Thrombolytics (Reteplase, Tenecteplase) – HEP
Rpa/Tnk and Adjunctive Heparin

<table>
<thead>
<tr>
<th>PRESENTATION</th>
<th>INDICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vials of reteplase</strong> 10 units for reconstitution with 10ml water for injection.</td>
<td>Acute myocardial infarction within six hours of symptom onset.</td>
</tr>
<tr>
<td><strong>Vials of tenecteplase</strong> 10,000 units for reconstitution with 10ml water for injection, or 8,000 units for reconstitution with 8ml water for injection.</td>
<td>Ensure patient fulfills the criteria for drug administration following the model checklist (below). Variation of these criteria is justifiable at local level with agreement of appropriate key stakeholders (e.g. cardiac network).</td>
</tr>
<tr>
<td><strong>NOTE:</strong> Whilst the strength of thrombolytics is traditionally expressed in ‘units’ these units are unique to each particular drug and are <strong>NOT</strong> interchangeable.</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>ACTIONS</th>
<th>JRCALC MODEL CHECKLIST</th>
</tr>
</thead>
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<tr>
<td><strong>Activates the fibrinolytic system, inducing the breaking up of intravascular thrombi and emboli.</strong></td>
<td><strong>PRIMARY ASSESSMENT</strong></td>
</tr>
</tbody>
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**JRCALC MODEL CHECKLIST**

**PRIMARY ASSESSMENT**

1. Can you confirm that the patient is conscious, coherent, and able to understand that clot dissolving drugs will be used?
2. Can you confirm that the patient is aged **80** or less?
3. Can you confirm that the patient has had symptoms characteristic of a heart attack (i.e. continuous pain in a typical distribution of 15 minutes duration or more)?
4. Can you confirm that the symptoms started less than 6 hours ago?
5. Can you confirm that the pain built up over seconds and minutes rather than starting totally abruptly?
6. Can you confirm that breathing does not influence the severity of pain?
7. Can you confirm that the heart rate is between 40-140 beats per minute.
8. Can you confirm that the systolic blood pressure is more than 80mmHg and less than 180mmHg and that the diastolic blood pressure is below 110mmHg?
9. Can you confirm that the electrocardiogram shows abnormal ST segment elevation of 2mm or more in at least 2 standard leads or in at least 2 adjacent precordial leads, not including V1? **NOTE:** ST elevation can sometimes be normal in V1 and V2.
10. Can you confirm that the QRS width is 0.16 seconds or less, and that left bundle branch block is absent from the tracing? **NOTE:** right bundle-branch block permitted only with qualifying ST elevation.
11. Can you confirm that there is **NO** atrio-ventricular block greater than 1st degree? **NOTE:** if necessary after treatment with IV atropine.
SECONDARY ASSESSMENT (CONTRA-INDICATIONS)

12. Can you confirm that the patient is not likely to be pregnant, nor has delivered within the last two weeks?
13. Can you confirm that the patient has not had an active peptic ulcer within the last 6 months?
14. Can you confirm that the patient has not had a stroke of any sort within the last 12 months and does not have permanent disability from a previous stroke?
15. Can you confirm that the patient has no diagnosed bleeding tendency, has had no recent blood loss (except for normal menstruation) and is not taking warfarin (anticoagulant) therapy?
16. Can you confirm that the patient has not had any surgical operation, tooth extractions, significant trauma, or head injury within the last 4 weeks?
17. Can you confirm that the patient has not been treated recently for any other serious head or brain condition? (This is intended to exclude patients with cerebral tumours).
18. Can you confirm that the patient is not being treated for liver failure, renal failure, or any other severe systemic illness?

Previous streptokinase treatment is a contra-indication to the later use of streptokinase. Whilst this is not relevant to the use of tenecteplase or reteplase, it is always worth noting that thrombolytic treatment has been used in the past.

CONSENT

NOTE: many patients with acute myocardial infarction (MI) will not be legally ‘competent’ to give informed consent, and the Paramedic must act in the individual patient’s best interest (refer to consent guideline).

The suggested information for a patient who is being considered for pre-hospital thrombolysis is as follows:-

“It is likely that you have suffered a heart attack, and the best treatment is a clot dissolving drug called ‘xxx’. The quicker you receive this drug, the lower the risk from the heart attack – which is why Doctors recommend the treatment is started as soon as possible. These drugs can cause serious side effects in a small minority of patients which I can explain to you in more detail if you so wish, but the risks attached to this treatment are very much less than the likely benefit. Would you like me to give you the injection or would you prefer to have more details?”

