**Intravenous Thrombolysis using Alteplase in Acute Ischaemic Stroke – in Adults**

**Document Registration Number:** HNELHD CG 12_22

<table>
<thead>
<tr>
<th>Sites where Clinical Guideline applies</th>
<th>All HNE Health sites providing thrombolytic therapy to patients presenting with acute ischaemic stroke.</th>
</tr>
</thead>
<tbody>
<tr>
<td>This Clinical Guideline applies to:</td>
<td></td>
</tr>
<tr>
<td>1. Adults</td>
<td>Yes</td>
</tr>
<tr>
<td>2. Children up to 16 years</td>
<td>No</td>
</tr>
<tr>
<td>3. Neonates – less than 29 days</td>
<td>No</td>
</tr>
<tr>
<td>Target audience</td>
<td>All clinicians working in sites caring for stroke patients including doctors, registered and enrolled nurses and allied health.</td>
</tr>
<tr>
<td>Description</td>
<td>All adults presenting to a HNE Health thrombolysis centre following ischaemic stroke and eligible for thrombolytic therapy should be managed within the framework of the IV Thrombolysis in Stroke Pathway and Guideline.</td>
</tr>
<tr>
<td>Keywords</td>
<td>alteplase, Actilyse®, clinical pathway, fibrinolytic, guidelines, ischaemic penumbra, ischaemic stroke, thrombolysis, recombinant tissue plasminogen activator, rt-PA</td>
</tr>
<tr>
<td>Replaces Existing Guideline?</td>
<td>No</td>
</tr>
<tr>
<td>Related documents (Policies, Australian Standards, Codes of Conduct, legislation etc)</td>
<td>See page 13</td>
</tr>
<tr>
<td>Position responsible for Clinical Guideline Governance</td>
<td>Louise Jordan, Clinical Lead Stroke Stream</td>
</tr>
<tr>
<td>Guideline Contact Officer</td>
<td>Louise Jordan, Clinical Lead Stroke Stream</td>
</tr>
<tr>
<td>Contact Details</td>
<td>Ph: 49214839 Email: <a href="mailto:Louise-A.Jordan@hnehealth.nsw.gov.au">Louise-A.Jordan@hnehealth.nsw.gov.au</a></td>
</tr>
<tr>
<td>Date authorised</td>
<td>27 August 2012</td>
</tr>
<tr>
<td>Authorising body</td>
<td>Leadership Committee, Stroke Clinical Stream</td>
</tr>
<tr>
<td>This guideline contains advice on therapeutics</td>
<td>Yes Approval gained from Area Quality Use of Medicines Committee on 13 August 2012</td>
</tr>
<tr>
<td>Issue Date</td>
<td>19 September 2012</td>
</tr>
<tr>
<td>Date for review</td>
<td>19 August 2015</td>
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<tr>
<td>TRIM number</td>
<td>12/28-3-23</td>
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GUIDELINE SUMMARY

This document establishes best practice for thrombolysis centres across Hunter New England LHD. While not requiring mandatory compliance, staff must have sound reasons for not implementing standards or practices set out within the guideline, or for measuring consistent variance in practice.

Introduction

Acute stroke is a medical emergency. Appropriate initial management can reduce disability and mortality resulting from stroke. Thrombolytic therapy is of proven and substantial benefit for select patients with acute ischaemic stroke. Thrombolytic agents such as recombinant tissue plasminogen activator (rt-PA), are powerful fibrinolytic or clot busting drugs, capable of dissolving the offending clot and restoring cerebral blood flow leading to improvement in or resolution of neurologic deficits.

Situation

Intravenous thrombolysis is a time dependent treatment offering substantial net benefits for patients with potentially disabling deficits who can be started on treatment within 4.5 hours of symptom onset. The administration of thrombolytic therapy in stroke, however, is also associated with risks, including intracerebral bleeding. It is important that staff administering and managing thrombolytic therapy in stroke, understand the principals and rationale of thrombolytic therapy to ensure safe and effective patient care.

Background

Currently only two centres within HNE Health have the infrastructure and expertise to deliver thrombolysis to patients with ischaemic stroke, the John Hunter Hospital and Tamworth Rural Referral Hospital. To ensure patients receive the best available evidence based care, a thrombolysis pathway and guideline have been produced.

Assessment

This guideline should be read in conjunction with the Drug Prescribing Guideline for the use of alteplase (Actilyse®), in Acute Ischaemic Stroke. These documents outline the specific principles of assessment and management for the care of patients receiving intravenous thrombolytic therapy for acute ischaemic stroke, and support the Intravenous Thrombolysis using Alteplase for Acute Ischaemic Stroke – in Adults: Clinical Pathway

The processes outlined have been written based on the literature and consensus of expert opinion. The document reflects and incorporates feedback from the Clinical Stroke Stream, network and stream leaders and other senior clinicians who wished to help clarify and inform the pathway.

