MONOGRAPH

Alteplase

Scope (Staff):	Medical, Pharmacy, Nursing, Anaesthetic Technicians
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

⚠ HIGH RISK MEDICINE ⚠

QUICKLINKS			
Dosage/Dosage Adjustments	Administration	Compatibility	Monitoring

DRUG CLASS

Alteplase is a recombinant tissue plasminogen activator (rt-PA).

Alteplase binds to fibrin in a thrombus and converts plasminogen to plasmin which causes local fibrinolysis with minimal systemic effects[1]

Alteplase is a High Risk Medicine

INDICATIONS AND RESTRICTIONS

- Restoration of thrombosed IV cannulae and Central Venous Access Devices (CVADs)
- Treatment of empyema to assist with chest drainage
- Systemic lytic treatment:
  - Emergency treatment of arterial ischemic stroke under the direction of a Neurologist
  - All other systemic lytic use must be used in consultation with a Haematologist.

CONTRAINDICATIONS[1]

Note: contraindications may not be relevant for CVAD clearance – discuss with prescriber.

- Hypersensitivity to alteplase, gentamicin (used in manufacturing process) or any component of the formulation
- Significant bleeding disorder
- History or evidence of intracranial haemorrhage
- History of CNS damage
- Severe uncontrolled hypertension
- Recent (<10 days) prolonged or traumatic CPR, obstetric delivery, organ biopsy or non-compressible large venous puncture
- Major surgery or significant trauma within last 3 months
- Gastrointestinal ulcer within last 3 months
- Arterial aneurysms or malformations
- Neoplasm with bleeding risk
- Bacterial endocarditis or pericarditis
- Acute pancreatitis
- Severe hepatic disease or dysfunction
- Patient receiving other thrombolytic agents or anticoagulants with INR >1.3
- Others: Please see product information[1]

PRECAUTIONS[1]

- Risk of bleeding (e.g. related to adverse effects, concurrent illness or drugs)
- Delay any invasive procedures post alteplase infusion where possible.[8]
- Spinal injection or puncture or intramuscular injection during treatment
- Right to left cardiac shunt
- Oncology patients – altered haematology, potential for surgery
- Product contains polysorbate 80 which can cause allergic reactions
- Others: Please see product information.

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

Vials containing powder for reconstitution:

10 mg, 50 mg[1]

Prefilled syringes:

Baxter 2 mg/2 mL packed in 10 mL syringe

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

All ages:

ADMINISTRATION OF ALTEPLASE TO RESTORE CATHETER PATENCY*:*

See also Central Venous Access Device and Midline Insertion and Management guideline

Product: 2 mg/2 mL supplied in a 10 mL syringe (frozen) from pharmacy

Dose: Maximum single dose 2 mg/2 mL (up to 2 doses in 24 hours)

- **If known intraluminal volume:** instil 110% of the internal lumen volume to a maximum of 2 mg per dose; the 2 mg/2 mL can be diluted further for lumen volumes larger than 2 mL.[2]
- **If unknown intraluminal volume** : Please refer to Central Venous Access Device and Midline Insertion and Management guideline (Appendix 7) for optimum volume for PICC and surgical devices and for multiple lumens.

SYSTEMIC LYTIC TREATMENT:

Product: 50mg vials – Available in ED Main 3 Cell ADM

Must be discussed with Haematologist prior to use, (except for emergency treatment of arterial ischemic stroke under the direction of a Neurologist)

Titrate dose and duration to patient response – higher doses are associated with a higher chance of bleeding

Administer fresh frozen plasma (FFP) prior to infusion if clinically indicated.

Standard dose intraVENOUS infusion:[3]

0.5 mg/kg/hour for 6 hours (range 0.1 - 0.6 mg/kg/hour; maximum 100 mg per day)

Low dose intraVENOUS infusion:[3-5]

0.02 - 0.03 mg/kg/hour for 12 - 70 hours **maximum 2 mg/hour**

(range 0.01 - 0.06 mg/kg/hour)

Arterial Ischemic Stroke – IntraVENOUS - PACS Study Patients Only[3,9]

Total dose 0.9 mg/kg to a maximum of 90 mg

- 10% of the total dose (0.09 mg/kg) is given as an IV push over 1 minute
- the remaining 90% of the dose (0.81 mg/kg) is given as an IV infusion over 60 minutes. See administration for additional information.

Catheter-directed infusion: intraVENOUS, intraARTERIAL [4]

Note: There is no current evidence that catheter-directed infusion is more effective than standard systemic administration in infants and children, however the risk: benefit may be favourable if a catheter tip is already proximal to the thrombus or if pharmacomechanical thrombectomy is being attempted.[3]

0.025 mg/kg/hour for 12 - 24 hours - **maximum 2 mg/hour**

CHEST DRAIN*:*

Administration of alteplase into a chest drain for empyema - Please refer to the Pleural Empyema Guideline (Clinical Practice Manual)

Dose: [6, 7]

For patients >10 kg, instil alteplase 0.1 mg/kg (maximum 6 mg) in 1 mL/kg sodium chloride 0.9% (maximum volume 50 mL) and clamp the drain for 1 hour. Give once daily for 3 days only.