In the unlikely event that patients do want more information they should be given the following information:-

“Treatment at this stage saves the lives of about 4 patients for every 100 we treat. But it can sometimes cause serious bleeding. The biggest risk is stroke which affects about 1 patient in every 200. Some patients also have allergic and other effects that do not usually cause any major problem.”
RETEPLASE – DOSAGE AND ADMINISTRATION

**Route:** IV bolus injections separated by 30 minutes.

<table>
<thead>
<tr>
<th>AGE</th>
<th>DOSE</th>
<th>VOLUME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>First dose 10 units – note time administered</td>
<td>10ml</td>
</tr>
<tr>
<td></td>
<td>Second dose 10 units – 30 minutes after first dose</td>
<td>10ml</td>
</tr>
</tbody>
</table>

Concentration – 10 units in 10mls.

A bolus intravenous injection of unfractionated heparin should be given before the first dose of reteplase and the cannula flushed well with saline OR a separate cannula used for reteplase since the two agents are physically incompatible.

HEPARIN

**Route:** IV single bolus unfractionated heparin.

<table>
<thead>
<tr>
<th>AGE</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>5,000U (prior to administration of reteplase)</td>
</tr>
</tbody>
</table>

If a heparin infusion HAS NOT commenced within 45 minutes of the original bolus of reteplase, administer a second dose of heparin 1,000U.

**AT HOSPITAL**

It is essential that care of the patient is handed over as soon as possible to a member of hospital staff qualified to administer the second bolus (if not already given) and commence a heparin infusion.
TENECTEPLASE – DOSAGE AND ADMINISTRATION

Route: IV single bolus adjusted for patient weight.

<table>
<thead>
<tr>
<th>AGE</th>
<th>DOSE</th>
<th>VOLUME</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60kg (&gt;9st6lbs)</td>
<td>6000 units</td>
<td>6.0ml</td>
</tr>
<tr>
<td>60-69kg (9st6lbs-10st12lbs)</td>
<td>7000 units</td>
<td>7.0ml</td>
</tr>
<tr>
<td>70-79kg (11st -12st6lbs)</td>
<td>8000 units</td>
<td>8.0ml</td>
</tr>
<tr>
<td>80-89kg (12st8lbs-14st)</td>
<td>9000 units</td>
<td>9.0ml</td>
</tr>
<tr>
<td>&gt;90kg (&gt;14st2lbs)</td>
<td>10000 units</td>
<td>10.0ml</td>
</tr>
</tbody>
</table>

Concentration – 1,000 U/ml.

A single bolus intravenous injection of unfractionated heparin should be given before administration of tenecteplase and the cannula flushed well with saline.

HEPARIN

Route: IV single bolus unfractionated heparin.

<table>
<thead>
<tr>
<th>AGE</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult &lt;67kg</td>
<td>4,000U (prior to administration of tenecteplase)</td>
</tr>
<tr>
<td>Adult &gt;67kg</td>
<td>5,000U (prior to administration of tenecteplase)</td>
</tr>
</tbody>
</table>

If the heparin infusion HAS NOT commenced within 45 minutes of the original bolus of tenecteplase, administer a second dose of heparin 1,000U.

AT HOSPITAL

It is essential that care of the patient is handed over as soon as possible to a member of hospital staff qualified to commence a heparin infusion.
### IN ALL CASES

Ensure a defibrillator is immediately available at all times.

Monitor conscious level, pulse, blood pressure and cardiac rhythm during and following injections. Manage complications (associated with the acute MI) as they occur using standard protocols. The main early adverse event associated with thrombolysis is bleeding, which should be managed according to standard protocols.

**AT HOSPITAL** – emphasise the need to commence a heparin infusion in accordance with local protocols.

### HEPARIN

Heparin is required as adjunctive therapy with reteplase and tenecteplase to reduce the risk of reinfarction.

It is extremely important that the initial bolus dose is given at the earliest opportunity prior to administration of thrombolytic agents and a heparin infusion is commenced immediately on arrival at hospital.

A further intravenous bolus dose of 1,000 units heparin may be required if a heparin infusion HAS NOT commenced within 45 minutes of the original bolus of thrombolytic agent.

Recent trials have suggested that low molecular weight heparin may be useful in patients under 75 years of age (older patients have much higher bleeding risk with this treatment). Research is ongoing and local protocols should be followed. Further information is available at www.warwick.ac.uk/go/emergencycare

### ADDITIONAL INFORMATION

**‘Time is muscle!’** Do not delay transportation to hospital if difficulties arise whilst setting up the equipment or establishing IV access. Qualified single responders should press on with administering a thrombolytic if indicated while awaiting arrival of an ambulance.

The increasing availability of primary percutaneous coronary intervention (PCI) means some patients with MI will be taken direct to a specialist cardiac centre instead of receiving thrombolysis (see acute coronary syndrome guideline). Local protocols should be followed.

### SIDE EFFECTS

**Bleeding:**
- major – seek medical advice and transport to hospital rapidly.
- minor e.g. at injection sites – use local pressure.

Arrhythmias – these are usually benign in the form of transient idioventricular rhythms and usually require no special treatment. Treat VF as a complication of MI with standard protocols; bradycardia with atropine as required.

Anaphylaxis – extremely rare (0.1%) with third generation bolus agents.

Hypotension often responds to laying the patient flat.