Recommendation

It is recommended that all adult patients presenting to the emergency department with ischaemic stroke within 4.5 hours of stroke onset who are potentially eligible for thrombolytic therapy, receive, as a minimum, the care outlined in the Intravenous Thrombolysis using Alteplase for Acute Ischaemic Stroke – in Adults: Guideline

OUTCOMES

1. All adult patients presenting or transferred to the John Hunter or Tamworth Emergency Department with ischaemic stroke within 4.5 hours of stroke onset who are potentially eligible for thrombolytic therapy receive the appropriate assessment, management and therapy.

2. Thrombolysis is administered in a safe and timely manner by staff who understand the risks and benefits associated with thrombolytic therapy.

3. Close observation and frequent monitoring of patients for neurologic changes, any signs or symptoms of intracranial haemorrhage, and any signs of adverse drug reactions to ensure prompt response to potential deterioration or complications.
## GLOSSARY

<table>
<thead>
<tr>
<th>Acronym or Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td><strong>aPTT</strong></td>
<td>Activated partial thromboplastin time – used to detect abnormalities in blood clotting</td>
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<tr>
<td><strong>BP</strong></td>
<td>Blood pressure</td>
</tr>
<tr>
<td><strong>CT</strong></td>
<td>Computed Tomography</td>
</tr>
<tr>
<td><strong>DBP</strong></td>
<td>Diastolic blood pressure</td>
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<tr>
<td><strong>ED</strong></td>
<td>Emergency Department</td>
</tr>
<tr>
<td><strong>Fibrinolytic drugs</strong></td>
<td>Thrombolytic drugs dissolve blood clots by activating plasminogen, which forms a cleaved product called plasmin. Plasmin is a proteolytic enzyme that is capable of breaking cross-links between fibrin molecules, which provide the structural integrity of blood clots. Because of these actions, thrombolytic drugs are also called &quot;plasminogen activators&quot; and &quot;fibrinolytic drugs.&quot;</td>
</tr>
<tr>
<td><strong>Haemorrhagic transformation</strong></td>
<td>Not long after an area of brain tissue has died, the vessels in the area lose their ability to retain blood within the vessel walls, increasing the risk that a haemorrhage will occur if blood flow were to return. This type of bleeding into dead tissue is called a hemorrhagic transformation. The risk of haemorrhagic transformation is increased in patients with large hemispheric strokes or in those who have received thrombolytic therapy.</td>
</tr>
<tr>
<td><strong>INR</strong></td>
<td>International Normalized Ratio - derived from the prothrombin time. It measures the extrinsic clotting pathway system, commonly used to measure the impact of warfarin.</td>
</tr>
<tr>
<td><strong>IV</strong></td>
<td>Intravenous</td>
</tr>
<tr>
<td><strong>JHH</strong></td>
<td>John Hunter Hospital</td>
</tr>
<tr>
<td><strong>mmHg</strong></td>
<td>Millimetres of mercury</td>
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<tr>
<td><strong>MRI</strong></td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td><strong>NIHSS</strong></td>
<td>National Institutes of Health Stroke Scale. A validated stroke specific tool used to quantify stroke severity. Measures: Level of consciousness, Visual fields, Extraocular movement, Motor function, Language, Comprehension, Sensory function, Coordination, Hemi inattention. NIHSS scores range from 0–42. Patients are given more points for greater deficiencies. A score of &quot;0&quot; indicates that the test is normal.</td>
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<tr>
<td><strong>NSF</strong></td>
<td>National Stroke Foundation</td>
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<tr>
<td><strong>PT</strong></td>
<td>Prothrombin time</td>
</tr>
<tr>
<td><strong>SAGO</strong></td>
<td>Adult General Observation Chart SMR110010</td>
</tr>
<tr>
<td><strong>SBP</strong></td>
<td>Systolic blood pressure</td>
</tr>
<tr>
<td><strong>Seizures</strong></td>
<td>Seizures can be precipitated by haemorrhagic and ischaemic strokes. When a group of neurons becomes provoked or irritated by a pathologic process or agent such as anoxia, compression, or blood, it may become hyperactive and begin discharging a high level of electrical signals. If the timing of such strong signal pulses becomes synchronised among all neurons in the group, a <em>motor</em> or <em>sensory</em> seizure can occur. If the hyperactivity spreads to adjacent or distant areas of the brain, a <em>more generalised</em> seizure can occur. People with haemorrhagic stroke or large cortical stroke are more at risk of seizures in the acute period. Delayed seizures may be experienced months or even years following the stroke. Scar tissue acts as a provocative irritant to the normal neurons</td>
</tr>
</tbody>
</table>

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*Seizures*
adjacent to it, precipitating a seizure.

<table>
<thead>
<tr>
<th>SSS</th>
<th>Scandinavian Stroke Score</th>
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</thead>
<tbody>
<tr>
<td>Thrombolysis and thrombolytic drugs</td>
<td>Thrombolytic drugs dissolve blood clots by activating plasminogen, which forms a cleaved product called plasmin. Plasmin is a proteolytic enzyme that is capable of breaking cross-links between fibrin molecules, which provide the structural integrity of blood clots. Because of these actions, thrombolytic drugs are also called &quot;plasminogen activators&quot; and &quot;fibrinolytic drugs.&quot;</td>
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<tr>
<td>rt-PA</td>
<td>recombinant tissue plasminogen activator – alteplase (Actilyse&lt;sup&gt;®&lt;/sup&gt;)</td>
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</tbody>
</table>

1.0 Guideline

1.1 Preamble
Stroke occurs when the blood supply to part of the brain is disrupted as the result of vessel occlusion or bleeding. A stroke is a medical emergency and can cause permanent neurological damage, complications and death. It is the leading cause of adult disability and the second leading cause of death in Australia<sup>2</sup>.

