Ballarat Health Services

DRUG GUIDELINE

ALTEPLASE - Restoring Patency to Central Venous Access Devices (CVADs)

HIGH RISK MEDICATION

SCOPE (Area): **FOR USE IN:** Dialysis, Day Oncology, General Wards, ICU, CCU, Emergency, GH Ballarat at Home
EXCLUSIONS: Paediatrics (seek Paediatrician advice), CVAD types not listed in Definitions section
SCOPE (Staff): Medical, Nursing and Pharmacy

Intraluminal alteplase 2mg vials are available via the Special Access Scheme (SAS), Medical Staff must complete a Category A SAS form online for all patients.

DEFINITIONS

- Central venous access device (CVAD) – a device inserted into the vascular system where the top lies within the central venous system. Types of CVAD included in this guideline:
  - Totally implantable venous access device (TIVAD): e.g. Port-a-cath®, Infusaport®, previously known as implanted venous port (IVP).
  - Peripherally inserted central venous catheter (PICC): single/double lumen, tunnelled (t-PICC) or non-tunnelled.
  - Tunnelled cuffed centrally inserted central catheter (tc-CICC): e.g. Hickman®, Broviac®.
  - Tunnelled cuffed apheresis catheters (tc-A-CICC) or tunnelled haemodialysis catheters: e.g. Permcath®, Permacath®.
- Partially occluded CVAD – CVAD may flush (easily or with some resistance) but blood return may be difficult/absent (does not yield freely). Some signs of a partial occlusion include - no blood return but flushes easily, flashback only but no frank blood return, slow blood return or increased resistance on flushing, blood remnants in catheter lumen/needless connector (see eviQ CVAD patency algorithm for more information).
- Completely occluded CVAD – no blood return and inability to inject fluids. Causes for this include:
  - Mechanical occlusion – obstruction of CVAD due to external (e.g. clamped/kinked tubing) or internal factors (e.g. CVAD tip malposition, pinch off syndrome - tubing caught between first rib and clavicle).
  - Thrombotic occlusion – obstruction of CVAD due to thrombus.
  - Chemical occlusion – obstruction of CVAD due to medication precipitation.

BRAND NAMES

Actilyse Cathflo®.
Cathflo®.
Also known as recombinant tissue plasminogen activator or rt-PA.

PHARMACOLOGY AND PHARMACOKINETICS

Alteplase binds to the fibrin in a thrombus and converts the entrapped plasminogen to plasmin. This initiates local fibrinolysis (clot breakdown). If a 2 mg dose of alteplase was inadvertently injected into the systemic circulation rather than instilled into the catheter, the concentration of circulating alteplase would be expected to return to undetectable limits within 30 to 60 minutes.

INDICATIONS

- For restoring patency to partially or completely occluded CVADs due to suspected thrombotic occlusion (following all other troubleshooting methods), by a nurse or medical officer with up to date competency in management of CVADs.

CONTRAINDICATIONS

- Hypersensitivity to alteplase or gentamicin (trace amount present).
- Active bleeding.
- High risk of haemorrhage, some examples include:
  - Bleeding disorders,
  - History of recent haemorrhagic stroke or intracranial bleeding in the previous 4 weeks,
  - Recent GI bleeding,
  - Within 48 hours of obstetric delivery, trauma or major surgery.
- Known or suspected catheter infection (localised infection may be inadvertently flushed into systemic circulation).
- Venous thrombosis around the area of the catheter.

PRECAUTIONS

- Both heparin and sodium citrate are incompatible with alteplase, therefore if either is used as a catheter lock, the locking solution must be removed and the catheter must be flushed with 0.9% sodium chloride prior to instillation of alteplase.
- Avoid excessive pressure when instilling alteplase into CVAD, excessive force can result in CVAD rupture or expulsion of clot into the circulation. When flushing implanted ports, PICCs or Tunnelled Venous Access Devices DO NOT USE SYRINGE SMALLER THAN 10 mL for flushing as these exert a higher pressure.
- Platelet count less than 75 x 10^9/L during the previous week – discuss with Consultant.

