

## Lothian University Hospitals NHS Trust

Department of Cardiology and Department of Pharmacy, Royal Infirmary of Edinburgh

### High Dose Tirofiban Protocol

<b>Indication</b>	<ul style="list-style-type: none"><li>• The prevention of early myocardial infarction in patients with unstable angina or non-ST-segment-elevation myocardial infarction (NSTEMI) and with last episode of chest pain within 12 hours (with angiography within 4 hours of diagnosis)</li><li>• The reduction of major cardiovascular events in patients with ST-segment elevation myocardial infarction (STEMI) intended for primary percutaneous coronary intervention (PCI)</li></ul>																					
<b>Presentation</b>	<ul style="list-style-type: none"><li>• 250mL infusion bag containing tirofiban 50 micrograms/mL</li><li>• 50mL vial containing tirofiban 250 micrograms/mL <b>concentrate</b> for infusion (<b>must be diluted before further use</b>)</li></ul>																					
<b>Method of preparation</b>	<ul style="list-style-type: none"><li>• 250mL infusion bag contains 12.5mg of tirofiban (50 micrograms/mL): it is a premixed solution in sodium chloride which is ready to use and does not need dilution</li></ul> <p>If infusion bag unavailable then consider using vials:</p> <ul style="list-style-type: none"><li>• Dilution of tirofiban 250 micrograms/mL <b>concentrate</b> vials:-<ul style="list-style-type: none"><li>○ Withdraw 50mL from a 250mL bag of sterile 0.9% sodium chloride or 5% glucose.</li><li>○ Replace the 50mL removed with 50mL tirofiban <b>concentrate</b> for infusion in order to give a concentration of 50 microgram/mL.</li><li>○ Mix well before use.</li></ul></li></ul>																					
<b>Dose and administration</b>	<ul style="list-style-type: none"><li>• Initial loading bolus dose 25 microgram/kg over <b>3 minutes</b> followed by an infusion of 0.15 microgram/kg/minute for 12-24 hours. Maximum duration of treatment 48 hours.</li><li>• Administer the initial bolus loading dose as an intravenous infusion over <b>3 minutes</b>. Volumes to be administered can be found in the table below.</li></ul> <table><tr><th></th><th colspan="2">Initial Loading Bolus Dose of 25 microgram/kg</th></tr><tr><th>Weight (kg)</th><th>Volume of 50 microgram/mL solution to be administered as intravenous infusion over three minutes (mL)</th><th>Infusion rate of 50 microgram/mL solution for initial <b>three minute</b> intravenous infusion (mL/hour)</th></tr><tr><td>45</td><td>22.5</td><td>450</td></tr><tr><td>50</td><td>25.0</td><td>500</td></tr><tr><td>55</td><td>27.5</td><td>550</td></tr><tr><td>60</td><td>30.0</td><td>600</td></tr><tr><td>65</td><td>32.5</td><td>650</td></tr></table>		Initial Loading Bolus Dose of 25 microgram/kg		Weight (kg)	Volume of 50 microgram/mL solution to be administered as intravenous infusion over three minutes (mL)	Infusion rate of 50 microgram/mL solution for initial <b>three minute</b> intravenous infusion (mL/hour)	45	22.5	450	50	25.0	500	55	27.5	550	60	30.0	600	65	32.5	650
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	70	35.0	700
	75	37.5	750
	80	40.0	800
	85	42.5	850
	90	45.0	900
	95	47.5	950
	100	50.0	999.9*
	105	52.5	999.9*
	110	55.0	999.9*
	115	57.5	999.9*
	120	60.0	999.9*
	* Will require administration over longer than 3 minutes. Continue administration until full volume is administered.		
<ul style="list-style-type: none"><li>At the end of the initial loading bolus dose, the rate setting for the maintenance infusion rate <b>must be</b> checked by two people.</li><li>The remaining solution should then be administered as 0.15microgram/kg/minute continuous intravenous infusion for 12 hours following PCI unless specifically requested by the consultant responsible for the patient.</li></ul>			
The following table contains information regarding maintenance infusion rates.			
	<b>Maintenance infusion of 0.15microgram/kg/minute</b>		
Weight (kg)	Infusion rate of 50microgram/ml solution (mL/hour)		
45	8.1		
50	9.0		
55	9.9		
60	10.8		
65	11.7		
70	12.6		
75	13.5		
80	14.4		
85	15.3		
90	16.2		
95	17.1		
100	18.0		
105	18.9		
110	19.8		
115	20.7		
120	21.6		
<ul style="list-style-type: none"><li>Tirofiban should be administered with unfractionated heparin (UFH) and oral antiplatelets including (but not limited to) aspirin unless contraindicated.</li><li>UFH should be administered as an intravenous bolus of 5000 units alongside the start of the tirofiban infusion then approximately 1000 units per hour titrated according to activated partial thromboplastin time (APTT).</li><li>Normally, not more than one bag is required for infusion (during PCI and ongoing treatment in Coronary Care Unit)</li></ul>			
Special Precautions	<ul style="list-style-type: none"><li>In <b>severe kidney failure (eGFR (/1.73m<sup>2</sup>) less than 30mL/min)</b> half both the loading dose and maintenance infusion rate.</li><li>If <b>angioplasty</b> is required, heparin should be stopped after PCI and the sheaths withdrawn once anticoagulation has returned to normal (activated clotting time is less than 180 seconds)<sup>1</sup>.</li></ul>		
Monitoring requirements	<ul style="list-style-type: none"><li>Baseline platelet count, haemoglobin and haematocrit levels should be taken before initiating treatment with tirofiban, then rechecked within 2 to 6 hours after starting therapy and at least daily thereafter whilst on therapy.<ul style="list-style-type: none"><li>If the platelet count is less than 90 x 10<sup>9</sup>/L, a repeat count should be taken in order to exclude pseudothrombocytopenia.</li></ul></li></ul>		

