Prescribing Protocol – SESLHDPR/711

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.

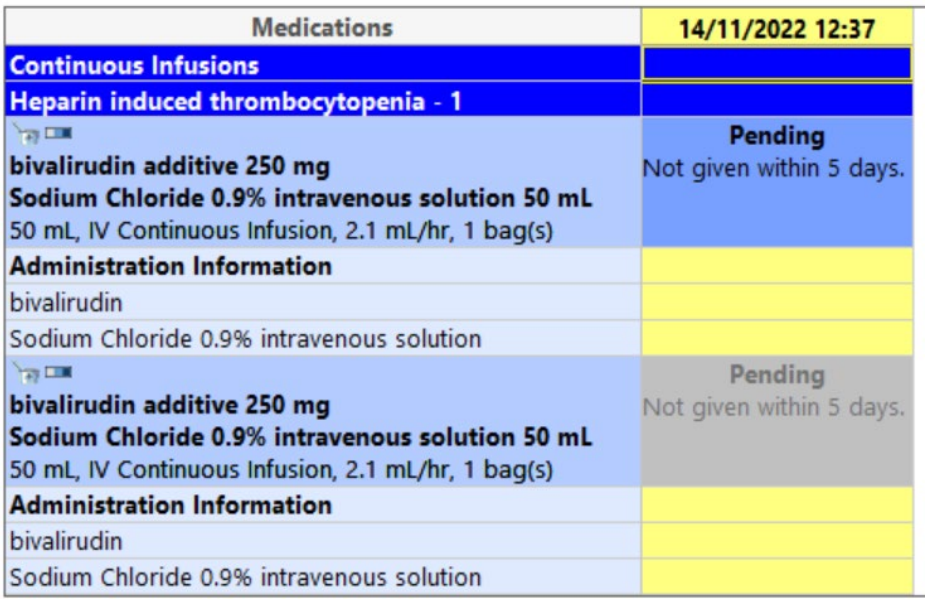
Bivalirudin for Heparin induced Thrombocytopenia (HIT)

Dosage	**Initial dosing**

Weight (kg)	Infusion volume rate (**mL/hour**) using Bivalirudin 250 mg in 50 mL sodium chloride 0.9% 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**) 0.05 mg/kg/hr	Patients Receiving Slow Low Efficiency Daily Dialysis (**SLEDD**) 0.075 mg/kg/hr
40	1.2	0.6	0.4	0.4	0.6
45	1.4	0.7	0.5	0.5	0.7
50	1.5	0.8	0.5	0.5	0.8
55	1.7	0.9	0.6	0.6	0.8
60	1.8	1.0	0.6	0.6	0.9
65	2.0	1.0	0.7	0.7	1.0
70	2.1	1.1	0.7	0.7	1.1
75	2.3	1.2	0.8	0.8	1.1
80	2.4	1.3	0.8	0.8	1.2
85	2.6	1.4	0.9	0.9	1.3
90	2.7	1.4	0.9	0.9	1.4
95	2.9	1.5	1.0	1.0	1.4
100	3	1.6	1.0	1.0	1.5
105	3.2	1.7	1.1	1.1	1.6
110 (maximum)	3.3	1.8	1.1	1.1	1.7

Duration of therapy	Patient dependent, until platelet recovery and / or able to be safely transitioned to warfarin or a separate non intravenous non heparin anticoagulant
Important Drug Interactions	Other anticoagulants. Prolongs INR will need specific consultation with haematologist when transitioning to warfarin.

Bivalirudin for Heparin induced Thrombocytopenia (HIT)

Prescribing Instructions	Prescribe in eFluids. Refer to Rate Change – Prescriber Initiated QRG.  Each order in eFluids corresponds to **one bag** only. Prescribers must ensure that new infusion orders are available in a timely manner, enabling nursing staff to continuously administer the drug infusion, where required. The number of bags prescribed at any one time should be considered in the context of: • Stability of dose at the time of prescribing • Predicted duration of one bag **Note:** A bivalirudin infusion must be recharted and replaced at least every 24 hours.
Administration Instructions	• 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

Bivalirudin for Heparin induced Thrombocytopenia (HIT)

Monitoring requirements

A baseline aPTT is required and repeated every 4 hours for the duration of the infusion.

Other monitoring: anticoagulation (routinely), FBC (daily), PT (daily).

