Prescribing Protocol

Bivalirudin for Heparin induced Thrombocytopenia (HIT)

Areas where Protocol/Guideline applicable	Medical Officers, Nurses/Midwives, Pharmacists
Authorised Prescribers:	Haematologists or Medical Officers under the direct supervision of a Haematologist
Indication for use	Heparin induced thrombocytopenia (HIT)
Clinical condition Patient selection: Inclusion criteria	Patients with HITT as diagnosed in consultation with a treating haematologist, based initially on clinical scoring (e.g. 4T score), which may be complemented via laboratory testing as time permits. This drug is most likely to benefit patients with HITT fulfilling the following criteria, and would be considered a first line therapy in these indications: 1. Undergoing percutaneous coronary or vascular intervention OR 2. Likely to require invasive procedures OR 3. Renal or Hepatic Failure OR 4. Deemed at high risk of bleeding 5. Suspected COVID-19 Vaccine Induced Thrombocytopenia with Thrombosis
Contra-indications	• Patients with active bleeding or increased risk of bleeding because of haemostasis disorders and/or irreversible coagulation disorders. • Severe uncontrolled hypertension or increased risk of severe uncontrolled hypertension • Subacute bacterial endocarditis • Hypersensitivity to bivalirudin or its components
Precautions	• Haemorrhage – Can occur at any site. An unexplained fall in blood pressure or haematocrit, or any unexplained symptom, should lead to serious consideration of a haemorrhagic event and cessation of Bivalirudin administration. • Renal Insufficiency – Clearance may be reduced in patients with renal impairment, dose adjustments necessary.
Proposed Place in Therapy	For patients not fulfilling one of these criteria, Bivalirudin would be a second line therapy only to be used if there is clear treatment failure with an alternative agent such as Fondaparinux, Danaparoid or a NOAC.

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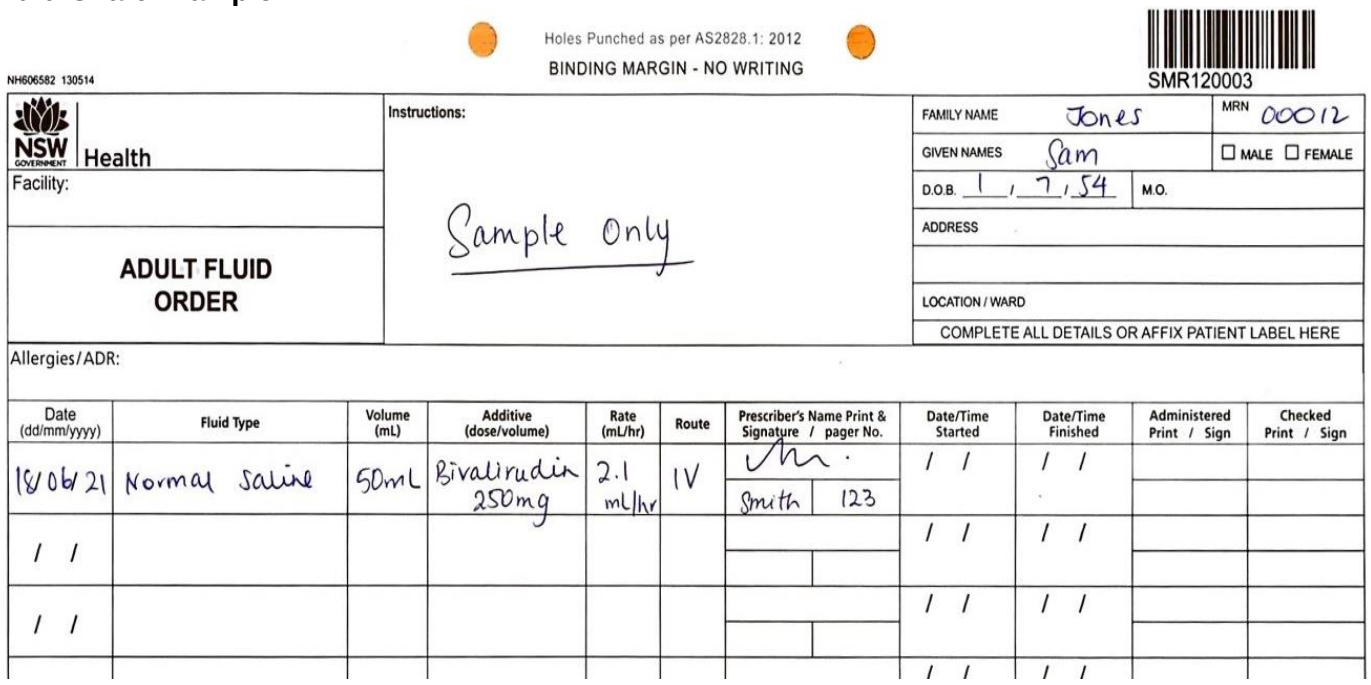
Health
South Eastern Sydney
Local Health District

Dosage	**Initial dosing**

Weight (kg)	Infusion volume rate (**mL/hour**) using Bivalirudin 250 mg in 50 mL NS Concentration 5 mg / mL PERIPHERAL LINE				
	CrCl > 60 mL/min 0.15 mg/kg/hr	**CrCl 30 – 60 mL/min** 0.08 mg/kg/hr	**CrCl < 30 mL/min** 0.05 mg/kg/hr	Patients receiving Continuous Renal Replacement Therapy (**CRRT**) 0.04 mg/kg/hr	Patients Receiving Slow Low Efficiency Daily Dialysis (**SLEDD**) 0.07 mg/kg/hr
40	1.2	0.6	0.4	0.3	0.6
45	1.4	0.7	0.5	0.4	0.6
50	1.5	0.8	0.5	0.4	0.7
55	1.7	0.9	0.6	0.4	0.8
60	1.8	1.0	0.6	0.5	0.8
65	2.0	1.0	0.7	0.5	0.9
70	2.1	1.1	0.7	0.6	1.0
75	2.3	1.2	0.8	0.6	1.1
80	2.4	1.3	0.8	0.6	1.1
85	2.6	1.4	0.9	0.7	1.2
90	2.7	1.4	0.9	0.7	1.3
95	2.9	1.5	1.0	0.8	1.3
100	3	1.6	1.0	0.8	1.4
105	3.2	1.7	1.1	0.8	1.5
110 (maximum)	3.3	1.8	1.1	0.9	1.5

