Urokinase

Information for use with tunnelled central venous catheters used for haemodialysis
GENERAL OVERVIEW AND BACKGROUND

Dialysis patients with tunnelled central venous catheters (CVC) used as access for haemodialysis need to achieve blood flow rates > 250mls/min in order to optimise dialysis adequacy. Failure to achieve an optimal blood flow rate in the first weeks after placement may be due to mechanical problems resulting in complete or intermittent loss of blood flow. These include:

- Incorrect dry weight assessment
- Catheter malposition
- Catheter migration
- Catheter kinking

It is important to establish that none of the above is responsible for the CVC flow inadequacy before any attempt is made at thrombolysis.

More commonly, loss of blood flow pre dialysis or gradual and intermittent loss of blood flow during dialysis with increasing positive venous pressure and negative arterial pressure may be caused by the build up of fibrin clots or fibrin sheaths around the internal and external aspects of the catheter causing occlusion. Clots may be intraluminal, or extraluminal (fibrin sheath).

Urokinase is a thrombolytic licensed to treat CVC occluded by fibrin clots/sheaths. It may be used as a:

1. Catheter push lock technique – useful for intraluminal clots.
2. Infusion – off dialysis – effective for fibrin sheaths.

Effective thrombolysis is preferable to line stripping or line replacement as both these options are costly and present a significant risk to the patient.

Urokinase converts plasminogen to plasmin, which degrades fibrin resulting in clot lysis. It has a half life of 20 mins and must be in direct contact with the fibrin clot to be effective. The dwell lock technique is considerably less effective than a push lock therefore patients treated with urokinase should receive standard line locks e.g. citralock. Interdialytic urokinase locks also have limited efficacy in view of the short half life and limited contact of the urokinase with the clot and should not be used. Overnight urokinase 25,000 unit infusions are also not recommended due to limited efficacy - less drug over longer period of time.
“A dysfunctional catheter usually is easier to salvage than a non-functional catheter, thereby preventing complications of a new placement. Early treatment also reduces the likelihood and minimises the extent of inadequacy of dialysis caused by catheter dysfunction. Increasing focus should be placed on prevention and control of growth of the fibrin sheath through periodic high dose lytic infusion triggered by a progressive decrease in achievable BFR”. (NKF-KDOQI Guidelines for vascular access 2006).

GUIDELINES FOR APPROPRIATE USE OF PROTOCOL

This guideline applies to the following:

1. Permanent tunnelled CVC used for haemodialysis. Temporary CVC may be more suitable for guidewire exchange.

2. CVC compromised by clot or fibrin formation. Other possible causes of insufficient blood flow such as hypovolaemia, line kinking or malposition should be excluded first (see line management algorithm).

Mode of prescription:

Unless the drug is contraindicated, patients who dialyse in a Satellite Dialysis Unit through a CVC should have urokinase push-lock and infusion prescribed on their drug chart by the doctor first receiving the patient in the dialysis unit (see page 3). This is to enable administration of urokinase according to verbal order from the assessing doctor where they are not present. The prescription should be written as detailed on page 3.

Before any urokinase is given, the patient should be fully assessed by a senior doctor (SpR level and above) in order to exclude other causes of line occlusion. This may have to be done by telephone. After this assessment, the doctor will then authorise administration of urokinase according to the pre-written prescription. The nurse receiving the verbal order must add the authorising doctor’s name to the chart.
## OXYGEN

**Circle Saturation target**
- 88-92%
- 94-96%
- Other

**Special Instructions**
Sign box to indicate that specified target saturations have been checked and achieved. Adjust flow rate and/or delivery device as necessary. Refer to Local Policy for further details.

