ALTEPLASE **This drug must be guardrailed**

Trade Name	Actilyse® (Boehringer Ingelheim)
Class	Fibrinolytic agent Human tissue plasminogen activator produced by recombinant DNA process
Mechanism of Action	Converts plasminogen to plasmin which then degrades fibrin causing lysis of intravascular thrombi
Indications	Documented intravascular thrombo-embolism causing vascular compromise. (Primarily catheter related in neonates). Eg: Arterial occlusion or symptomatic vena caval thrombosis Documented intracardiac thrombi considered to be at high risk of embolism or symptomatic. (Primarily catheter related in neonates). Renal venous thrombosis. Central line occlusion if access is critical and alternatives not available or desirable. Early therapy (within 12 hours of onset of thrombo-embolism) is important
Contraindications	Recent haemorrhage (intracranial, pulmonary) or uncontrolled bleeding tendency Thromocytopenia of below 100 X 10^9 /L Fibrinogen below 1 gram/L
Supplied As	10 mg vials of powder for reconstitution with10 mL of sterile water Reconstitution gives a **1 mg/mL** concentration.
Dilution ***TWO dilution steps required***	**Step 1. Reconstitute the vial**

Drug	Add Diluent Water for injection	Total Volume	Concentration
10mg (dry powder)	10 mL	10 mL	1 mg / mL

Step 2. Further dilute the 1 mg/mL solution in step 1

Drug	Add Diluent 0.9% sodium chloride	Total Volume	FINAL CONCENTRATION
10mg = 10mL	10 mL	20 mL	**500 microgram/mL**

DO NOT SHAKE

Dosage ***Must chart guardrail and use Alaris pump***	**Prescribe as Alteplase 500 microgram / mL** **Loading dose:** 500 microgram/kg over 30 minutes Infuse at a rate of **2mL/kg/hr** (1000 microgram/kg/hr) **Maintenance Infusion**: 200 microgram/kg/hour if loading dose is not effective. Infuse at a rate of **0.4 ml/kg/hr = 200 microgram/kg/hr** Increase to a maximum of **0.8ml/kg/hr = 400 microgram/kg/hour** For critical catheter occlusion instil solution of 1 mg/mL at a volume equivalent to the catheter volume.
Guardrails	Concentration: 500 microgram/mL Soft Min: 100 microgram/kg/hr Hard Max: 1000 microgram/kg/hr Soft Max: 400 microgram/kg/hr Default: 200microgram/kg/hr
Interval	Continuous infusion if initial loading dose fails to result in clinical and sonographic resolution. Administer for 24 hours with repeat sonographic and clinical assessment before deciding to continue for a further 24 hours.
Administration	Intravenous infusion only for systemic thrombolysis. Local thrombolysis is possible via arterial line if arterial or umbilical arterial line associated thrombo-embolism requires treatment.
Compatible With	**Solutions:** Sterile water for reconstitution and 0.9% sodium chloride if dilution needed. (No other IV solutions have been shown to be compatible with alteplase) **Y-site compatibility:** Lidocaine, propranolol, tobramycin and vancomycin.
Incompatible With	Do not mix with any other drug in the same infusion solution or administer via the same venous line. Dobutamine, Dopamine, Heparin, Nitroglycerine, Balanced Salt Solution, Bacteriostatic water for injection (containing benzyl alcohol or parabens). Further dilution with sterilised water for injection or dextrose solutions is not recommended due to increased turbidity.
Monitoring…	Monitor fibrinogen, platelet count, APTT/PT, antithrombin III and haemoglobin before starting therapy, after the initial infusion and if on continuous infusion, 4-6 hourly. Maintain fibrinogen level of > 1.5 gram/L and platelet count of > 100 X 10^9 /L. If necessary use platelet and cryoprecipitate infusions to maintain levels…..

… Monitoring	Aim for Prothrombin time of 30-40 seconds and APTT 50-60 sec. Daily sonographic assessment of thrombus lysis. Cranial ultrasound scans before and daily while on treatment.
Stability	Use immediately after reconstitution, and discard opened vial after use. Use a new vial for drawing up each dose. Give loading dose and if maintenance dose is required then continue to use the same diluted solution until the infusion is no longer needed / the syringe runs out / or at 24 hours
Storage	Powder for reconstitution: store at room temperature, protect from light. Reconstituted solution: prepare immediately before use, however stable when refrigerated for up to 24 hours, and at room temperature for up to 8 hours.
Adverse Reactions	Excessive bleeding if thrombocytopenia and low fibrinogen present as above. Intracranial haemorrhage. Additive bleeding risk if given with other antiplatelet medication eg aspirin or anticoagulant medication eg heparin or enoxaparin
Metabolism	Relatively inactive until it binds to fibrin. Rapidly destroyed by the liver. Plasma half life ($t_{1/2}$) is 5 minutes.
Comments	There is limited data and experience of this agent in preterm babies. Infusion locally in the region of the thrombosis is desirable eg if confirmed thrombosis complicates arterial lines causing ischaemia of a limb. Early therapy (within 12 hrs of thrombo-embolism) is best. After thrombolysis, consider low dose heparin.
References	1. Neonatal Formulary 4th edition 2003 2. Micromedex ® Healthcare Series 3. Hartmann J et al Arch Dis Child Fetal Neonatal Ed 2001;85:F18-F22 4. Cochrane Library Protocol. *Thrombolytic agents for arterial and venous thromboses in neonates*. 2003. 5. Notes on Injectable drugs 7th Edition
Updated By	Glynn Russell May 2004 A Lynn, B Robertshawe, F Robertson May 2009 (new pumps) A Lynn, B Robertshawe, September 2009 A Lynn, B Robertshawe Dec 2012 (re-order profile) A Lynn, B Robertshawe, M Young Aug 2016 (change name) A Lynn, M Wallenstein, B Robertshawe, A Evison May 2020 (review & update) ALynn B Robertshawe March 2023 (Reformat dilution box, update compatibility)