PREGNANCY AND BREASTFEEDING

Seek specialist advice before prescribing, information may update regularly. Refer to the Royal Women's Pregnancy and Breastfeeding Medicines Guide for more information.

DRUG INTERACTIONS

- Physically incompatible with heparin and sodium citrate locking solution.
- Patients receiving therapeutic anticoagulation may have increased risk of bleeding if alteplase is inadvertently systemically administered.

DOSAGE AND ADMINISTRATION

Staff attempting to restore patency to CVADs with alteplase must have completed mandatory CVAD management competency training as per CPG0059 Principles of Central Venous Access Device (CVAD) Management – In Adults. Seek advice from oncology or dialysis unit if unsure.

Full procedure for intraluminal alteplase administration available from:
All areas except Dialysis:

- eviQ Clinical Procedure- Restoring Patency to a Central Venous Access Device (CVAD) – Partial and Complete Occlusion
- Note – there are 2 different techniques depending on type of occlusion:
  - Partial occlusion: injection into catheter lumen with needleless connector (Key-Part),
  - Complete occlusion: 3-way-tap technique to create negative pressure.

Dialysis:

- Appendix 7 – Obstructed Perm Catheter, CPG0065 Haemodialysis Perm Catheter Procedures.

Prefilled frozen syringes are no longer manufactured by pharmacy, alteplase 2 mg powder vial for reconstitution (an overseas product) is now available – a Category A SAS form must be completed for each order.

Usually ordered by renal, oncology or haematology physicians and Advanced Trainees, however it can be ordered by, or under the direction of, prescribers with experience and expertise in CVADs.

Alteplase should remain in the CVAD and be subsequently withdrawn after required dwell time. Note that inadvertent systemic administration may occur but the dose involved is much less than that used in thrombolysis for other conditions.

Avoid excessive pressure when instilling alteplase into CVAD, excessive force can result in CVAD rupture or expulsion of clot into the circulation. When flushing implanted ports, PICCs or Tunneled Venous Access Devices; DO NOT USE SYRINGE SMALLER THAN 10mL for flushing as these exert a higher pressure.

This procedure should only be performed at a time and location where medical support is readily available.

1.) Assessment of CVAD patency:

Prompt and thorough assessment of CVAD patency is essential prior to the decision to administer intraluminal alteplase, see:

- Central venous access device (CVAD) patency algorithm (eviQ).
- BHS CVAD troubleshooting guide (located in appendix of CPP0059).

Exclusion criteria for unblocking CVAD (ensure none present before continuing):

- CVAD clamped or tubing kinked.
- Incorrect needle placement in the case of implanted port blockage.
- Malposition or migration of the catheter tip.
- Blockage thought to be due to drug precipitation or another non-thrombotic occlusion.
- CVAD cap malfunction or blocked, cap change should be performed prior to alteplase instillation.
- Intraluminal CVAD infection.

2.) Ordering of intraluminal alteplase:

- Complete SAS Category A form.
- Write order on Once Only Orders section of the National Standard Medication Chart (MR/700.2) as "alteplase 2 mg/2 mL to volume of CVAD" for each affected lumen.
  - In the case of a multi-lumen CVAD each lumen should be treated separately.
  - A maximum dosage of 2 mg may be administered per lumen.
- If the first dose is unsuccessful, a second dose requires a new order and SAS form.

3.) Reconstitution of intraluminal alteplase:

Intraluminal alteplase is an overseas product available as a 2 mg vial.
The total amount of alteplase in the vial is 2.2 mg, this includes a 0.2 mg overage.