Observe for signs and symptoms of bleeding. If patient actively bleeding, notify medical registrar or haematology registrar / consultant on call 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.

aPTT	Dose Adjustment	Calculation	Action
< 50	Increase infusion rate by 20%	New rate = current rate x 1.2	Monitor aPTT every 4 hours
50 – 80	**GOAL RATE = NO CHANGE**	**No Change**	Monitor aPTT every 4 hours
80 - 100	Decrease dose by 10%	New rate = current rate x 0.9	Monitor aPTT every 4 hours
> 100	Hold infusion for 2 hour, reduce rate at 50% less than previous rate	New rate = current rate x 0.5	Monitor aPTT every 4 hours

Medical officers are responsible for monitoring aPTT. Nursing staff may request a medical officer review when aPTT results become available.

Medical officers are responsible for prescribing any rate changes in eFluids. Any future infusion orders, already prescribed, must also be updated each time a rate change is required. See Quick Reference Guide: Modifying the Rate of an Infusion.

Nursing staff MUST document the administration of rate changes in MAR and note when the next aPTT is next due in the Comment box. If no adjustments are required, document this and other details relevant for the infusion in the progress notes. If the infusion has been paused (i.e., rate is 0 mL/hr) for longer than 2 hours, nursing staff to contact the doctor for clarification unless clearly documented. See Quick Reference Guide: Documenting a Rate Change (Prescriber Initiated).

Ensure that the patient has ongoing infusions charted unless Haematology or the treating team has specifically documented or advised to cease the bivalirudin infusion.

Management of Complications

- 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.

Bivalirudin for Heparin induced Thrombocytopenia (HIT)

Basis of Protocol/Guideline: (including sources of evidence, references)	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 2. Jyoti A, Maheshwari A, Daniel E, Motihar A, Bhathiwal R, Sharma D. Bivalirudin in venous extracorporeal membrane oxygenation. The Journal of ExtraCorporeal Technology. 2014:46: 94-97 3. St Vincent's Hospital Intensive Care Unit. Extracorporeal membrane oxygenation (ECMO) in the intensive care unit. 2016: Oct: 26-27 4. Liverpool Hospital Intensive Care Unit. ICU: bivalirudin policy. 2015 5. Tsu L, and Dager W. Bivalirudin dosing adjustments for renal function with or without hemodialysis in the management of heparin-induced thrombocytopenia. The annals of Pharmacotherapy. 2011;45: 1185-1192 6. Sangali F, Patroniti N, Pesenti A. ECMO – Extracorporeal Life Support in Adults. 2014. Springer Verlag: Italy 7. University of Washington Medicine. Bivalirudin Dosing Algorithm. https://depts.washington.edu/anticoag/home 8. UC Davis Medical Health. Guideline for bivalirudin dosing in HIT/HITTS. 2014. https://www.ucdmc.ucdavis.edu/anticoag/pdf/BivalirudinHIT.pdf 9. Gilmore J, Adams C, Blum R, Fanikos J, Hirning B, Matta L. Evaluation of a multi-target direct thrombin inhibitor dosing and titration guideline for patients with suspected heparin-induced thrombocytopenia. 2015. American Journal of Hematology. 90;8: E143-E145 10. Runyan C, Cabral K, Riker R, Redding D, May T, Seder D, Savic M, Hedlund J, Abramson S, Fraser G. Correlation of bivalirudin dose with creatinine clearance during treatment of heparin-induced thrombocytopenia. American Journal of Hematology. 2011;31 (9): 850-856 11. UpToDate. Bivalirudin: Drug information. 2017. www.uptodate.com.acs.hcn.com.au 12. Joseph L, Casanegra M, Dhariwal M, Smith M, Raju M, Militello M, Gomes M, Gorink H, Bartholomew J. Bivalirudin for the treatment of patients with confirmed or suspected heparin-induced thrombocytopenia. Journal of Thrombosis and Haemostasis. 2014;12: 1044-1053 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.

Bivalirudin for Heparin induced Thrombocytopenia (HIT)

AUTHORISATION	
Author (Name)	Charles Shuttleworth
Position	Staff Specialist Haematology
Department	Haematology Department
Department Contact	Charles Shuttleworth charles.shuttleworth@health.nsw.gov.au

GOVERNANCE	
Enactment date *Reviewed* (Version 2) *Reviewed* (Version 3)	July 2021 July 2022 February 2023
Expiry date:	February 2025
Ratification date by SESLHD DTC	2nd March 2023
Chairperson, DTC	Dr John Shephard
Version Number	3