**UROKINASE - ADMINISTRATION OF INTRA-ARTERIAL UROKINASE IN *SPECIFIC CLINICAL AREAS**

*Administration of intra-arterial urokinase is limited to the Intensive Care Units (ICU/ICU2) and the Medical Imaging Department (MID) at St George Hospital (SGH).*

This drug information clinical business rule is **NOT** a standing order.

| Cross references (including NSW Health/ SESIAHS policy directives) | NSW Health Consent to Medical Treatment – Patient Information PD2005_406
NSW Health Correct Patient, Correct Procedure and Correct Site PD2007_079
NSW Health Medication Handling in NSW Public Health Facilities PD2013_043
SGSHHS CLIN198 Arterial Sheath Removal |
|---|---|
| 1. Accreditation requirements | This clinical business rule (CIBR) refers specifically to the administration of an **intra-arterial** urokinase infusion in ICU/ICU2 and MID at SGH.
- Medical officers (MO) and Registered Nurses (RN) administering an intra-arterial Urokinase infusion will have a thorough and clear understanding of Urokinase including indications, contraindications, adverse effects and the correct administration.
- MO and RN will safely administer an intra-arterial Urokinase infusion using the recommended procedure described in this CIBR |
| 2. Risk rating | Medium |
| 3. Description | • Urokinase is a plasmin activator, thrombolytic enzyme
• It works by converting plasminogen to plasmin, which then catalyses the breakdown of fibrin
• Urokinase can be administered intra-arterially and intravenously
• With the administration of a urokinase infusion, clearance of a thrombosis can take from 4-18 hours
• Urokinase is available in vials containing 100,000 units and 500,000 units of powder for reconstitution
• Urokinase requires a special access scheme (SAS) form to be completed by the radiologist or an MO from the admitting medical team – contact pharmacy for forms/further information. |
| 4. Indications | An intra-arterial Urokinase infusion may be indicated in the management of the following conditions:
- Acute arterial embolism, to restore circulation to occluded vessels
- Thrombosis of an arterial bypass graft, where there is a threat to the viability of limbs or vital organs |
| 5. Contraindications and/or Precautions | If any signs or symptoms of adverse reaction develop, the infusion is to be stopped immediately and medical assistance called for.
- Hypersensitivity to Urokinase
- Acute gastrointestinal bleed
- Severe uncontrolled hypertension (SBP>175; DBP>110)
- Recent (<1 month) major surgery or trauma, obstetric delivery, organ biopsy
- History of having cardiopulmonary resuscitation (CPR) attended within the last 10 days |
- Intracranial neoplasm, arteriovenous malformation or aneurysm
- History of cerebrovascular accident (CVA)
- Hepatic or renal disease
- Haemostatic disorders
- Subacute bacterial endocarditis
- Pregnancy
- Atrial fibrillation
- Any other condition in which bleeding is likely or would be difficult to manage.

**Adverse Effects – Common**

**Common**
- Bleeding, including bleeding at injection sites, intracerebral bleeding, internal bleeding (eg. Gastrointestinal, genitourinary)
- Decreased haematocrit, less than 0.37.

**Adverse Effects – Infrequent**
- Infusion reactions, including anaphylaxis, fever, chills, rigors, rash, nausea, headache, dyspnoea, bronchospasm, hypotension, tachycardia, acidosis, back pain, nausea, vomiting, vasculitis, nephritis
- Reperfusion ventricular arrhythmias, chest pain, vascular embolisation.

**Adverse Effects – Rare**
- Cholesterol embolism

6. PROCESS
In addition to the following processes, all relevant policy directives and CIBR must be adhered to when prescribing, preparing and administering an intra-arterial urokinase infusion.

6.1 Patient Preparation
- Informed, written consent is required as per NSW Health PD2005_406
- Pathology required prior to administration of urokinase - full blood count (FBC), fibrinogen, prothrombin time (PT) and activated partial thromboplastin (APTT)
- The referring MO must arrange for a bed in the Intensive Care Units, or other critical care area post procedure
- Two Agilia infusion pumps must be sent to the Medical Imaging Department with the patient.

