Lothian University Hospitals NHS Trust

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

High Dose Tirofiban Protocol

<table>
<tr><td>Indication</td><td>For unlicensed use as an adjunct to “Primary PCI” for patients with ST-elevation MI. It may also be used in patients undergoing PCI in other clinical situations, if it is felt that a rapid onset of drug action would be beneficial.</td></tr>
<tr><td>Presentation</td><td>• 50ml vial containing tirofiban 250 micrograms/ml concentrate for infusion (must be diluted further before use)
• 250ml Intravia® infusion bag containing tirofiban 50 micrograms/ml</td></tr>
<tr><td>Method of preparation</td><td>• Dilution of tirofiban 250 microgram/ml vials:-
o Withdraw 50ml from a 250ml bag of sterile 0.9% sodium chloride or 5% glucose.
o Replace the 50ml removed with 50ml tirofiban concentrate for infusion in order to give a concentration of 50 microgram/ml.
o Mix well[1].
Alternatively, 250ml Intravia® infusion bag containing tirofiban 50 micrograms/ml is available</td></tr>
<tr><td>Dose and administration</td><td>• Initial loading bolus dose 25 microgram/kg over 3 minutes followed by an infusion of 0.15 microgram/kg/minute for up to 24 hours[2,3,4].
• Administer the initial bolus loading dose as an intravenous infusion over 3 minutes. Volumes to be administered can be found in the table below.

<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 three minute 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>
<tr><td>70</td><td>35.0</td><td>700</td></tr>
<tr><td>75</td><td>37.5</td><td>750</td></tr>
<tr><td>80</td><td>40.0</td><td>800</td></tr>
<tr><td>85</td><td>42.5</td><td>850</td></tr>
<tr><td>90</td><td>45.0</td><td>900</td></tr>
<tr><td>95</td><td>47.5</td><td>950</td></tr>
<tr><td>100</td><td>50.0</td><td>999.9*</td></tr>
<tr><td>105</td><td>52.5</td><td>999.9*</td></tr>
<tr><td>110</td><td>55.0</td><td>999.9*</td></tr>
<tr><td>115</td><td>57.5</td><td>999.9*</td></tr>
<tr><td>120</td><td>60.0</td><td>999.9*</td></tr>
</table>
* Will require administration over longer than 3 minutes. Continue administration until full volume is administered.
• At the end of the initial loading bolus dose, the rate setting for the maintenance infusion rate must be checked by two people.
• 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.

The following table contains information regarding maintenance infusion rates.</td></tr>
</table>

	<table><tr><th></th><th>Maintenance infusion of 0.15microgram/kg/minute</th></tr><tr><td>Weight (kg)</td><td>Infusion rate of 50microgram/ml solution (ml/hour)</td></tr><tr><td>45</td><td>8.1</td></tr><tr><td>50</td><td>9.0</td></tr><tr><td>55</td><td>9.9</td></tr><tr><td>60</td><td>10.8</td></tr><tr><td>65</td><td>11.7</td></tr><tr><td>70</td><td>12.6</td></tr><tr><td>75</td><td>13.5</td></tr><tr><td>80</td><td>14.4</td></tr><tr><td>85</td><td>15.3</td></tr><tr><td>90</td><td>16.2</td></tr><tr><td>95</td><td>17.1</td></tr><tr><td>100</td><td>18.0</td></tr><tr><td>105</td><td>18.9</td></tr><tr><td>110</td><td>19.8</td></tr><tr><td>115</td><td>20.7</td></tr><tr><td>120</td><td>21.6</td></tr></table> • Tirofiban should be administered with unfractionated heparin unless contraindicated. • Heparin 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 thromboplastin time (APTT). • Normally, not more than one bag is required for infusion (during PCI and ongoing treatment in Coronary Care Unit)
Special Precautions	• In **severe kidney failure** (creatinine clearance **less than 30ml/min**) half both the loading dose and maintenance infusion rate[5]. • If **angioplasty** 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)[1].
Monitoring requirements	• 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[1]. o If the platelet count is less than 90 x 10^9/L, a repeat count should be taken in order to exclude pseudothrombocytopenia. o If thrombocytopenia is confirmed, stop tirofiban and heparin and monitor for signs of bleeding. • Activated thromboplastin time (APTT) should be measured before starting tirofiban and monitored at regular intervals throughout heparin treatment[1].
Compatibility at Y-site	• There is no compatibility information for running glyceryl trinitrate 1mg/ml alongside tirofiban and therefore this should be avoided. • Tirofiban is compatible with heparin at Y-site[1,6].
References	1. Aggrastat solution for infusion and concentrate for solution for infusion Summary of Product Characteristics, last update April 2005. Accessed via http://emc.medicines.org.uk 2nd June 2009. 2. Danzi GB, Capuano C, Sesana M, Baglini R. Preliminary experience with a high bolus dose of tirofiban during percutaneous coronary intervention. Current Medical Research and Opinion. 2003;19:1-6. 3. Danzi BG, Capuano C, Sesana M, Baglini R. Safety of a high bolus dose of tirofiban in patients undergoing coronary stent placement. Catheterization and Cardiovascular Interventions. 2004;61:179-84. 4. Valgimigli M, camp G, Percoco G, Bolognese L, Vassanelli C, Colangelo S et al. Multicentre evaluation of single high-dose bolus tirofiban vs. abciximab with sirolimus-eluting stent or bare metal stent in acute myocardial infarction study (MULTISTRATEGY) Investigators. Comparison of angioplasty with infusion of tirofiban or abciximab and with implantation of sirolimus-eluting or uncoated stents for acute myocardial infarction:the MULTISTRATEGY randomised trial. JAMA. 2008;299:1788-99. 5. Ashley C, Currie A, editors. The renal drug handbook. Oxon: Radcliffe publishing Ltd. 2009, page 732. 6. Trissel, LA. Ed. Handbook on injectable drugs, 15th ed. Bethesda: American Society of Health-System Pharmacists Inc. 2009.

This protocol should be used in conjunction with the Aggrastat® Summary of Product Characteristics available via http://emc.medicines.org.uk listing details of contraindications and special precautions.