1.2 Ischaemic stroke and haemorrhagic stroke
There are two major types of stroke: ischaemic stroke – usually caused by a clot blocking a cerebral, carotid or vertebral artery, is the most common (85% of strokes in the Anglo Saxon population); and haemorrhagic stroke – caused by a bleed into the brain (15% of strokes)<sup>2</sup>. It is important to distinguish between ischaemic and haemorrhagic stroke (using CT or MRI), prior to treatment, as therapies for ischaemic stroke are usually contraindicated in haemorrhagic stroke and vice versa.

1.3 The ischaemic penumbra
In ischaemic stroke, the ischaemic lesion consists of two distinct areas, the infarct core and the ischaemic penumbra which surrounds the core. The ischaemic penumbra is an area of "hypoperfused brain tissue which has capacity to recover if perfusion is improved"<sup>3</sup>. Hypoperfusion results in an area of hypoxia and loss of function, but is not enough to cause permanent damage. If perfusion is restored quickly the ischaemic penumbra may be salvaged and neurological damage minimised. If perfusion is not restored, irreversible necrosis propagates from the core to include the penumbra<sup>4</sup>. The goal of thrombolytic therapy, therefore, is to dissolve the clot and restore perfusion to the ischaemic penumbra.

1.4 Thrombolytic therapy
Thrombolytic therapy is of proven and substantial benefit for select patients with acute ischaemic stroke. Thrombolytic therapy, however, is time dependent, offering substantial net benefits for patients with potentially disabling deficits who can be started on treatment within 4.5 hours of symptom onset<sup>5</sup>.

Recombinant tissue plasminogen activator (rt-PA, alteplase) combines with the plasminogen in the thrombus and converts the plasminogen to plasmin. Plasmin destroys the thrombus by initiating local fibrinolysis or clot breakdown. Alteplase is relatively selective for clot-associated fibrin. It is cleared rapidly (80% within 10 minutes of ceasing the infusion<sup>4</sup>) from circulating plasma primarily by the liver.

Common adverse effects of thrombolytic drugs include bleeding complications related to systemic fibrinogenolysis and lysis of normal haemostatic plugs. The bleeding is often noted at a catheterisation site, although gastrointestinal and cerebral hemorrhages may occur. Therefore, patients who have experienced traumatic injury or who have a history of cerebral hemorrhagic stroke are not usually administered thrombolytics<sup>7–8</sup>.

Because of the risks associated with thrombolytic therapy, thrombolysis should only be given by experienced physicians and staff, in centres with adequate infrastructure, imaging technology, and intensive care support. The two thrombolytic centres in HNE Health are John Hunter Hospital and Tamworth Rural Referral Hospital.
1.5 Thrombolytic agents

Alteplase (Actilyse®), is the only thrombolytic drug currently licensed in Australia for the treatment of acute ischaemic stroke. Other thrombolytic agents, such as tenecteplase (Metalyse®), and desmoteplase (recombinant Desmodus rotundus salivary plasminogen activator alpha 1), are still under investigation and are only available for use in the clinical trial setting.

This guideline refers specifically to the administration of alteplase (Actilyse®).
2.0 Patient and staff preparation

2.1 A Patient preparation:

It is mandatory to ensure that the patient/family has received appropriate information to provide informed consent and that patient identification, correct procedure and correct site process is completed prior to any procedure.

2.2 B Staff preparation:

It is mandatory for staff to follow relevant “Five moments of hand hygiene”, infection control, moving safely, safe manual handling and documentation practices.

2.3 C Drug administration

The decision to administer alteplase in acute ischaemic stroke should only be made by a Senior Medical Officer who is EXPERIENCED in the use of this medication in stroke.

3.0 Triage of patient with ischaemic stroke

3.1 Stroke is a medical emergency

Delays to triage, assessment, brain imaging and expert management should be avoided.

3.2 Suspected stroke in the Emergency Department

If stroke symptoms are suspected by staff in the Emergency Department, the Emergency Department Acute Stroke and TIA Pathway is to be activated and the Thrombolysis Screen attended (see Figure 1). The Stroke Physician is to be notified immediately in order to instigate urgent assessment and management.

