the children's hospital at Westmead

INTRAVENOUS TIROFIBAN - CHW

DRUG PROTOCOL©

DOCUMENT SUMMARY/KEY POINTS

- Overview of tirofiban for use in emergent neuro-interventional procedures
- Indicated to prevent platelet aggregation in neuro-interventional procedures where oral therapy unsuitable, or where ultra-rapid platelet blockade is required
- To be administered as a loading dose over 30 minutes, followed by continuous infusion
- Dilute to a concentration of 50 microg/mL in glucose 5% or sodium chloride 0.9% before infusion
- Transition to oral anti-platelet therapy when clinically appropriate.

CHANGE SUMMARY

- This is a new document

READ ACKNOWLEDGEMENT

- Medical, pharmacy, and nursing staff who care for patients being treated with tirofiban are required to read and acknowledge the document.

Note: Separate Practice Guidelines may be required to cover all aspects of management.

Approved by:	SCHN Policy, procedure and Guideline Committee	
Date Effective:	3rd May 2022	**Review Period**: 3 years
Team Leader:	VMO	**Area/Dept**: Radiology

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NSW GOVERNMENT

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Introduction / Background

Tirofiban is an antiplatelet agent that prevents fibrinogen binding to glycoprotein (GP) IIb/IIIa receptors, the major interaction involved in platelet aggregation. It is a reversible agent with a short half-life of 1.4 – 1.8 hours in healthy adults where platelet aggregation returns to normal 4—8 hours post discontinuation.

Registered Use

Tirofiban is registered for use in Australia for patients with unstable angina or non-Q-wave myocardial infarction to prevent cardiac ischaemic events. This policy would indicate tirofiban for use in off-label indications.

Approved Indications

- Intra-procedural treatment of platelet aggregation or intravascular thrombus.
- Patient requiring ultra-rapid platelet blockade (e.g. acute requirement for intracranial flow diverter stent or bare metal stent).
- Urgent requirement for anti-platelet therapy in patients without nasogastric access and when oral therapy is unsuitable or not possible.

Specific patient groups most likely to benefit

Patients undergoing neuro-interventional procedures requiring urgent antiplatelet therapy, without nasogastric access and where oral therapy is unsuitable or not possible.

Contraindications

- Allergy to tirofiban.
- Active internal bleeding or known bleeding diathesis.
- Intracranial haemorrhage, AV malformation, or neoplasm (but allowing for possibility of urgent flow diverter placement in ruptured blister aneurysms causing subarachnoid haemorrhage and requiring urgent anti-platelet action).
- Major surgical procedure or severe traumatic injury in last 30 days.
- Aortic dissection.
- Acute pericarditis.
- Severe uncontrolled hypertension.
- Concomitant use of another parenteral GP IIb/IIIa inhibitor.
- Severe thrombocytopaenia (platelet count <50 x 10^9/L) or history of thrombocytopenia following prior exposure to tirofiban.

Precautions

- Platelet count of <150 x 10^9/L or any other known platelet disorder.
- Coagulopathy
- Chronic haemodialysis.
- Recent epidural procedure.
- Recent significant bleeding, or risk of bleeding.

- Haemorrhagic retinopathy.
- When used with other antiplatelet or thrombolytic agents, monitor closely for additive bleeding risk.
- Impaired renal function (creatinine clearance <30 mL/min).

Presentation

- Injection 12.5 mg in 50 mL as tirofiban (250 micrograms/mL) clear colourless sterile solution for intravenous use.
- Storage ≤25°C. Protect from light during storage and do not freeze.
    - Storage locations:
        - Neurovascular angiography suite – stroke equipment mobile cupboard.
        - Pharmacy.
- Available brands: *Aggrastat, Tirofiban Juno*

Dose

- Weight <30 kg
    - Load: 10 microg/kg over 30 minutes
    - Maintenance infusion: 0.15 microg/kg/min
    - No minimum age or weight limit applies, but caution should be taken in infants less than 6 months of age
- Weight ≥30 kg
    - Load: 12 microg/kg over 30 minutes
    - Maintenance infusion: 0.1 microg/kg/min
- In severe renal impairment (CrCl <30 mL/min):
    - Reduce both loading dose and maintenance dose by half.

