Health Quality & Safety Commission New Zealand
Kupu Taurangi Hauora o Aotearoa

Alert 18
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Medication alert

Thrombolysis for acute ischaemic stroke

For attention: Lead stroke physicians, stroke resource nurses and chief pharmacists

For information: Quality and risk managers, cardiology services and emergency department staff

Purpose of this alert

Both alteplase and tenecteplase can be used for stroke thrombolysis. This alert highlights action for all providers and issues where organisations have chosen to use tenecteplase. It identifies the need to differentiate clearly between the different dosages when using tenecteplase thrombolysis to treat acute ischaemic stroke or myocardial infarction. Serious errors, including fatalities, have occurred when there is confusion between thrombolytic medicine or dosages.

What you need to do

1. Have clear protocols and guidelines on stroke thrombolysis.
2. Other than in specific circumstances, such as research trials, chose only one thrombolytic agent for ischaemic stroke (either tenecteplase or alteplase).
3. Stroke thrombolysis always needs to be supervised by clinicians experienced in, and ideally credentialed for, the activity.
4. Never use abbreviations[1,‡] to describe thrombolytic medicines. Always prescribe, dispense and document these medicines using their full generic name (eg, tenecteplase).
5. Check all clinical pathways, guidelines and protocols that include thrombolysis use the full generic name of which thrombolytic to use.
6. Include the indication in the prescription, for example, 'tenecteplase (for stroke thrombolysis)'.
7. Always check the dose for the intended indication against your local guidelines before prescribing, dispensing or administering any thrombolytic.
8. Review where thrombolytics are held as imprest (stock). Remove agents from areas where they are not used or used rarely.
9. Only hold the thrombolytic appropriate to the clinical specialty. For example, in haemodialysis units, where thrombolytics are required for the treatment of occluded central venous access devices, only hold alteplase as stock.
10. Ensure a stroke kit clearly labelled for stroke thrombolysis is available in the hospital area(s) where this is carried out. The stroke kit should contain tenecteplase (Metalyse) 50 mg injection and clearly identify the dose (0.25 mg/kg, maximum 25 mg) – or alteplase (Actilyse) if this is the preferred thrombolytic in your hospital. Tenecteplase for other uses (eg, myocardial infarction) should be in kits clearly labelled for those indications, including dose. The stroke thrombolysis kit could also contain:
    - a copy of the local stroke thrombolysis guideline, or how to access this if it is electronic
    - other medicines for the management of hypertension (as per local guidelines, eg, labetalol, nitroprusside and/or hydralazine)
    - other recommended items: needles, sodium chloride 0.9% 10 mL to flush the line, stationery (eg, checklist, monitoring form, sticker if using a paper chart).
11. Establish a reliable process for managing the stroke kit, including refilling, ongoing content checks for expiry and use, and review of the contents.

‡ Never use abbreviations for medicine names. For the thrombolytics, never use abbreviations such as tpa, tPA, t-PA, rtPA, rTPA, rPA, TNK, or any other variants.

Background

The 2019 update of the Australian Stroke Guidelines[2] (endorsed by the National Stroke Network of New Zealand) recommends both tenecteplase and alteplase for the treatment of ischaemic stroke. Historically, tenecteplase was used for myocardial infarction thrombolysis and alteplase for ischaemic stroke thrombolysis. Currently, tenecteplase is an unapproved indication for stroke thrombolysis in Australia and New Zealand, however a number of DHBs are changing to tenecteplase for this indication.

Issues relating to tenecteplase

Tenecteplase is essentially a molecule of alteplase genetically engineered at three points. Compared with alteplase, it has higher fibrin affinity, greater resistance to plasminogen activator inhibitor-1 (PAI-1) and a longer half-life (allowing for a single intravenous bolus instead of one-hour infusion), with low effects on general haemostasis.[3] This translates to (a) higher efficacy in clot lysis, (b) lower haemorrhagic complications and (c) simpler and faster administration, reducing the door-to-needle time.

There is a risk of overdosing or underdosing if the incorrect dosing schedule for tenecteplase is used for a specific indication.

- For ischaemic stroke, the dose of tenecteplase (0.25 mg/kg with a maximum dose of 25 mg) is different to the dose for alteplase (0.9 mg/kg, maximum 90 mg).
- Tenecteplase is also established as the first-line intravenous thrombolytic for myocardial infarction (approved indication) and is increasingly used for pulmonary embolism (unapproved indication). **However the dosing and maximum dosage for each indication are different**.
- The syringe in the commercial tenecteplase kit available in New Zealand (Metalyse) is calibrated and marked for weight-based dosing specifically for myocardial infarction. **When providing tenecteplase for stroke thrombolysis, ignore the weight-based (kg) markings and use the volume markings (mL) only**.
- The syringe in the Metalyse pack is calibrated in 0.2 mL increments. Some local guidelines provide dosing in 0.1 mL increments, requiring estimation of the measured volume for some doses. This could result in minor errors of ±0.5 mg (approximately ±7% maximum). These differences are not clinically important.

Fatal and serious harm adverse events have been reported where tenecteplase was:

- administered but alteplase was prescribed
- prescribed and administered but the dose used was the alteplase dose because of confusion over the abbreviation tpa and use of another hospital's protocol[4]
- prescribed and administered because alteplase was unavailable in the clinical area. The dose used was the tenecteplase dose for the treatment of myocardial infarction but the administration method was for alteplase (with a 10% bolus followed by an infusion).[5]

References

1. Institute for Safe Medication Practices. 2015. FDA Advise-ERR: Avoid using the error-prone abbreviation, TPA. URL: www.ismp.org/newsletters/acutecare/showarticle.aspx?id=120 (accessed January 2020).
2. Stroke Foundation. 2019. (Australian) clinical guidelines for stroke management – Chapter 3 of 8: Acute medical and surgical management. v7.0. Melbourne, Australia: Stroke Foundation. URL: app.magicapp.org/public/guideline/QnoKGn (accessed January 2020).
3. Keyt BA, Paoni NF, Refino CJ, et al. 1994. A faster-acting and more potent form of tissue plasminogen activator. Proc Natl Acad Sci, USA. 91: 3670–4.
4. Health and Disability Commissioner Decision 11HDC01434. URL: www.hdc.org.nz/media/1744/11hdc01434.pdf.
5. Health and Disability Commissioner Decision 13HDC01676. URL: www.hdc.org.nz/media/1591/13hdc01676.pdf.

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