

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