For patients < 10 kg, instil alteplase 0.1 mg/kg in 10 mL sodium chloride 0.9% and clamp the drain for 1 hour. Give once daily for 3 days only.

RECONSTITUTION & ADMINISTRATION

10 mg vial: 10 mL Water for Injections

50 mg vial: 50 mL Water for Injections

Water for injections should be directed via a large bore needle or transfer cannula directly into the powder. The solution should be gently agitated to avoid excess foam formation. A slight amount of foam is normal and should be allowed to dissipate before a dose is measured.[1]

Repacked reconstituted syringes are supplied frozen and should be completely thawed at room temperature before use. Rolling the syringe between hands can assist the thawing process.

For administration of alteplase to restore CVAD access please refer to the Central Venous Access Device and Midline Insertion and Management guideline.

For administration of alteplase into a chest drain for empyema please refer to the Pleural Empyema Clinical Practice Guideline.

For blocked renal dialysis catheters contact the Renal CNS via Vocera – only nurses with specific training in care and management of peritoneal or haemodialysis catheters are to access these devices.

Therapeutic thrombolysis:

Infuse via syringe pump either as neat 1 mg/1 mL solution or dilute to an appropriate volume in sodium chloride 0.9% to a minimum concentration of 0.2 mg/mL (Precipitation can occur below this dilution)[1]

Arterial Ischemic Stroke:

Dilute the appropriate strength of vial(s) as per reconstitution directions above to 1 mg/mL concentration, no further dilution is required. Prepare 2 syringes at the same time, the first syringe with 10% of the dose for IV push (0.09 mg/kg) over 1 minute, the second syringe with 90% of the dose for infusion (0.81 mg/kg) is given over 60 minutes.

- Where the IV infusion dose is > 50 mg, the dose should be split equally into 2 equal volumes in syringes of the same size

COMPATIBILITY

Compatible fluids: Sodium chloride 0.9%

Incompatible fluids: glucose solutions, precipitation will occur[1]

Compatible at Y-site: lidocaine, metoprolol

Only commonly used drugs are listed below. This is not a complete list of incompatible drugs. Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

INCOMPATIBLE drugs:

Dobutamine, dopamine, glyceryl trinitrate, heparin sodium

MONITORING

Only relevant for systemic lytic treatment:

No therapeutic drug monitoring is required for alteplase blood level however a fibrinogen level is useful to guide practice and should be above 2 g/L.

aPTT level should be interpreted with caution in the presence of low plasminogen and concurrent heparin therapy. Measurement of fibrin degradation products and D-Dimer may be useful to determine a fibrinolytic effect.

Maintaining platelet count above 100 x 10^9/L is recommended during thrombolysis.[8]

ADVERSE EFFECTS

Common: Bleeding (major and minor, many body systems can be affected), transient hypotension[1]

Rare: Neurological symptoms (may be associated with intracranial haemorrhage), reperfusion arrhythmias, symptoms of hypersensitivity, cholesterol embolism[1]

STORAGE

Vial: below 30°C

Reconstituted solution: 8 hours < 25°C, 24 hours at 2 - 8°C

Diluted or thawed solution: Use immediately[1]

INTERACTIONS

Use with other drugs known to cause bleeding will increase bleeding risk[1]

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of alteplase. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

Central Venous Access Device and Midline Insertion and Management guideline

High Risk Medicines Policy

Medication Administration Policy

Medication Preparation, Checking and Administration Procedure

Medication Safety Policy

Pleural Empyema Clinical Practice Guideline

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File Path:	W:\Safety & Quality\CAHS\CLOVERS MEDICAL Pharmacy\Procedures Protocols and Guidelines\Medication Monographs_Word\PCH.MED.Alteplase.DOCX		
Document Owner:	Chief Pharmacist		
Reviewer / Team:	Consultant – PCC, Haematologist, CVAD Nurse Practitioner, Senior Pharmacist, Haematologist, Neurologist		
Date First Issued:	September 2016	**Last Reviewed:**	August 2024 (interim update)
Amendment Dates:	*July 2020, November 2023, January 2025*	**Next Review Date:**	November 2026
Approved by:	Medication Safety Committee	**Date:**	November 2023
Endorsed by:	Drugs and Therapeutics Committee	**Date:**	December 2023
Standards Applicable:	NSQHS Standards: NSMHS: N/A Child Safe Standards: N/A		

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