg/hour is required, using a solution containing 0.04mg/mL ^(ref 3)
- Maximum rate of administration 1mg/hour ^(ref 3)

Table 1: Alteplase: Dose in mL/hour using 20mg in 500ml (0.04mg/ml) infusion									
Weight	40kg	50kg	60kg	70kg	80kg	90kg	100kg	110kg	120kg
Equates to Alteplase dose per hour	0.4mg	0.5mg	0.6mg	0.7mg	0.8mg	0.9mg	1mg	1mg	1mg
Rate in ml/hour	10	12.5	15	17.5	20	22.5	25	25	25

These are starting doses only based on 0.01mg/kg/hour. May be adjusted according to number of catheters, CLAUSS fibrinogen levels and other patient factors

- A separate catheter is required for unfractionated heparin
- **All catheters must be labeled appropriately**
- Alteplase infusions are usually continued for 24 to 72 hours. When prolonged administration is required, close monitoring of CLAUSS fibrinogen, Hb, platelet count and Creatinine is essential - see under Monitoring below
- A dose reduction may be required for longer infusion durations

Heparin infusion

- The patient is also anti-coagulated with unfractionated heparin (patients receive heparin bolus during procedure)
- Run through side arm of 6F sheath
- An optimum target **APTT** is between 55 and 80 is suggested based on a mean average aPTT of 28 in GUH (prescribe on the green Heparin prescription)
- The mean **aPTT is specific to each laboratory**, and is reagent and analyser specific. It is also important to look at the patient's baseline APTT. Aim for APTT ratio or 2 to 3 times the patient's or laboratory baseline
- Note: in certain circumstances, patients may remain on LMWH instead of UFH after discussion with consultant haematologist

Monitoring

Blood tests

- Inform laboratory that patient is receiving alteplase (tPA) infusion as this interferes with assays
- Check FBC, PT, APTT, CLAUSS fibrinogen before starting the infusion
- Recheck above after 4 to 6 hours
- Then recheck every eight hours for first 24 hours
- If stable, need to recheck bloods every 12 hours, but this depends on the clinical situation
- Monitor for bleeding
- If Hb or CLAUSS fibrinogen falls, more frequent monitoring is required
- **Stop alteplase and heparin infusions** if major bleeding
- Consider halving alteplase rate if Fibrinogen falls precipitously and is less than 1.5g/L
- **Stop alteplase** if CLAUSS fibrinogen is less than 1g/L (continue UFH unless bleeding)

- Consider restarting alteplase at half original rate if CLAUSS fibrinogen is greater than 1g/L as long as no bleeding. Clinical judgement required

What to watch out for: see protocol below

- **Headache: Intracranial bleeding** occurs in approximately 2/1000 patients. CT scan is indicated as an emergency for any patient complaining of a new or unusual headache. Call the Interventional Radiologist if in doubt.
- **Low BP:** could signal **internal bleeding**. Approximately 2-4/100 patients. Watch Hb carefully. Appropriate fluid challenge. Call the Interventional Radiologist if in doubt.
- **Increased heart rate:** may signal early bleeding

What to expect:

- Oozing around puncture sites
- Drop in Hb by 0.5 to 1g/day

What to avoid:

- Intramuscular injections
- Arterial puncture/blood gases while on infusion
- If venous access may be an issue, consider an arterial line prior to starting heparin and tPA infusion

Recommendations:

- Strict bed rest
- Regular diet
- Good analgesia- PCA ideal

Further information

- **A lower dilution may be used, on consultant request (when a larger volume/lower concentration is required)** ^(ref 4)
- **If this is required, use the 10mg vial to prepare the infusion** (reconstitute with 10ml Water for Injection provided)

Table 2: Alteplase: Dose in mL/hour using 10mg in 1000mL (0.01mg/ml) infusion									
Weight	40kg	50kg	60kg	70kg	80kg	90kg	100kg	110kg	120kg
Rate in ml/hour	40	50	60	70	80	90	100	100	100
Equates to Alteplase dose per hour	0.4mg	0.5mg	0.6mg	0.7mg	0.8mg	0.9mg	1mg	1mg	1mg
These are starting doses only based on 0.01mg/kg/hour. May be adjusted according to number of catheters, CLAUSS fibrinogen levels and other patient factors									

Storage

Store below 25°C

References

1. Guideline prepared in consultation with Dr Ruth Gilmore (Consultant haematologist), Prof Gerry O'Sullivan (Consultant interventional radiologist) , Prof Stephen Kee (Consultant interventional radiologist) and Dr George Rahmani (Radiology Fellow)
2. Actilyse (SPC). 06/2021. Accessed at <https://www.medicines.org.uk/emc/medicine/308#gref> on 01/09/2021.
- 3: [Feasibility of low-dose infusion of alteplase](#) for unsuccessful thrombolysis with urokinase in deep venous thrombosis Gong et al, Exp Ther Med. 2019 Nov;18(5):3667-3674..
- 4: Alteplase: [stability and bioactivity after dilution in normal saline solution](#), J Vasc Interv Radiol . 2003 Jan;14(1):99-102
- 5: Stability data exists for 24 hour infusion containing 0.01mg/mL. We do not have stability data for the 0.04mg/mL infusion for a 24 hour period- however, anecdotally, this has not caused any issues in use