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**THROMBOLYSIS SCREEN (F A S T + glucose)**

1. Does patient have at least one of the following symptoms?
   - \( \text{F} \)acial droop
   - \( \text{A} \)rm or leg weakness
   - \( \text{S} \)peech abnormal
   - \( \text{T} \)ime stroke symptoms started (i.e., time patient last seen well and awake)

2. Did stroke symptoms start within the last 3.5 hours?
   - \( \text{Y} \)es
   - \( \text{N} \)o
   - Unknown

3. Glucose – is BGL between 2 and 22 mmol/L?
   - \( \text{Y} \)es
   - \( \text{N} \)o

If ‘YES’ to all three questions contact Thrombolysis centre below

<table>
<thead>
<tr>
<th>In Hours</th>
<th>Out of Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>John Hunter Hospital</strong></td>
<td>Stroke fellow page 6404</td>
</tr>
<tr>
<td><strong>Tamworth Hospital</strong></td>
<td>Senior ED MO 67677435 or 67677438</td>
</tr>
</tbody>
</table>

**Name**

**Signature**

**Date/Time**

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**Figure 1** Thrombolysis Screen on page one of Emergency Department Acute Stroke and TIA Pathway
4.0 Care of the patient with suspected stroke

4.1 Assessment and management

• Ascertain the time of symptom onset (last time that the patient was seen without stroke symptoms)
• A baseline neurological examination is to be attended using the National Institutes of Health Stroke Scale (NIHSS)
  • The NIHSS quantifies level of consciousness, visual fields, motor function, language, comprehension, sensory function, coordination, hemi inattention
  • NIHSS scores range from 0–42. Patients are given more points for greater deficiencies. A score of "0" indicates that the test is normal
  • NIHSS ≥ 25 indicates very severe neurological impairment and high probability of death
  • NIHSS 5–14 indicates mild to moderately severe neurological impairment
  • NIHSS < 5 indicates mild impairment13
• Increase in NIHSS level of consciousness sub-scores (1a, 1b, 1c) by ≥ 2 points indicates early deterioration and should prompt medical review and repeat CT (Professor Chris Levi, personal communication, 09/02/2011)
• Patient monitoring should be performed in accordance with HNE Health Intravenous Thrombolysis using Alteplase for Acute Ischaemic Stroke – in Adults: Clinical Pathway (Appendix A)
• All patients should have an electrocardiograph (ECG) recording as early as possible. Attending to the ECG should not delay the transfer to computerised tomography (CT) scan.

4.2 Medical history

• A comprehensive medical history should be taken to exclude other causes of neurological symptoms, determine actual stroke onset time and screen for appropriate inclusion and exclusion criteria for thrombolysis.
• A comprehensive list of patient medications should be obtained from the patient or immediate family. If the family or patient is unable to supply, every effort should be made to contact the patient’s local medical officer or pharmacy to obtain a recent patient history.
• The patient and family members or carers must be provided with detailed explanations about the patient’s condition, tests, procedures and treatments, and potential outcomes.

4.3 IV access and blood tests

• Two intravenous access lines should be established where possible (one for thrombolysis and the other for other drugs). If CT Perfusion is to be performed, one cannula should be minimum size of 18 gauge in the cubital fossa
• Bloods should be collected for haematology, chemistry, blood glucose, coagulation and INR (if patient on warfarin)
• Arterial and venous puncture sites will require increased observation due to the potential for bleeding following administration of thrombolysis

4.4 Imaging

• Urgent head CT should be ordered as routine on all suspected acute stroke patients. The CT is predominantly used to rule out intracranial haemorrhage (ICH) or tumour
• Where appropriate, contrast CT or MRI brain imaging will be ordered by the treating neurologist to determine size and location of lesion, volume of infarct core and penumbra and suitability for thrombolysis
• Brain imaging is repeated within 24 hours of thrombolytic therapy before starting anticoagulants or antiplatelet therapy and to determine final infarct size and response to thrombolytic therapy

5.0 Inclusion and Exclusion criteria for Alteplase (Actilyse®)

Important note: These inclusion and exclusion criteria are Alteplase specific. (Refer to HNE Health Drug Prescribing Guideline: Alteplase for Acute Ischaemic Stroke in Adults).
Other fibrinolytic agents, (such as those used in the clinical trial setting) are not approved and therefore not recommended for acute stroke.
If other fibrinolytic agents are used, these inclusion and exclusion criteria do not necessarily apply.
### Inclusion Criteria
- Age ≥ 18
- Onset of acute stroke symptoms less than 4.5 hours
- Computed Tomography (CT) scan of brain to exclude haemorrhage
- Clinical diagnosis of hemispheric ischaemic stroke causing measurable neurological deficits (defined as impairment of language, motor function, cognition, and/or gaze, vision, or neglect)

**The decision to administer alteplase in acute ischaemic stroke should only be made by a Senior Medical Officer who is EXPERIENCED in the use of this medication in stroke.**

### Exclusion Criteria (Contraindications are marked with*)
- Seizure at onset of stroke
- Gentamicin hypersensitivity
- Diabetic haemorrhagic retinopathy or other ophthalmic conditions
- History of suspected intracranial haemorrhage, including subarachnoid haemorrhage
- Arterial aneurysms, arterial or venous malformations
- Neoplasms with increased risk of bleeding
- Severe hepatic (LFT 3 x upper normal range) or renal disease (GFR < 15)
- INR > 1.5
- Administration of heparin in 48 hours preceding the onset of stroke and with an elevated aPTT at presentation

