

## ALTEPLASE thrombolysis of massive pulmonary embolism

- PRESENTATION:** Alteplase (rtPA) 50mg vials containing powder for reconstitution.  
Vials of solvent: water for injections 50ml.
- INDICATION:**
- Massive PE proven on CTPA, with persistent hypotension (SBP<90mmHg or pressure drop of ≥40 mmHg for >15 minutes with evidence of poor perfusion, despite adequate fluid resuscitation, or in patients where cardiac arrest is imminent.
  - Suspected massive PE in patients where cardiac arrest is imminent and who are too unstable for CTPA, and in whom alternative diagnoses are unlikely. Echocardiography is of value in suggesting the diagnosis in this group of patients, particularly if there is evidence of right ventricular dilatation and inter-ventricular septal displacement.
- In the event of cardiac arrest due to suspected massive PE all contra-indications are "relative" and should not defer thrombolysis where appropriate.
- ABSOLUTE CONTRA-INDICATIONS:**
- Known hypersensitivity to the active substance, gentamicin (a trace element from the manufacturing process) or to any of the excipients.
  - Active gastrointestinal/gastric ulcer bleeding or severe active bleeding from any site.
  - Severe liver disease, including hepatic failure, cirrhosis, oesophageal varices, active hepatitis and portal hypertension.
  - Any history of central nervous system damage (i.e. neoplasm, aneurysm, intracranial or spinal surgery).
  - Significant head or facial trauma or brain injury within past 3 months.
  - Structural intracranial disease (i.e. neoplasms, aneurysm, AVM).
  - Known history of ischaemic stroke or transient ischaemic attack in the preceding 6 months, except current acute ischaemic stroke within 4.5 hours.
  - Known history of or suspected intracranial/subarachnoid haemorrhage or haemorrhagic stroke.
  - Bleeding diathesis.
  - Suspected aortic dissection.
- RELATIVE CONTRA-INDICATIONS:**  
(seek specialist advice where appropriate)
- Recent bleeding (non intracranial).
  - Recent major surgery (within 3 weeks).
  - Recent invasive procedure (including non compressible vascular punctures).
  - Anticoagulation (including Vitamin K Antagonists).
  - Acute endocarditis, pericarditis, pericardial effusion.

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## Critical Care Directorate Guidelines

**RELATIVE  
CONTRA-INDICATIONS:**  
(seek specialist advice  
where appropriate)

- Pregnancy or recent delivery.
- Uncontrolled hypertension.
- Diabetic retinopathy.
- Traumatic cardiopulmonary resuscitation.
- Age > 75 years.
- Acute pancreatitis

For full list of contraindications, see current Summary of Product Characteristics. Actilyse 50 mg powder and solvent for solution for injection and infusion:

[Actilyse 50 mg powder and solvent for solution for injection and infusion - Summary of Product Characteristics \(SmPC\) - \(emc\) \(medicines.org.uk\)](#)

### ICU STANDARD INTRAVENOUS INFUSION

**DOSE AND  
ADMINISTRATION:**

*Reconstitute each 50mg vial with 50ml of solvent using a syringe. The mixture should only be agitated gently until complete dissolution. Avoid vigorous agitation in order to prevent foam formation. Withdraw 10ml to give the 10mg bolus. Withdraw 90ml to give the 90mg infusion.*

**For patients who weigh 65kg or greater:**

Give a bolus of alteplase, 10mg IV over 1-2 minutes, followed by an IV infusion of 90mg over 2 hours.

**For patients who weigh less than 65kg:**

The total dose is 1.5mg/kg. Give a bolus of 10mg IV over 1-2 minutes, followed by the remainder of the dose as an IV infusion over 2 hours.

- **If the patient was not anticoagulated prior to alteplase infusion:**  
Check the APTT ratio immediately after the alteplase infusion is complete and commence IV unfractionated heparin once the APTT ratio is less than **1.5**, at a rate of 1200units/hour (**no loading bolus dose should be given**).
- **If the patient was anticoagulated with IV unfractionated heparin prior to alteplase infusion:**  
Check the APTT ratio immediately after the alteplase infusion is complete and recommence IV unfractionated heparin once the APTT ratio is less than **1.5**, at previous rate (**no loading bolus dose should be given**).

If the APTT ratio is still greater than **1.5** after the end of the alteplase infusion, recheck it every 2 hours until conditions for commencing unfractionated heparin are met.

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- **If the patient was therapeutically anticoagulated with dalteparin prior to alteplase infusion (prophylactic dose dalteparin is not considered relevant):**  
Once the alteplase infusion is complete and 12 hours after the last dose of dalteparin (whichever is later), check APTT ratio and LMW heparin assay. If the APTT ratio is less than **1.5 AND** the LMW heparin assay is <0.5 iu/ml, commence IV unfractionated heparin at a rate of 1200 units/hour (**no loading bolus dose should be given**). Otherwise, repeat APTT ratio and LMW heparin assay every 4 hours until the conditions for commencing IV unfractionated heparin are met.

**If the patient has been therapeutically anticoagulated with an alternative agent, discuss management with on-call haematologist.**

**In all instances, check APTT 6 hours after starting IV heparin, and aim for APTT ratio of 2.0-3.0.**

**In a cardiac arrest due to likely/confirmed massive PE, treatment is the following: 50 mg intravenous bolus of alteplase, repeated after 30 minutes if no return of spontaneous circulation.**

**CONCENTRATION:** 1mg/ml

**STABILITY:** After reconstitution, solution is stable for 8 hours at 25°C.

**ADDITIONAL INFORMATION** Ensure adequate intravenous access is established and take blood for group and save.

## References

1. Summary of Product Characteristics Actilyse, last updated 06/09/2022 <https://www.medicines.org.uk/emc/product/898/smpc>
2. Anti – Thrombotic Guide. Version 4.0. Lothian University Hospitals Division. October 2018.
3. Venous Thromboembolic Disease: The management of venous thromboembolic diseases and the role of thrombophilia testing. NICE clinical guideline 144. Issued June 2012.
4. BTS Guidelines. British Thoracic Society Guidelines for the management of suspected acute pulmonary embolism. British Thoracic Society Standards of Care Committee Pulmonary Embolism Guideline Development Group. Thorax 2003;58: 470-484.
5. Thrombolytic therapy in acute pulmonary embolism and lower extremity deep vein thrombosis. [www.uptodate.com](http://www.uptodate.com). Accessed July 2015.
6. Bottiger B, Bode C et al. Efficacy and safety of thrombolytic therapy after initially unsuccessful cardiopulmonary resuscitation: a prospective clinical trial. The Lancet 2001; 357:1583-1585.
7. Resuscitation guidelines UK 2015. Adult Advanced Life Support.
8. Jaff M R et al. Management of Massive and Submassive Pulmonary Embolism, Iliofemoral Deep Vein Thrombosis and Chronic Thromboembolic Pulmonary Hypertension: A Scientific Statement from the American Heart Association. Circulation.2011; 123:1788-1830.
9. Kearon C, Akl E A, Comerota AJ et al. Antithrombotic Therapy for VTE Disease: Antithrombotic Therapy and Prevention of Thrombosis: American College of Chest Physicians Evidence Based Clinical Practice Guidelines. Chest 2012;141:e419s
10. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141:e419S. Copyright © 2012

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