Ballarat Health Services

DRUG GUIDELINE

Tenecteplase in STEMI

HIGH RISK MEDICATION

SCOPE (Area): **FOR USE IN:** ED, Intensive Care Unit and Coronary Care Unit
EXCLUSIONS: Paediatrics (seek Paediatrician advice), any other area
SCOPE (Staff): Medical, Nursing and Pharmacy

DEFINITIONS
STEMI – ST elevated myocardial infarction.

BRAND NAMES
Metalyse®.

PHARMACOLOGY AND PHARMACOKINETICS
Tenecteplase is a recombinant plasminogen activator that is derived from native tissue plasminogen activator. It binds to the fibrin component of the thrombus and converts thrombus bound plasminogen to plasmin, which degrades the fibrin matrix of the thrombus. Tenecteplase is hepatically metabolised demonstrating a biphasic clearance with an initial half-life of 22 minutes, and a terminal half-life of 90-130 minutes.

INDICATIONS
- Thrombolysis of acute STEMI within 12 hours of symptom onset, where percutaneous coronary intervention is not available or not appropriate. **This document must be used in conjunction with CPP0379 Acute Myocardial Infarction: Management.**

CONTRAINDICATIONS
Absolute contraindications
- Active bleeding or bleeding diathesis (excluding menses).
- Significant closed head or facial trauma within 3 months.
- Suspected aortic dissection (including new neurological symptoms).
- Any prior intracranial haemorrhage.
- Ischaemic stroke within 3 months.
- Known structural cerebral vascular lesion (e.g. arteriovenous malformation).
- Known malignant intracranial neoplasm (primary or metastatic).

Relative contraindications
- Current use of anticoagulants. With warfarin the higher the international normalised ratio (INR), the higher the risk of bleeding.
- Non-compressible vascular puncture in the past 24 hours (eg liver biopsy, lumbar puncture).
- Recent major surgery (within 3 weeks).

- Traumatic or prolonged (more than 10 minutes) cardiopulmonary resuscitation.
- Recent (within 4 weeks) internal bleeding (e.g. gastrointestinal or urinary tract haemorrhage).
- Active peptic ulcer.
- History of chronic, severe, poorly controlled hypertension.
- Severe uncontrolled hypertension on presentation (greater than 180 mm Hg systolic or greater than 110 mm Hg diastolic).
- Ischaemic stroke greater than 3 months ago, dementia, or known intracranial abnormality not covered in absolute contraindications.
- Transient ischaemic attack in preceding 6 months
- Advanced liver disease
- Infective endocarditis
- Pregnancy (seek Specialist advice) or within 1 week postpartum.
- Serious hypersensitivity reaction to tenecteplase or gentamicin (trace amount present in vial).

PRECAUTIONS

- **Intrathecal or epidural analgesia or anaesthesia, or lumbar puncture** – risk of epidural haematoma which can cause paralysis, seek specialist advice post tenecteplase administration before performing any of these procedures.

In the following conditions, the risk of bleeding with tenecteplase may be increased and should be weighed against the anticipated benefits:

- Consider advanced age, frailty and comorbidities that influence the overall chance of survival.
- Recent trauma.
- High likelihood of left heart thrombus, e.g. mitral stenosis with atrial fibrillation.
- Acute pericarditis.
- Subacute bacterial endocarditis.
- Acute pancreatitis.
- Haemostatic defects, including those secondary to severe hepatic or renal disease.
- Severe hepatic dysfunction.
- Diabetic haemorrhagic retinopathy or other haemorrhagic ophthalmic conditions.
- Recent administration of GP IIb/IIIa inhibitors (abciximab, eptifibatide, tirofiban).

PREGNANCY AND BREASTFEEDING

Relative contraindication in pregnancy. Seek specialist advice before prescribing, information may update regularly.

DRUG INTERACTIONS

- **The following medications given in combination with tenecteplase increase the risk of bleeding. Monitor closely for signs of bleeding. This risk may continue for several days after discontinuation of agent depending on the duration of action of the interacting drug.**

Other thrombolytics	alteplase, reteplase, urokinase.
Heparin and low molecular weight heparins	dalteparin, danaparoid, enoxaparin, heparin (can be used), nadroparin.
Direct thrombin inhibitors	bivalirudin, dabigatran
Vitamin K antagonists	warfarin.