### MEDICINE (Approved Name)

<table>
<thead>
<tr>
<th>DATE</th>
<th>ROUTE</th>
<th>SPECIFY TIME IF REQUIRED</th>
<th>DOSE</th>
<th>SIGN</th>
<th>DOSE CHANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**PRESCRIBER’S SIGNATURE**

**DATE**

**PHARMACIST**

**SUPPLY**

**RE-WRITE CHART**

**To be reviewed by GP**

**Continuous**

**Limited Duration**

**Other Instructions**

---

### UROKINASE

**Medicine (Approved Name)**

**Special Instructions**

**PRESCRIBER’S SIGNATURE**

**DATE**

**PHARMACIST**

**SUPPLY**

**RE-WRITE CHART**

**To be reviewed by GP**

**Continuous**

**Limited Duration**

**Other Instructions**

**TO ONLY BE GIVEN ONCE AUTHORISED BY A SENIOR DOCTOR - SEE PROTOCOL**

**MAXIMUM 3 DOSES - THEN REVIEW BY DR**

**DATE, TIME, NURSE’S SIG, DR’S NAME**

---

### UROKINASE

**Medicine (Approved Name)**

**Special Instructions**

**PRESCRIBER’S SIGNATURE**

**DATE**

**PHARMACIST**

**SUPPLY**

**RE-WRITE CHART**

**To be reviewed by GP**

**Continuous**

**Limited Duration**

**Other Instructions**

**TO ONLY BE GIVEN ONCE AUTHORISED BY A SENIOR DOCTOR - SEE PROTOCOL**

**DATE, TIME, NURSE’S SIG, DR’S NAME**

---

### NON-ADMINISTRATION OF MEDICINES

When a patient does not receive a prescribed dose, the nurse should enter one of the code numbers given below in the administration box, to explain the reason for non-administration. Please attempt to obtain any unavailable medicines.

- X. Prescriber’s request
- 3. Patient unable to receive medicines/or no access
- 5. Medicine unavailable
- 2. Patient not on ward
- 4. Patient refused medicine
- 6. See Notes

Prescriber’s Signature authorising TTO  Bleep No.  Date  Pharmacy Date
Each prescription of urokinase containing push lock (3 doses) and infusion (1 dose) will be valid for a 4 week period from the date of when first dose is given to the patient. The prescription and contraindications will be reviewed by the unit doctor at the monthly blood meeting. The prescription will need to be rewritten 4 weeks after patient receive 1st dose of urokinase.

IMPORTANT NOTE

This protocol is designed as a guide for each satellite dialysis unit. Theoretically, the 3 push lock doses could be given in the same session as could the infusion. However, you should discuss each individual patient case with the authorising doctor.

Indications for urokinase lock/infusion

- Repeated saline flushes do not establish sufficient blood flow to commence HD
- Insufficient blood flow to maintain HD (less than 250ml/min) with increasing negative arterial pressure and / or increasing positive venous pressure for two consecutive dialysis sessions
- Progressive reduction in URR

Contraindications to urokinase treatment include the following:

- Active bleeding
- Severe trauma
- Major surgery within the past 10 days
- Malignant hypertension
- Stroke/TIA within the last 3 months
- Recent head injury
- Pregnancy/ Immediate post partum/ breastfeeding
- Hypersensitivity to urokinase or excipients
- Hepatic failure

Special precautions for use

- If bleeding occurs, urokinase must be stopped immediately
- Caution should be used in patients at risk of GI bleed

Incompatibilities

- Urokinase is not compatible with glucose solutions therefore it must be diluted in sodium chloride 0.9%
PATIENT INFORMATION FOR UROKINASE INFUSION AND UROKINASE PUSH LOCK

The staff looking after you have been having some problems getting the best flow rates from the line you use for dialysis. This may be caused by a small clot around the end of your line. The most effective way to dissolve this clot is by administering a solution called UROKINASE through your line. The staff looking after you will ask you a few questions to ensure that this treatment is safe for you to have.

The urokinase can be administered by what is called a ‘push lock’. This is done by attaching a syringe with urokinase solution to the end of each lumen of your line and injecting a small amount into your line in 10 minute intervals.

Sometimes this is enough to dissolve the clot. If the push lock is unsuccessful we may need to give a bigger dose and infuse it through your line over 90 minutes. In this case you may have a shortened dialysis session, i.e. 2 hours. The staff looking after you will have established before hand that this is safe for you.