Fluid Chart Example:



Holes Punched as per AS2828.1: 2012
BINDING MARGIN - NO WRITING

NH606582 130514

SMR120003

NSW Health
Facility:

ADULT FLUID ORDER

Instructions:
Sample Only

FAMILY NAME Jones
GIVEN NAMES Sam
D.O.B. 1/7/54
MRN 00012
☐ MALE ☐ FEMALE
M.O.
ADDRESS
LOCATION / WARD
COMPLETE ALL DETAILS OR AFFIX PATIENT LABEL HERE

Allergies/ADR:

Date (dd/mm/yyyy)	Fluid Type	Volume (mL)	Additive (dose/volume)	Rate (mL/hr)	Route	Prescriber's Name Print & Signature / pager No.	Date/Time Started	Date/Time Finished	Administered Print / Sign	Checked Print / Sign
18/06/21	Normal Saline	50mL	Bivalirudin 250mg	2.1 mL/hr	IV	Smith 123	/ /	/ /		
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							/ /	/ /		

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<table>
<tr><td></td><td></td></tr>
<tr><td>Duration of therapy</td><td>Patient dependent, until platelet recovery and / or able to be safely transitioned to warfarin or a separate non intravenous non heparin anticoagulant</td></tr>
<tr><td>Important Drug Interactions</td><td>Other anticoagulants.
Prolongs INR, will need specific consultation with haematologist when transitioning to warfarin.</td></tr>
<tr><td>Administration Instructions</td><td>• Reconstitute 250 mg vial with 5 mL Water for Injection (swirl to dissolve)
• Further dilute reconstituted solution to total 50 mL with Glucose 5% or NS for final concentration of 5 mg/mL
• Dose should be based on actual body weight (kg) up to a maximum of 110kg</td></tr>
<tr><td>Monitoring requirements</td><td>A baseline APTT is required
Routine anticoagulation monitoring
Daily FBC, PT
Observe for signs and symptoms of bleeding. If patient actively bleeding, notify ICU Consultant/Senior Registrar immediately
Perform daily urinalysis checking for presence of blood
Bivalirudin infusions must be closely monitored to achieve an aPTT 1.5 to 2.5 times baseline or aPTT50-80sec
<table>
<tr><th>aPTT</th><th>Dose Adjustment</th><th>Calculation</th><th>Action</th></tr>
<tr><td>< 50</td><td>Increase infusion rate by 20%</td><td>New rate = current rate x 1.2</td><td>Monitor aPTT every 4 hours</td></tr>
<tr><td>50 – 80</td><td>GOAL RATE = NO CHANGE</td><td>No Change</td><td>Monitor aPTT every 4 hours</td></tr>
<tr><td>80 - 100</td><td>Decrease dose by 10%</td><td>New rate = current rate x 0.9</td><td>Monitor aPTT every 4 hours</td></tr>
<tr><td>> 100</td><td>Hold infusion for 2 hour, reduce rate at 50% less than previous rate</td><td>New rate = current rate x 0.5</td><td>Monitor aPTT every 4 hours</td></tr>
</table></td></tr>
<tr><td>Management of Complications</td><td>• There is no reversal agent for Bivalirudin.
• Elimination half-life: 25mins.
• Prolonged coagulation times return to normal approximately one hour after discontinuation.
• Bivalirudin is cleared by dialysis.</td></tr>
<tr><td>Basis of Protocol/Guideline:
(including sources of evidence, references)</td><td>Based on St George Hospital ICU Bivalirudin protocol, modified with permission of ICU Pharmacist and CNC.
1. Kiser T, Pharm D, and Fish D. Evaluation of bivalirudin treatment for heparin-induced thrombocytopenia in critically ill patients with hepatic and/or renal dysfunction. Pharmacotherapy. 2006:26 (4): 452-460
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6. Sangali F, Patroniti N, Pesenti A. ECMO – Extracorporeal Life Support in Adults. 2014. Springer Verlag: Italy</td></tr>
</table>

7. University of Washington Medicine. Bivalirudin Dosing Algorithim. https://depts.washington.edu/anticoag/home
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13. SGSHHS/ Extracorporeal Membrane Oxygenation (ECMO) http://seslhnweb/SGSHHS/Business_Rules/Clinical/SGH/ICU/documents/ECMO_SGH_SGSHHS_CLIN_ICU.pdf
14. Peiri M, Agracheva N, Bonaveglio E, Greco T, De Bonis M, Covello R, Zangrillo A, Pappalardo F. Bivalirudin versus heparin as an anticoagulant during extracorporeal membrane oxygenation: A case-control study. Journal of Cardiothoracic and Vascular Anaesthesia. 2013; 27:1 30-34

Groups consulted in development of this guideline	Intradepartmental discussion amongst all haematologists. Discussion with ICU CNC and Pharmacist regarding modification of their existing protocol. Consultation with Haematology CNC and Pharmacist regarding administration and protocolisation.

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GOVERNANCE	
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Chairperson, QUM Committee	Dr John Shephard
Version Number	1