**Recent (within last 10 days) prolonged or traumatic:**
- cardiopulmonary resuscitation (> 2 minutes)
- obstetric delivery
- organ biopsy
- puncture of non-compressible blood vessel (e.g., subclavian or jugular)

**In the last 30 days:**
- suspected recent myocardial infarction
- biopsy of a parenchymal organ or surgery
- trauma, with internal injuries or ulcerative wounds
- pregnancy, lactation or parturition

**In the last 3 months:**
- major surgery
- significant trauma, including cranium
- ulcerative gastrointestinal disease
- history of stroke

**In the last 6 months:**
- Active haemorrhage
- Significant bleeding disorder
- Clinical presentation suggestive of subarachnoid haemorrhage, even if initial CT is normal
- Severe symptoms suggesting total anterior circulation syndrome (coma or severe obtundation with fixed eye deviation and complete hemiplegia)
- Minor stroke symptoms or those that are rapidly improving
- Any pre-existing neurological illness resulting in a modified Rankin Score > 3
- Uncontrolled baseline hypertension: Systolic BP > 185 mmHg or Diastolic BP > 110 mmHg, despite acute treatment
- Presumed septic embolus
- Bacterial endocarditis or pericarditis
- Acute pancreatitis
- Hypoglycaemia (baseline serum glucose < 2.8 mmol/L)
- Hyperglycaemia (baseline serum glucose > 22 mmol/L)
- Thrombocytopenia (platelet count < 100 x 10^9/L)
- Other serious, advanced or terminal illness or any other condition the treating medical officer feels would impose a significant hazard to the patient if intravenous thrombolysis were initiated

### Precautions
In 2009, the American Stroke Association published a science advisory recommending expanding the window for alteplase administration in eligible patients from 3 to 4.5 hours. Unless the decision for alteplase is made on advanced imaging results (CT Perfusion or MRI), extreme caution should be used in the following circumstances for this extra 1.5 hour period:
- age older than 80
- baseline NIHSS greater than 25
- history of both previous stroke and diabetes
6.0 Prescribing and dosage

6.1 Prescribing guideline
For prescribing information, indications and contraindications, refer to HNE Health Drug Prescribing Guideline: Alteplase for Acute Ischaemic Stroke – in Adults (HNELHD DPG 12-02) at:

6.2 Dosage
Dosage is determined by patient's body weight. Refer to Alteplase (Actilyse ®) Dosing Schedule for Acute Ischaemic Stroke for dosing instructions (Appendix B).

7.0 How to give ALTEPLASE (ACTILYSE) for Stroke
- Draw up the entire vial of (Water for Injection) that comes with the alteplase (Actilyse®). If water vial broken use 50 mL of water for injection
- Add water carefully to vial of alteplase (Actilyse®), “dribble down side of vial”
- Mix gently by swirling until dissolved. DO NOT SHAKE. (The solution will foam and you will lose a percentage of the alteplase (Actilyse®) for administration
- Draw up the required dose of alteplase (Actilyse®) in two, 50 mL syringes
- The dose is to be calculated at 0.9 mg/kg body weight
- DO NOT EXCEED a 90 mg dose of alteplase (Actilyse®).
- Give 10% of the dose as a BOLUS
- Connect IV tubing to a bag of 0.9% sodium chloride and attach an empty burette. Do not prime the line or burette with 0.9% sodium chloride
- Add the remaining 90% of reconstituted alteplase solution to the empty IV burette and prime the line carefully with the alteplase solution
- The infusion should commence immediately after the bolus
- Set the pump to the amount you can see in the burette chamber. (i.e., you may have drawn up 50 mL but can only see 37 mL in the burette after priming the line)
- Following administration of alteplase from the burette, flush the line with approx. 30 mL of 0.9% sodium chloride to ensure all the dose of alteplase is administered and continue to run at the same rate. (The 30 mL of 0.9% sodium chloride must only be used to flush the solution AFTER the alteplase administration)

Precautions
- Use dedicated cannula
- Alteplase must not be mixed with other drugs, fluids or blood products and should be infused via a separate IV line and cannula
- Avoid any invasive therapies during alteplase administration (including application of TED stockings)
- FLUSH the burette port with 0.9% sodium chloride after the alteplase has been infused
- Flush the line with 30 mL of 0.9% sodium chloride

ALTEPLASE IS NOT COMPATIBLE WITH ANY OTHER DRUGS; THE LINE MUST BE FLUSHED FIRST
8.0 Alteplase (Actilyse®) Instructions for reconstitution.

1. Remove caps
2. Insert transfer cannula into sterile water (provided)
3. Keep sterile water upright
4. Invert powder vial and pierce it with transfer cannula so that the two bottles are joined together with the cannula.
5. Invert both vials so that the sterile water vials is uppermost. Allow 2 minutes for water to transfer and dissolve powder. SWIRL – but DO NOT SHAKE

Figure 2: Diagrammatic representation of instructions for reconstituting alteplase (Actilyse®)
9.0 Post thrombolysis care

9.1 The first 24 hours

**The first 24 hours are critical when alteplase is administered**

In the National Institute of Neurological Disorders (NINDS) trial, all fatal intracerebral haemorrhages following thrombolytic therapy occurred in the first 24 hours.