6.2 Medical Imaging Department Responsibilities
- Radiologist must confirm correct patient, correct procedure and correct site according to NSW Health 2007_079 prior to prepping the groin for catheter insertion
- A femoral angiogram is attended, and an arterial catheter +/- an arterial sheath is inserted
- The urokinase infusion is administered via the arterial catheter
- If an arterial sheath is inserted, heparinised saline is infused via the sheath. No other medication is to be administered through the intra-arterial sheath
- The first dose of intra-arterial urokinase is loaded and commenced in the Medical Imaging Department
- Further doses are to be written up by the treating team.
6.3 Angiography Set Up
- Standard angiography kit.

**Under Trolley**
- 6 fr sheath (Short or long Check with MO)
- 2 x 500ml normal saline bags for intravenous (IV) infusion
- 2 x Agilia giving sets
- Urokinase 500 000 units
- 5 000 units/ 5 mls heparin for IV injection ampoule
- 2 x additive labels
- IV Fluid Order Chart and red pen
- 2 x water for IV injection ampoule (for mixing urokinase)
- Arterial sheath if required
- Labels for arterial sheath and arterial catheter
- UniFuse infusion catheter, with copper wire
- Visipaque – Urokinase infusion usually follows a femoral angiogram.

6.4 Preparation of Urokinase Infusion
Refer to table 1 for summary
- Urokinase dose and infusion rate must be ordered by the Radiologist on a on a separate IV Fluid Order chart (i.e. other fluids or medications must not be ordered on this chart).
- The word ‘intravenous’ on the IV fluid order must be crossed out and replaced with ‘INTRA-ARTERIAL’
- Use of intra arterial labels to be placed on the line as per MOH http://www0.health.nsw.gov.au/policies/pd/2012/pdf/PD2012_007.pdf
- This must be written in full (i.e. Not I/A), and in RED pen. A urokinase infusion is usually administered at a rate of 100,000 units/ hour...
- The dose per treatment ranges from 500,000 units up to 4 million units of urokinase.
- Urokinase is usually administered in 500ml bags of normal saline solution for infusion, with 500,000 units of urokinase added.
- Urokinase is obtained from the SGH Pharmacy
- Each 100,000 unit vial of urokinase powder is reconstituted with 2mls of sterile water for injection and each 500,000 unit vial is reconstituted with 10mls of sterile water..
- The required urokinase dose is aseptically added to 500mls of sterile normal saline solution for infusion
- An additive label is to be completed and signed by the two people who have checked the drug and calculation rate.
- The additive label must be affixed to the flask in such a way that the contents and infusate label may still be inspected. The IV should be crossed out and INTRA - ARTERIAL written on the additive label.

As a minimum, the label must include:
- Patient’s name and ward
- Name and volume of the IA fluid (if volume not on the bag)
- Name of drug and the amount (dose) added
- Date and time of preparation
- Date and time to be discarded (to be changed every 24 hours)
- Signature of person making the addition and the person checking.
6.5 Commencement of Urokinase Infusion

- The urokinase infusion is commenced in the MID
- The urokinase infusion is administered via an arterial catheter, inserted in the MID
- A bolus dose of intra-arterial urokinase may be administered by the Radiologist prior to commencing the infusion. This must be recorded on the IV fluid order chart
- The urokinase infusion must be administered via an Agilia pump. Staff must ensure that the infusion is kept running at all times
- If an arterial sheath has been used, this must also be kept patent with a separate continuous infusion, via an Agilia pump. Usually 500mls of normal saline loaded with 5000 units of heparin, is administered at 50mls/ hour via the arterial sheath. A concurrent infusion of heparin is required to prevent peri-catheter thrombosis formation, distal clot propagation and rethrombosis proximal to the catheter tip during thrombolysis infusion
- This is ordered by the Radiologist on the IV fluid order chart
- The sheath and the arterial catheter should be clearly labelled as “Sheath” and “Arterial Catheter”
- Prior to transfer to the unit, the Radiology nursing and medical staff must ensure there is sufficient volume of the urokinase infusion remaining in order to run at least another hour, to allow the unit staff time to obtain further amounts from pharmacy
- If the urokinase infusion is stopped for any reason, both the arterial catheter and arterial sheath must be kept patent using either a normal saline or a normal saline with heparin infusion, administered via an Agilia pump
- In addition, patients usually require a systemic intravenous heparin infusion. This is arranged by the admitting medical team. The SGH Heparin 60:15 protocol specifically states that it is not for use with thrombolytic therapy. However, this protocol is an exception. No bolus dose should be given, only an infusion of 1,000 units per hour whilst urokinase is in progress and adjusted to the APTT as per nomogram once urokinase finished.