- Draw up 2.2 mL of water for injection, and inject into the vial, directing the stream of water for injection onto the powder. Slight foaming is not unusual, allow vial to stand to dissipate large bubbles.
- Gently swirl the vial until completely dissolved. **Do not shake**.
- Inspect the solution: the reconstituted solution must be clear and colourless to pale yellowish.
- Draw up the required volume of reconstituted solution (up to 2 mL) in an appropriately sized syringe.
- **Final concentration of reconstituted solution: alteplase 1 mg/mL.**

4.) Check lumen volume and for locking solution:

- Both heparin and sodium citrate are incompatible with alteplase, therefore if either is used as a catheter lock, the locking solution must be removed and the catheter must be flushed with 0.9% sodium chloride prior to instillation of alteplase.
- For lumen volumes greater than 2 mL – alteplase 2 mg in 2 mL can be diluted further with sterile sodium chloride 0.9% to the volume of the catheter lumen. Check carefully the volume required for the lumen before administering.
- For patients with a weight less than 30 kg, the volume of alteplase to instill into the lumen should correspond to 110% of the lumen volume, to a maximum dose of 2 mg (2 mL).
  Practical example: for a catheter with internal volume of 1 mL, instill 1.1 mL of reconstituted alteplase solution, i.e. a dose of 1.1 mg.

5.) Abbreviated procedure for alteplase administration:

- Attempt to gently instill the appropriate volume of alteplase into the affected lumen of the CVAD as per the relevant full procedure listed in the Dosage & Administration box above.
- Label the catheter lumen with the dose, volume and time of alteplase instillation.
- After the prescribed dwell time (e.g. 30 to 60 minutes) assess catheter function by attempting to aspirate 4 to 5 mL of blood and catheter contents, this should remove the alteplase solution and any residual thrombus.
  - If catheter is functional and all alteplase appears to have been aspirated, the catheter may be flushed with 10-20 mL of sodium chloride 0.9%.
  - If catheter is not functional, leave alteplase for an additional 60 minutes, and again assess catheter function by attempting to aspirate 4 to 5 mL of blood and catheter contents.
  - If blood cannot be aspirated from the lumen after a total dwell time of 2 hours, a second dose of alteplase may be warranted (see below).

Second dose (if required):

- If the above procedure fails to unblock the CVAD, it may be repeated once at the discretion of the prescriber. Note: a second dose of alteplase requires a second order and a second SAS form.
- All attempts to remove the first dose should be made before instilling the second dose.
- Extended dwell time of up to 24 hours may be ordered by the prescriber.

If two attempts fail at unblocking the CVAD, the treating clinician must be informed for consideration of further diagnostic investigation of the CVAD or, removal of the CVAD.

General Administration Information

- **Routes of administration:** this guideline covers intraluminal injection only.

IV injection:	No
IV intermittent infusion:	No
IV continuous infusion:	No
IM injection:	No
Subcut injection:	No

- **Compatible/incompatible IV drugs/fluids:** incompatible with heparin and sodium citrate. Consult the Australian Injectable Drugs Handbook ('Yellow book') in your ward area. **Assume all unlisted drugs and IV fluids are incompatible – contact Pharmacy for further advice.**

MONITORING (INCLUDING BLOOD TESTS)

- Nil required.

NURSING PRACTICE POINTS

- Observe patient for signs of hypersensitivity reactions as listed below.
- Educate patient to report any signs of infection post procedure (e.g. fever, chills, rigors and pain, tenderness or swelling at the CVAD site).
- Watch for fever and signs of sepsis for up to 72 hours post alteplase instillation.
- All injections are to be labelled as per CPP0022 User Applied Labelling Of Injectable Medicines, Fluids and Lines.

ADVERSE EFFECTS

As the alteplase will be withdrawn after use, adverse effects are unlikely unless accidentally administered systemically.

- Sepsis (especially if localised infection flushed into systemic circulation).
- Catheter related complications.
- Fever.
- Hypersensitivity reactions:
  - Rarely - rash, urticaria, bronchospasm, angioedema, hypotension.
  - Very rarely – anaphylaxis.

DRUG PRESENTATIONS AND STORAGE

Alteplase 2 mg powder vial for reconstitution.
Store original package in refrigerator at 2 °C to 8 °C.
The reconstituted solution is stable for 24 hours at 2 °C to 8 °C and for 8 hours at 25 °C.
Protect from light.