	<ul style="list-style-type: none"> <li>○ If thrombocytopenia is confirmed, stop tirofiban and heparin and monitor for signs of bleeding.</li> <li>● Activated partial thromboplastin time (APTT) should be measured before starting tirofiban and monitored at regular intervals throughout heparin treatment.</li> </ul>
<b>Compatibility at Y-site</b>	<ul style="list-style-type: none"> <li>● Tirofiban is compatible with heparin and glyceryl trinitrate at Y-site</li> </ul>
<b>Pharmacokinetics</b>	<ul style="list-style-type: none"> <li>● Elimination half life is about 2 hours</li> <li>● Antiplatelet effect persists for 4 – 8 hours</li> </ul>

### References

1. INJECTABLE MEDICINES GUIDE. Tirofiban – *Intravenous Adult monograph*. [online]. Available from: <http://medusa.wales.nhs.uk/Home.asp> [Accessed 6 October 2016].
2. ELECTRONIC MEDICINES COMPENDIUM (EMC), 2015. Tirofiban 50 micrograms/ml solution for infusion - *Beacon Pharmaceuticals Summary of Product Characteristics*. [online]. Available from: [www.medicines.org.uk/emc](http://www.medicines.org.uk/emc) [Accessed 6 October 2016]
3. JOINT FORMULARY COMMITTEE, 2016. *British National Formulary*. 71. London: BMJ Group and Pharmaceutical Press.
4. GRAY, A. et al., 2011. *Injectable Drugs Guide*. London: Pharmaceutical Press.
5. CRC PRESS TAYLOR AND FRANCIS GROUP, 2014. *The Renal Drug Database – Tirofiban Monograph*. [online]. Abingdon: CRC Press Taylor and Francis Group. Available from: <https://renaldrugdatabase.com/> [Accessed on 13 October 2016]
6. MICROMEDEX SOLUTIONS, 2016. *Trissels's™ 2 Clinical Pharmaceuticals Database (Parenteral Compatibility)*, 2016. [online]. Available from: <https://www.micromedexsolutions.com/home> [Accessed 6 October 2016]