6.6 Post Procedure Care

6.6.1 General

- The patient is to go to ICU/ICU2 post procedure
- Check that all infusion connections are secure and running at all times
- Review angiography report for post procedure instructions – nursing and medical entries
- Check whether patient has an arterial sheath in situ
- Patients must remain on strict bed rest. Head of bed may be elevated to 30 degrees
- Patient may eat and drink as normal. A strict fluid balance chart must be maintained.
- Patient may take their regular medications
- A check urokinase angiogram is usually attended approximately 6 hours after the infusion commences, to assess the progress of thrombolysis. Clearance of thrombosis can take from 4-18 hours. The Radiologist will arrange the check angiogram
- Central lines must not be inserted until the patient has a full recovery of normal coagulation
- NO intramuscular injections are to be administered until the patient has a full recovery of normal coagulation.

6.6.2 Observations

- Observe vascular puncture site for bleeding and swelling ¼ hourly for 2 hours post angiogram. Observations may then be decreased to hourly, if observations have been normal
- Attend a comprehensive neurovascular assessment of both the affected limb and the limb with arterial sheath in situ ½ hourly for 2 hours post angiogram. Observations may then be decreased to hourly, if observations have been normal. A neurovascular assessment involves assessing the
• Assess vital signs (blood pressure, pulse) ½ hourly for 2 hours. Observations may then be decreased to hourly, if observations have been within normal parameters. Vital signs must continue to be observed until at least one hour post cessation of the urokinase infusion. Urokinase remains effective for up to 20 minutes post cessation of infusion due to the half life of the drug. Therefore the risk of bleeding remains high during this time frame.
• Neurological observations (Glasgow Coma Scale) must be attended 4th hourly.
• Urinalysis must be attended and recorded 4th hourly. Urine must be checked for the presence of microscopic and macroscopic blood.
• An accurate stool chart must be maintained. Faeces must be checked for the presence of microscopic and macroscopic blood.

6.6.3 Pathology
• Daily and PRN fibrinogen, activated partial thromboplastin time (APTT), prothrombin time (PT) and FBC must be ordered and attended. It is the responsibility of the admitting medical team to follow up pathology results.
• However, there is no reliable correlation between the severity of clinical bleeding complications and the degree of derangement of any of the coagulation/haemostasis tests. A normal test result does not preclude bleeding. Queries should be discussed with oncall Haematologist.

6.6.4 Arterial Sheath and Arterial Catheter Removal
• At the completion of an intra-arterial Urokinase infusion, the Radiologist will usually remove the arterial catheter during the check angiogram, leaving the sheath insitu.
• If no check angiogram is attended, in the absence of an accredited RN the ICU or ICU2 MO can remove the arterial catheter. The urokinase infusion must be ceased for at least two hours prior to sheath removal.
• Systemic IV Heparin infusion should also be stopped two hours prior to sheath removal. IV Heparin should be recommenced 60 minutes after sheath removal, without a bolus heparin injection.
• The arterial sheath must be kept patent until removal using either an infusion of normal saline or normal saline with heparin. Stop heparin 90 minutes prior to sheath removal and recommence heparin infusion 60 minutes after removal. Do not administer a bolus.
• The arterial sheath must be removed by an accredited RN or medical officer, such as the ICU/ICU2 Resident. as per CLIN198 Arterial Sheath Removal.

• 6.6.5 Troubleshooting
• If arterial catheter or sheath becomes dislodged or pulled out 5cm or more, patient **must immediately** be reviewed by the admitting medical team.
• The patient may need to return to angiography for replacement/ repositioning of the catheter/sheath.
• If swelling or bleeding occurs at the insertion site, apply pressure just above the catheter entry point for at least 25 minutes, and seek medical advice immediately.
6.7 Nursing Care Post Removal of Arterial Sheath

6.7.1 Options for achieving haemostasis:

a) Manual pressure
   • Pressure over the arterial puncture site with gloved fingers. Sufficient pressure to be able to feel the underlying femoral pulse, not so much pressure that the pulse is obliterated. Typically takes 10-15 minutes to achieve haemostasis.

b) Arterial Clamp Device
   Follow manufacturer’s instructions for deployment.