- The patient to nurse ratio for these patients should not exceed 2:1 for the first 24 hours.
- Close observation and frequent monitoring of patients for neurologic changes, signs or symptoms of increased intracranial pressure, or signs of adverse drug reactions are important in patient recovery.
- Observations should include frequent neurological and vital signs monitoring; bleeding assessments and precautions; continuous cardiac monitoring (refer to Intravenous Thrombolysis using Alteplase for Acute Ischaemic Stroke – in Adults: Clinical Pathway (Appendix A)
- NIHSS attended and compared with previous results whenever neurological deterioration is suspected. This will help quantify and clarify level of deterioration.
- NIHSS repeated at 24 hours to help quantify response to therapy.
- Complete Adult inpatient assessment screen and transfer of care risk assessment.

9.2 Patient deterioration

**The attending medical officer should be notified immediately if the patient develops signs of neurological deterioration**

1. An emergency CT scan will need to be obtained
2. The alteplase infusion may need to be discontinued

9.3 Signs of neurological deterioration

- Restlessness, confusion, agitation or severe headache may be the earliest sign of an increase in intracranial pressure (ICP) associated with hemorrhagic transformation or oedema in large ischaemic strokes.
- Pupillary changes (sluggish or reduced reaction to light, and/or unequal size or shape may also indicate increased ICP.
- A drop of 2 points or more on the Glasgow Coma Scale or an increase of 2 or more points in NIHSS level of consciousness sub-scores, indicates the need for a complete reassessment and evaluation.
- Nausea or vomiting.
- Cardiac monitor signs including Q waves with ST segment depression; large upright T waves which have long QT intervals; atrial fibrillation; and a variety of other dysrhythmias. Arrhythmias contributing to the stroke or resulting from the stroke, including atrial fibrillation, may be detected in this acute period. The incidence of cardiac arrhythmias will be about the same for thrombolysis patients as those who have not been treated with thrombolysis.
- Seizures may be focal or generalised and are more common in patients with haemorrhagic stroke or large cortical stroke.
- Indications of gastrointestinal, retroperitoneal or genitourinary haemorrhages must also be reported immediately.
- Observations in the yellow or red zone on the adult Standard Adult General Observation (SAGO) or ED observation charts. NSW Health observation charts have Yellow and Red Zones corresponding to early and late signs of deterioration, which require a Clinical Review (Yellow Zone), or Rapid Response (Red Zone).

9.4 Risks of thrombolytic therapy and associated controls

<table>
<thead>
<tr>
<th>Risks of thrombolytic therapy</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial bleeding</td>
<td>The patient <strong>MUST</strong> have had a non-contrast CT scan prior to administration of thrombolysis. Observe for signs of increased intracranial pressure or neurological deterioration and report to medical officer immediately. Repeat CT scan is usually required if intracerebral bleeding suspected. <strong>Antiplatelet and anticoagulant therapy should not be commenced until 24 hour brain imaging has been reviewed by medical team and intracerebral haemorrhage has been excluded.</strong></td>
</tr>
<tr>
<td>Neurological deterioration</td>
<td>The patient who has received thrombolysis is to be nursed in a high dependency area for a minimum of 24 hours post administration of drug. Close regular observations with particular attention to changes in level of</td>
</tr>
</tbody>
</table>
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Treatment interruptions and delays due to cannula difficulties: The patient is to have two intravenous cannulae inserted (where possible) prior to administration of thrombolysis.

Thrombolysis delivered at incorrect dose and rate: Medication to be prepared and administered in accordance with Australian Injectable Drugs Handbook, fifth edition July 2011 (see Appendices C, D). Medication is to be administered using an infusion pump.

Bruising from automated blood pressure device: Use manual sphygmomanometer where possible, particularly where patient has irregular heart rate.

Bleeding risk: Have a high index of suspicion for potential bleeding, particularly gastrointestinal, retroperitoneal or genitourinary haemorrhages. Report evidence of bleeding or swelling to medical officer: regularly check cannula sites, mouth, tongue, gums, joints, wounds, lacerations, vomitus, faeces and urine (test all urine for blood). Avoid safety razors. Oral mouth care should be in the form of sponges and rinsing. Hard tooth brushes should be avoided. Avoid invasive procedures where possible. Maintain bed rest for initial 24 hours to minimise risk of fall associated trauma and bleeding.

Development of DVT due to immobilisation: Attend regular leg and feet movements or passive limb exercises. DVT prophylactic medication as per neurologist.

Development of Pressure wounds due to immobilisation: Pressure area care to be given to the patient 4 hourly and as necessary.

Latex reaction: If either the staff or patient has a latex allergy, use latex free gloves and equipment.