Factor Xa inhibitors	apixaban, fondaparinux, rivaroxaban.
Glycoprotein IIb/IIIa inhibitors	eptifibatide, tirofiban.
Non-steroidal anti-inflammatory agents	aspirin (can be used), diclofenac, ibuprofen, indomethacin, ketoprofen, ketorolac, mefenamic acid, naproxen, piroxicam, sulindac. Note: Selective NSAIDs (celecoxib, etoricoxib, meloxicam, parecoxib) do not directly affect clotting, but increase the risk of gastrointestinal bleeding
Selective serotonin reuptake inhibitors	citalopram, dapoxetine, escitalopram, fluoxetine, fluvoxamine, paroxetine,
Serotonin and Noradrenaline Reuptake Inhibitors	desvenlafaxine, duloxetine, milnacipran, venlafaxine
Prostacyclin analogues	epoprostenol, iloprost.
Other	anagrelide, cilostazol, clopidogrel (can be used), dipyridamole, prasugrel (can be used), protein C concentrate (human), ticagrelor, ticlopidine.
Herbal medications	Alfalfa, anise, bilberry, bladderwrack, bromelain, cat's claw, celery, chamomile, coleus, cordyceps, dong quai, evening primrose, fenugreek, feverfew, garlic, ginger, ginkgo biloba, ginseng (american), ginseng (panax), ginseng (siberian), grape seed, green tea, guggul, horse chestnuts, horseradish, licorice, prickly ash, red clover, reishi, S-adenosylmethionine, sweet clover, taurine, turmeric, white willow

DOSAGE AND ADMINISTRATION

Requires continuous ECG monitoring, life threatening reperfusion arrhythmias may occur. Resuscitation equipment must be available.
For administration only

- **in ED (resuscitation bay) or Intensive Care Unit**
- **in Coronary Care Unit on the order of a Cardiologist with the Cardiologist in attendance**

All patients require discussion with an interventional Cardiologist. This document must be used in conjunction with CPP0379 Acute Myocardial Infarction: Management.

Only to be prescribed by ED, Cardiology or Intensive Care Consultants, or Registrars under their supervision. Contraindications and Precautions above MUST be reviewed prior to prescribing, and consent obtained from patient/family where possible.

Ensure aspirin 300 mg has been administered preadmission or on admission, and that a clopidogrel 300 mg load has also been administered (only $P2Y_{12}$ inhibitor to be used in the 24 hrs post thrombolysis).

Commence a heparin infusion as soon as is practicable with dosing rounded by actual body weight as outlined in DRG0038 Heparin (and Heparin Intravenous Infusion Chart MR/700.3) adjusting to APTT, and continue for 48-72 hours post thrombolysis.

- **Loading dose heparin of approximately 60 units/kg (maximum 4000 units) IV bolus from 5000 units/5mL ampoule, followed by**
- **IV infusion approximately 12 units/kg/hr (maximum 1000 units/hr) from heparin premixed bag 25,000 units in 250 mL.**

Administer via CVC, midline or peripheral line. Two access sites are required, separate IV lines must be used for heparin and tenecteplase. Tenecteplase is incompatible with glucose.

On ED imprest tenecteplase for STEMI must be stored in its own tub with a sign stating 'STEMI - Tenecteplase ONLY' in the Thrombolytic Cupboard.

Reconstitution:

Reconstitute the vial by slowly adding all of the water for injection from the prefilled syringe supplied as outline below. Gently swirl. **Do not shake**. The concentration is 5 mg/mL.

Detailed injection reconstitution and preparation information:

1. Use aseptic technique
2. Remove the protective flip-off cap from the vial of tenecteplase and clean the rubber vial closure with an alcohol swab.
3. Remove the tip-cap from the pre-filled syringe of water for injection and immediately screw the prefilled syringe securely onto the vial adapter.
4. Penetrate the rubber vial closure in the middle with the spike of the vial adapter.
5. Add the water for injection into the tenecteplase vial by pushing the syringe plunger down slowly to avoid foaming.
6. Reconstitute by swirling gently. **Do not shake**.
7. The reconstituted preparation results in a colourless to pale yellow clear solution. Only clear solution without particles should be used.
8. Directly before administration, invert the vial with the syringe still attached, so that the syringe is below the vial.
9. Based on the patient's weight, transfer the appropriate volume of reconstituted solution (as described below) into the syringe.
10. Disconnect the syringe from the vial adapter and attach the sterile needle provided.
11. Administer as a single intravenous bolus injection over 10 seconds. It should not be administered in a line containing glucose.
12. Any unused solution should be discarded.