- Dosing chart for patients ≥30 kg using concentration of tirofiban 50 microg/mL

Patient Weight (kg)	Most Patients		Severe Kidney Failure	
	30 Min Loading Infusion Rate (mL/hr)	Maintenance Infusion Rate (mL/hr)	30 Min Loading Infusion Rate (mL/hr)	Maintenance Infusion Rate (mL/hr)
30-37	16	4	8	2
38-45	20	5	10	3
46-54	24	6	12	3
55-62	28	7	14	4
63-70	32	8	16	4
71-79	36	9	18	5
80-87	40	10	20	5
88-95	44	11	22	6
96-104	48	12	24	6
105-112	52	13	26	7
113-120	56	14	28	7
121-128	60	15	30	8
129-137	64	16	32	8
138-145	68	17	34	9
146-153	72	18	36	9

Source: http://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2020-PI-01774-1

Duration of treatment

- Until oral or nasogastric aspirin can be safely initiated (typically 12–48 hours). Use beyond 72 hours has not been well studied and should be avoided if possible.
- Discontinuation: Cease the tirofiban infusion one hour after administration of loading or maintenance doses of oral anti-platelet agents (e.g. oral aspirin, clopidogrel).

Authorised Prescribers

- Neuro-interventionalists.
- Intensivists.
- Other prescribers under the supervision of an intensivist or neuro-interventionist.

Place in therapy in relation to alternatives

- As antiplatelet agent where oral anti-platelets are not suitable. To be transitioned to oral antiplatelet agent (aspirin +/- clopidogrel or prasgurel) as soon as clinically appropriate/feasible.
- Heparin infusion may run concurrently with tirofiban infusion with caution.

Administration

- Dilute solution immediately before use.
- Dilution instructions:

  - Remove 50 mL from a 250 mL bag of sodium chloride 0.9% OR glucose 5% and replace with contents of the 50 mL vial of tirofiban to a final concentration 50 microgram/mL.
  - If using a 500 mL bag, remove 100 mL and replace with 2 x 50 mL vials of tirofiban to a final concentration of 50 micrograms/mL

- Mix well before infusion.
- Loading dose: Infuse over 30 minutes followed by a continuous infusion.
- Maintenance dose: Dilute to 50 microgram/mL with G5W or NS and infuse continuously.
- Rate:
  - Weight <30 kg: 0.15 microgram/kg/minute
  - Weight ≥30 kg: 0.1 microgram/kg/minute
- Refer to the Paediatric Injectable Medicines Handbook for further information.

Safety and Patient Monitoring

- Neurological observations should be undertaken every 30 minutes for 4 hours after initiation of infusion, then hourly for 8 hours, then every 2 hours until infusion ceased.
- Signs of bleeding.
- Hypersensitivity reactions.
- Blood testing: Platelet count and haemoglobin level must be measured before treatment, 6 hours after starting tirofiban, and every 24 hours thereafter. A persistent reduction in platelet count (drop of 25% below baseline) may require discontinuation.
- Brain imaging: CT or MRI brain to be performed 12–24 hours after commencement to exclude new intracranial haemorrhage prior to transition to oral anti-platelet medications.
- Invasive procedures:
  - Central venous access procedures should be avoided during tirofiban infusion, and where appropriate alternatives such as peripheral venous cannulation or PICC line insertion should be considered. It would be preferable that central venous access be performed before infusion commencement. If there is no central venous access, the neuro-interventionist should consider placement of femoral central venous line under imaging guidance prior to case completion.
  - Radial or dorsalis pedis arterial line insertion should be undertaken with caution, and using ultrasound guidance, during tirofiban infusion. It would be preferable that such a line be placed prior to commencement of the infusion.
  - Nasogastric tube insertion should be undertaken with caution during tirofiban infusion, preferably under imaging guidance to minimize mucosal trauma. It would be preferable for the neuro-interventionist or anaesthesiologist to place a nasogastric tube whilst in the angiography suite.

Adverse effects

- Bleeding (major bleeding fulfilling TIMI {thrombolysis in myocardial infarction} criteria in 1.4-2.2% when used in combination with heparin infusion compared with 0.8-1.6% with heparin alone), thrombocytopenia, dizziness, bradycardia (4% in an adult cohort with cardiac disease when used in combination with heparin, 3% with heparin alone), leg or pelvic pain, swelling, increased sweating, fever, chills, nausea and vomiting.

Management of complications

- Management of hypersensitivity reactions.
- Management of severe bleeding.

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