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**Â 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 (option 1)

Dose in adults

- Administer via catheter as per consultants instructions
- Dose range is 12.5ml/hour (0.5mg/hour) to 50ml/hour (2mg/hour)
- UsualÂ rate is 25ml/hour (1mg/hour)
- In general, two catheters are inserted, one for tPA and one for unfractionated heparin
    - These are labelled appropriately
- The infusion could be infused for up to five days but generally is infused for 24 toÂ 72 hours
- A dose reduction may be required for longer infusion durations
- A separate catheter is required for unfractionated heparin
- **All catheters must beÂ labelled appropriately**
- Alteplase infusions are usually continued for 24 to 72 hours.Â 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
- Occasionally, a weight based approach may be required- see under Further Information (option 2)

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 Fibrinogin 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 signalÂ **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

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Options available

1:Option 1 - Using lower concentrationÂ

- A lower dilution may be used, on consultant request (when a larger volume/lower concentration is required) (ref 4)
- If this is required, add one 10mg vial (reconstituted with 10mL Water for Injection) to 1000mL infusion bag (0.01mg/mL)
- 0.5mg/hour = 50ml/hourÂ
- 1mg/hour = 100ml/hour
- 2mg/hour = 200ml/hour

2: Option 2 -Â Using a weight based approach

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

Storage

Store below 25^{0}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