IMPLEMENTATION PLAN

The implementation of the Intravenous Thrombolysis using Alteplase for Acute Ischaemic Stroke – in Adults: Guideline and the Intravenous Thrombolysis using Alteplase for Acute Ischaemic Stroke – in Adults: Clinical Pathway will be limited to the two sites involved in thrombolysis delivery i.e., John Hunter Hospital and Tamworth Rural Referral Hospital. Implementation of the guideline and pathway has been nominated as a Stroke Stream priority and is therefore the responsibility of the Stroke Stream Translational Team and its representatives. The process includes the development and support of site specific pathway implementation and evaluation strategies.

An online self-directed learning and assessment package is under development and will be available across HNE Health through MyLink in February 2012. The learning and assessment package will be linked to professional development learning points via Pathlore.

EVALUATION PLAN

1. Implementation, compliance and clinical effectiveness of the pathway will be evaluated at site level with the support of the SSTT.

   Web based pre- and post-implementation audit surveys will be developed by the Hunter Stroke Service using Select Survey. The audit surveys will allow monitoring and evaluation of clinical effectiveness and staff uptake of the guideline and pathway. The audit surveys will take a few moments to complete.

   Audit results are generated automatically by Select Survey and can be customised to reflect activity across at individual sites.

CONSULTATION WITH KEY STAKEHOLDERS

The Intravenous Thrombolysis using Alteplase for Acute Ischaemic Stroke – in Adults: Guideline and the Intravenous Thrombolysis using Alteplase for Acute Ischaemic Stroke – in Adults: Clinical Pathway have been examined by the following individuals and groups:

1. Clinical Stroke Stream
2. Emergency Department Clinical Stream
3. Cardiac Clinical Stream
REFERENCES


Appendices

Appendix A HNE Health Intravenous Thrombolysis using Alteplase for Acute Ischaemic Stroke – in Adults: Clinical Pathway

Appendix B Alteplase (Actilyse®) Dosage Schedule For Acute Ischaemic Stroke

**Hunter New England Local Health District**

**Facility:**

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**Intravenous Thrombolysis Using Alteplase for Acute Ischaemic Stroke – in Adults: Clinical Pathway**

In the event of patient DETERIORATION contact Dr [Name] Ph [Number] for urgent review

**Stroke onset**

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
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</table>

Attending nurse to initial appropriate box (Yes, No or NA) after attending/checking each item. Sign and date below.

**CT**

- CT attended and reviewed to exclude haemorrhage

**Thrombolytic administration**

- Baseline NIHSS stroke severity score attended
- Baseline temperature, pulse, blood pressure and respiration rate recorded
- All drug specific inclusion and exclusion criteria met (see over for alteplase inclusion and exclusion criteria)
- Patient's weight is obtained or estimated to calculate drug dose

**Manufacturer administration guidelines followed**

- Alteplase and diluent mixed gently (avoid excessive agitation during reconstitution)
- IV cannula patent and secured. Alteplase infused via separate IV line and cannula.
- 10% of total dose given as an IV push over one minute
- Remaining 90% of dose MUST be given via Infusion pump and burette over one hour
- Patient to nurse ratio not less than 2:1 in first 24 hours
- Invasive procedures avoided for first 24 hours where possible

**Intravenous Thrombolysis using Alteplase for Acute Ischaemic Stroke – in Adults: Guideline**

Baseline NIHSS stroke severity score attended

Baseline temperature, pulse, blood pressure and respiration rate recorded

All drug specific inclusion and exclusion criteria met (see over for alteplase inclusion and exclusion criteria)

Patient’s weight is obtained or estimated to calculate drug dose

Manufacturer administration guidelines followed

- Alteplase and diluent mixed gently (avoid excessive agitation during reconstitution)
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- Patient to nurse ratio not less than 2:1 in first 24 hours
- Invasive procedures avoided for first 24 hours where possible

**Thrombolysis specific interventions during initial 24 hours – in addition to acute stroke pathway**

- Booking made for 24 hour brain imaging
- MRI procedural checklist completed if applicable
- Antiplatelet agents and anticoagulants withheld until intracerebral haemorrhage has been excluded as evidenced by 24 hour brain imaging
- Metformin withheld (if applicable) for 48 hours if contrast medium used during CT brain imaging and patient has renal failure (eGFR < 60 mL/min/1.73 m²)

**Vitals**

BP, pulse, respirations every 15 min for 2 hours; 30 min for 6 hours; then hourly for 16 hours.

More frequently if patient unstable.

**BP range**

Acceptable BP range for this patient determined by MO.

**Neurological Obs**

Level of consciousness & neurological observations every 30 min for 6 hours; then hourly for 18 hours.

More frequently if patient unstable.

**Cardiac**

Continuous cardiac monitoring for 48 hours

Atrial fibrillation and or arrhythmias reported to MO

**NIHSS**

NIHSS attended when neurological change suspected

NIHSS repeated 24 hours after thrombolysis

**Intracerebral bleeding or infarct expansion**

- Evidence of neurological deterioration observed. (e.g., confusion, restlessness, vomiting, decrease in GCS or increase in NIHSS, deteriorating level of consciousness or worsening stroke symptoms, change in pupil size or reaction, seizures).
- Neurological deterioration reported to MO
- Evidence of bleeding/swelling observed
- Regularly check cannula sites, mouth, tongue, gums, joints, wounds, lacerations, vomitus, faeces, urine (test all urine for blood).
- Bleeding reported to MO

**Excretion of contrast**

IV fluids infusing to aid in excretion of imaging contrast

**Mobility**

Bed rest for 24 hours following thrombolysis

**Urinary retention**

In cases of urinary retention, IDC preferred over in/out catheter.