Like all medicines, there can be side effects but not everybody will get them. Please inform the staff immediately if you notice

• Any bleeding
• Any sign of allergic reaction, such as difficulty breathing, swelling of the face, lips or throat, skin rash or hives (raised, itchy rash).

If you have any questions you want to ask please feel free to talk to the dialysis staff.
CVC MANAGEMENT ALGORITHM

Mechanical problems - check line for any kinks or clamp on. Patient volume depleted - to infuse with prescribed colloid/0.9% normal saline appropriate to patient condition. Be wary of fluid overload. Check U & E urgently and inform SpR on call at UHW

None of the above or No changes from intervention

Force push both lumens with 10 mL of sodium chloride 0.9% over 5 secs.

Line not working - unable to withdraw or flush lumens Bloodpump speed 150 ml/min or less

Standard line lock e.g. citralock

Successful dialysis i.e. Dialysis pump speed >250 ml/min for duration of treatment

Urokinase push lock

See protocol 1

If line requires 3 push lock procedures within a 4 week period then proceed to infusion (as below) (Please see overleaf for maximum dosage)

No effect

90 minute Urokinase infusion (Off dialysis)

Prepared per prescription

See protocol 2 If this is
A) Ineffective within one month or
B) used on 3 occasions proceed to step below

No effect

No effect or Previously tried

Rate patient to SpR on 8D
Urgent review of current and past access with Consultant Nephrologist in charge and surgery; radiology
ACCESS MEETING Personal discussion Consultant to Consultant outside of arranged meetings with surgery and/or radiology teams.

Consider line change
Alternative access
Radiological intervention for complex / precious access
PROTOCOL ONE (PUSH LOCK)

The volumes involved in the push lock depend on the lumen size of the patient’s CVC. Please refer to the table below to identify the patient’s line and hence the volumes required to undertake the push lock.

1. Identify the lumen volume of the patients CVC
2. Reconstitute a vial of Urokinase 25000 units with volume A of sodium chloride 0.9%
3. Draw up solution into two syringes, one containing volume B for the venous line and one with volume C for the arterial lumen.
4. Inject the solution into each lumen of the line; volume D in the venous lumen and volume E in the arterial lumen.
5. Wait 10 minutes
6. Inject a further 0.5ml of solution into each lumen of the line
7. Wait 10 minutes
8. Inject a further 0.5ml of solution into each lumen of the line
9. Wait 10 minutes
10. Remove the lumen volume of urokinase solution

<table>
<thead>
<tr>
<th>Venous lumen volume</th>
<th>Arterial lumen volume</th>
<th>Reconstitution lumen volume (A)</th>
<th>Volume for venous syringe (B)</th>
<th>Volume for arterial syringe (C)</th>
<th>Volume for first venous push (D)</th>
<th>Volume for first arterial push (E)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2ml</td>
<td>2.1ml</td>
<td>7.3ml</td>
<td>3.7ml</td>
<td>3.6ml</td>
<td>2.7ml</td>
<td>2.6ml</td>
</tr>
<tr>
<td>1.8ml</td>
<td>1.7ml</td>
<td>6.5ml</td>
<td>3.3ml</td>
<td>3.2ml</td>
<td>2.3ml</td>
<td>2.2ml</td>
</tr>
<tr>
<td>2.3ml</td>
<td>2.3ml</td>
<td>7.6ml</td>
<td>3.8ml</td>
<td>3.8ml</td>
<td>2.8ml</td>
<td>2.8ml</td>
</tr>
<tr>
<td>1.8ml</td>
<td>2.0ml</td>
<td>6.8ml</td>
<td>3.3ml</td>
<td>3.5ml</td>
<td>2.3ml</td>
<td>2.5ml</td>
</tr>
<tr>
<td>2.0ml</td>
<td>1.9ml</td>
<td>6.9ml</td>
<td>3.5ml</td>
<td>3.4ml</td>
<td>2.5ml</td>
<td>2.4ml</td>
</tr>
<tr>
<td>2.3ml</td>
<td>2.2ml</td>
<td>7.5ml</td>
<td>3.8ml</td>
<td>3.7ml</td>
<td>2.8ml</td>
<td>2.7ml</td>
</tr>
<tr>
<td>2.8ml</td>
<td>2.7ml</td>
<td>8.5ml</td>
<td>4.3ml</td>
<td>4.2ml</td>
<td>3.3ml</td>
<td>3.4ml</td>
</tr>
</tbody>
</table>