Dose:

Dose is weight based and often only part vials are administered, with a maximum of 50 mg (see table below). After reconstituting, the required dose is injected IV over 10 seconds. Flush the line with sodium chloride 0.9% before and after injection to prevent precipitation in the line, and to ensure complete administration of the drug.

Tenecteplase dosing calculation table
(Consider halving the dose for patients 75 years and older to minimise the risk of intracranial bleeding)

Weight	Tenecteplase dose (mg)	Volume of reconstituted tenecteplase required (mL)
Less than 60 kg	30	6
60 to 69 kg	35	7
70 to 79 kg	40	8
80 to 89 kg	45	9
90 kg or more	50	10

General Administration Information

- **Routes of administration:**

IV injection:	Yes (only method)
IV intermittent infusion:	No
IV continuous infusion:	No
IM injection:	No
Subcut injection:	No

- **Compatible/incompatible IV drugs/fluids:**
  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)

- Blood tests as outlined in CPP0379 Acute Myocardial Infarction: Management.

NURSING PRACTICE POINTS

- **Continuous cardiac and BP monitoring are mandatory during and for 24 hours after administration of tenecteplase (with patient in ED, Intensive Care Unit, Coronary Care Unit), with an ECG taken post tenecteplase.**
- **Monitor continuously for any signs of bleeding** for the first few hours after tenecteplase. Should serious bleeding (not controlled by local pressure) occur, any concomitant heparin or antiplatelet agents should be discontinued immediately and contact ED/ICU/Cardiology registrar. See DRG0030 Protamine if heparin reversal is required.
- **Perform the following observations for 4 hours:**
  - Monitor continuously for signs of internal bleeding (tachycardia, hypotension, pallor, restlessness, lower back pain, new muscle weakness/numbness in lower extremities).
  - Assess for external bleeding (e.g. IV sites, gums) hourly.
  - Urine full ward test each void or 1/24 post dose for indwelling catheter.
  - Faecal occult blood test if bowels opened.
  - Blood pressure (with manual blood pressure cuffs to avoid bruising from over-inflation from automatic blood pressure machines), HR, RR, Sa02, temp and GCS at baseline, then every 15 minutes for the first hour post tenecteplase, followed by half hourly. A change in 2 points of GCS should be reported to the ED/ICU/Cardiology Registrar immediately.
- **Strict rest in bed** is required for 24 hours.
- **Avoid** the use of rigid catheters, intramuscular injections, other invasive procedures and nonessential handling of the patient for the first few hours following tenecteplase.
- **Venepuncture** must only be undertaken as outlined in the Thrombolysis for Acute Ischaemic Stroke (CPP0012) – Post Administration of Alteplase section..
- **Arterial puncture** should be avoided during the first few hours following tenecteplase, if necessary use an upper extremity vessel that is accessible to manual compression. Pressure should be applied for at least 30 minutes, a pressure dressing applied and the puncture site checked frequently for evidence of bleeding.
- If required, supplemental oxygen must be administered via a mask as nasal prongs can cause nasal mucosa damage.
- Falls prevention.
- Use only electric shavers.
- All injections are to be labelled as per CPP0022 Labelling of Injectable Medicines and Lines.

ADVERSE EFFECTS

This is a selected list of adverse reactions, for a more comprehensive list see MIMS at https://www.mimsonline.com.au.acs.hcn.com.au//Search/Search.aspx?acc=36265.

- **Common (>1%)**
  bleeding, including bleeding at injection sites, intracerebral bleeding, internal bleeding (e.g. gastrointestinal, genitourinary), transient hypotension
- **Infrequent (0.1–1%)**
  allergic reactions including angioedema, fever, chills, rash, nausea, headache, bronchospasm, anaphylaxis, vasculitis, nephritis
- **Rare (<0.1%)**
  cholesterol embolism

DRUG PRESENTATIONS AND STORAGE

Tenecteplase 50 mg vials.
Store below 30°C. Protect vials from light.

Appendix 1: Abbreviated dosing information for tenecteplase (Metalyse®) in STEMI

Note: see Tenecteplase in STEMI full drug guideline for other information (e.g. contraindications, precautions, monitoring).

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