6.7.2 Observations

a) Neurovascular observations
   • 15 minutely for 2 hours
   • 30 minutely for 2 hours
   • hourly for 8 hours
   • 4th hourly for 24 hours, after 24 hours - every shift until discharged

b) Blood pressure/ heart rate / respiratory rate / $\text{SpO}_2$
   • hourly for 4 hours
   • After 4 hours - as clinically indicated

| Table 1: Summary table for administration of intra-arterial urokinase and heparin |
|---------------------------------|---------------------------------|---------------------------------|
| **INTRA-ARTERIAL** | **INTRAVENTOUS** | **INTRA-ARTERIAL** | **INTRAVENTOUS** |
| Intra-arterial heparin/saline via arterial sheath | Intra-arterial Urokinase via Blue Catheter | Intravenous Systemic heparin via venous access device |
| Usual infusion | 5000 units heparin in 500mls normal saline | 500,000 units urokinase in 500mls normal saline | 5000 units heparin in 100mls normal saline |
| Usual dose/rate | 50mls/hr = 500units/hour | 100,000 units/hour = 100mls/hour | As per protocol |
| Responsibility for prescribing | Radiologist | Radiologist | Admitting medical team |
| Responsibility for ceasing | Radiologist or consultant/registrar from admitting medical team | Radiologist or consultant/registrar from admitting medical team | Consultant/registrar from admitting medical team |
| Removal of blue catheter | Radiologist, RMO or accredited RN | | |
| Removal or arterial sheath | Arterial sheath must be kept patent with infusion until removal by accredited RN/RMO (preferably during business hours) | | Stop systemic IV heparin 2 hours prior to sheath removal. Recomence 1 hour after sheath removal without a bolus. |
| Responsibility of SAS form for urokinase | Radiologist or admitting medical team by contacting pharmacy. | | |
7. **Keywords** | Urokinase, intra-arterial
---|---
8. **Functional Group** | Intensive Care St George Hospital  
Medical Imaging  
Surgery (Vascular)
---|---
9. **External References** | Not applicable
---|---
8. **Consumer Advisor Group (CAG) approval of patient information brochure (or related material)** | This CIBR will be implemented through local inservice programs and communication at relevant department committee meetings and evaluated on a case by case basis.  
Monitoring IIMS – Clinical performance incidents / Medication
---|---
9. **Implementation and Evaluation plan Including education, training, clinical notes audit, knowledge evaluation audit etc** | Q1: What is the immediate response if the patient shows signs of adverse reaction to urokinase?  
A: Stop the infusion immediately and call for medical assistance.

Q2: Does urokinase use require completion of a Special Access Scheme (SAS form)?  
A: Yes, the SAS form must be completed by the radiologist or an MO from the admitting medical team – contact pharmacy for forms/further information

Q3: What action is required if the arterial sheath or catheter becomes dislodged?  
If arterial catheter or sheath becomes dislodged or pulled out 5cm or more, the patient must immediately be reviewed by a MO from the admitting medical team.
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10. **Compliance evaluation** | **Nursing Co-director Critical Care**  
**Medical Director Critical Care**  
**Director of Medical Imaging**  
**Nursing Unit Manager – Medical Imaging**
---|---
11. **Who is responsible**
Approval For Urokinase - Administration Of Intra-Arterial Urokinase In *Specific Clinical Areas

| *Specialty/Department Committee | Committee title: Drug and Therapeutics Committee  
|                               | Chairperson name/position  A/Prof Winston Liauw |
| *Nursing/Midwifery Co-Director | Julie Cosgrove |
| *Medical Director approval     | Dr Kush Deshpande |
| *Drug and Therapeutics Committee (SGH) | A/Prof Winston Liauw |
| Executive Sponsor              | Dr Martin Mackertich, Director of Clinical Services |
| Contributors to CIBR development | Stuart Ford, NUM Medical Imaging, Dr Kevin Hanel, Vascular Surgery, Dr Theresa Jacques, Director ICU, Sarah Jones CNC ICU |

Revision and approval history

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