Note
Urokinase push lock may be administered 3 times within a 4 week period. Theoretically the 3 push lock doses could be given in the same session, however you should discuss each individual patient case with the doctor authorising the prescription.

Your local policy will apply for the infection control aspects of CVC handling.
PROTOCOL TWO (OFF DIALYSIS INFUSION)

1. Reconstitute 2 vials of 100,000 units of urokinase using 5mls of sodium chloride per vial of urokinase.

2. Dilute the prescribed amount of urokinase into two 100ml bags of sodium chloride 0.9%, one for each lumen.

3. Attach one 100ml bag to each lumen of the catheter and infuse, using an infusion pump, over 90 minutes.

Note
If this is ineffective within 1 month or used for 3 occasions you should proceed to the next step on algorithm.

Your local policy will apply for the infection control aspects of CVC handling.
## Contra-indications Urokinase checklist

<table>
<thead>
<tr>
<th>Has the patient had any of the below: (PLEASE COMPLETE)</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Active bleeding?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Severe trauma?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Major surgery within past 10 days?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Malignant hypertension (rapid onset of severe hypertension)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Today's blood pressure is _____________________________</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Stroke/TIA within the last 3 months?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Recent head injury?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Pregnancy/Immediate post partum/breastfeeding?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Hypersensitivity to urokinase or excipients?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Hepatic failure?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Discussed with doctor:** ____________________________ **Bleep no.** __________

**Date:** __________ **Time:** __________

**Nurse signature:** __________________________________________

**and designation:** __________________________________________

Once form is completed fax to 029 2074 4875

File this copy in the patients notes
## Transfer letter for problematic permcath flows

### Addressograph
- Have next of kin been informed: Y  N
- Next of kin Tel no:
- Dialysis unit:
- Dialysis days: M/W/F  T/TH/S  Hours per session

### Blood results
- Please tick blood samples taken: U&E  □  FBC  □  INR  □
- Is patient on warfarin?
- If yes what dose _______ and why ___________________________________________

### Permcath history (if known)
- Date inserted: ____________  Right: ____________  Left: ____________

### History of recent flow problem
- Is this a new problem? Y  N  Is it an ongoing problem? Y  N
- Please explain: __________________________________________________________
- How long has patient dialysed today? ______________________________________

### Recent Urokinase push lock:
- Date: ____________  Dose: ____________  Outcome: _____________________________
- Date: ____________  Dose: ____________  Outcome: _____________________________
- Date: ____________  Dose: ____________  Outcome: _____________________________

### Recent/last urokinase infusion:
- Date: ____________  Dose: ____________  Outcome: _____________________________

### Summary from onset of problem: __________________________________________

- Signature (print name): __________________________  Grade: ______
- Date: __________________________
<table>
<thead>
<tr>
<th>Date</th>
<th>Push Lock</th>
<th>Infusion</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Please complete after each urokinase intervention

Please keep with dialysis chart.
Cardiff and Vale LHB is a teaching hospital and at times medical and nursing staff may be in attendance at the time of your consultation. If you want to opt out of this please inform your doctor.

Devised by Sister Elaine Saunders & Sister Lynn Davies, with much appreciated help from Dr Kieron Donovan & Dr Ruth Benzimra Renal pharmacists Helen Thomas & Robert Bradley.
Effective date: August 2014
Review date: July 2015
Issue 1
Approved by Dialysis Access team.