**Hygiene**

Use of razors (blades), hard toothbrushes avoided.

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<tr>
<th>AM Name</th>
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<tr>
<td>ND Name</td>
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</table>
Inclusion Criteria
- Age ≥ 18
- Onset of acute stroke symptoms less than 4.5 hours
- Computed Tomography (CT) scan of brain to exclude haemorrhage.
- Clinical diagnosis of hemispheric ischaemic stroke causing measurable neurological deficits (defined as impairment of language, motor function, cognition, and/or gaze, vision, or neglect).

The decision to administer alteplase in acute ischaemic stroke should only be made by a Senior Medical Officer who is EXPERIENCED in the use of this medication in stroke.

Exclusion Criteria (Contraindications are marked with*)
- Seizure at onset of stroke*
- Gentamicin hypersensitivity*
- Diabetic haemorrhagic retinopathy or other ophthalmic conditions*
- History of suspected intracranial haemorrhage, including subarachnoid haemorrhage*
- Arterial aneurysms, arterial/venous malformations*
- Neoplasm with increased risk of bleeding*
- Severe hepatic (LFT 3 x normal range) or renal disease (GFR < 15) *
- INR > 1.5
- Administration of heparin in 48 hours preceding the onset of stroke and with an elevated aPTT at presentation*

Recent (within last 10 days) prolonged or traumatic:
- cardiopulmonary resuscitation (> 2 minutes)*
- obstetric delivery*
- organ biopsy*
- puncture of non-compressible blood vessel (e.g., subclavian or jugular)*

In the last 30 days:
- suspected recent myocardial infarction
- biopsy of a parenchymal organ or surgery
- trauma, with internal injuries or ulcerative wounds
- pregnancy, lactation, or parturition

In the last 3 months:
- major surgery*
- significant trauma, including cranium*
- ulcerative gastrointestinal disease*
- history of stroke*

In the last 6 months:
- Active haemorrhage*
- Significant bleeding disorder*
- Clinical presentation suggestive of subarachnoid haemorrhage, even if initial CT is normal*
- Severe symptoms suggesting total anterior circulation syndrome (coma or severe obtundation with fixed eye deviation and complete hemiplegia).
- Minor stroke symptoms or those that are rapidly improving
- Any pre-existing neurological illness resulting in a modified Rankin Score > 3
- Uncontrolled baseline hypertension: **Systolic BP > 185 mmHg or Diastolic BP > 110 mmHg**, despite acute treatment*
- Presumed septic embolus*
- Bacterial endocarditis or pericarditis*
- Acute pancreatitis*
- Hypoglycaemia (Baseline serum glucose < 2.8 mmol/L) * Hyperglycaemia (Baseline serum glucose > 22 mmol/L)*
- Thrombocytopenia (Platelet count < 100 x 10^9/L) *
- Other serious, advanced or terminal illness or any other condition the treating medical officer feels would impose a significant hazard to the patient if intravenous thrombolysis were initiated.

Precautions
In 2009, the American Stroke Association published a science advisory recommending expanding the window for alteplase administration in eligible patients from 3 to 4.5 hours. Unless the decision for alteplase is made on advanced imaging results (CT Perfusion or MRI), extreme caution should be used in the following circumstances for this 1.5 hour period:
- age older than 80
- baseline NIHSS greater than 25
- history of both previous stroke and diabetes.
### Alteplase (Actilyse®) Dosage Schedule For Acute Ischaemic Stroke

**PATIENTS MUST BE CONTINUOUSLY MONITORED** prior to and during drug administration, and for at least 12 hours following administration.

- **Total dose:** 0.9 mg/kg. **MAXIMUM DOSE IS 90 mg.**
- 10% of total dose given as an IV push over 1–2 minutes
- Remaining 90% of dose given as an IV infusion over 60 minutes via infusion pump.

<table>
<thead>
<tr>
<th>Patient Weight (kg)</th>
<th>Total dose (mg)</th>
<th>Alteplase 1 mg/mL strength</th>
<th>Patient Weight (kg)</th>
<th>Total Dose (mg)</th>
<th>Alteplase 1 mg/mL strength</th>
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<td>10% Bolus (mL) 90% Infusion (mL)</td>
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Appendix B

Alteplase (Actilyse®) Reconstitution instructions

1. Remove caps
2. Insert transfer cannula into sterile water (provided)
3. Keep sterile water upright

4. Invert powder vial and pierce it with transfer cannula so that the two bottles are joined together with the cannula.

5. Invert both vials so that the sterile water vials is uppermost. Allow 2 minutes for water to transfer and dissolve powder. SWIRL – but DO NOT SHAKE