GUIDELINE FOR BIVALIRUDIN DOSING IN HIT/HITTS

Immune Mediated Heparin Induced Thrombocytopenia (HIT) is a hypercoaguable condition occurring with recent exposure to a heparin based anticoagulant. Patients who are diagnosed or have a high suspicion for heparin induced thrombocytopenia with/without thrombosis (HITTS) should have all forms of heparin discontinued (including low molecular weight heparins) and initiate an alternative anticoagulant. Direct thrombin inhibitors (DTI) are the recommended alternative anticoagulant.

Currently **Bivalirudin** is the DTI of choice at UCDMC. Bivalirudin has the shortest half-life among all DTI's with lower dependence on renal or liver function for removal (~80% enzymatic) which is a benefit in patients who have a high risk of bleeding, organ failure, or who may require an invasive procedure.

The dosing presented below is a guide to aid in the initiation of Bivalirudin infusion; however alterations may occur based on the clinical presentation of the patient. All other uses including for surgical procedures/intraoperative use, call Anticoagulation Service.

Bivalirudin initial dosing guide: (*Note this is not the package insert dose)*

- Range: 0.03-0.2 mg/kg/hr
  - *If deemed necessary by physician, bolus dose: 0.1-0.2 mg/kg*
- **Dose reduction is recommended** in patients with hepatic or renal failure, critically ill or very high bleeding risk—please see below for guidance.

CrCL (ml/min)	Bivalirudin Initial Dose (mg/kg/hr)
>60	0.13 ± 0.1
30-60	0.08 ± 0.04
<30	0.05 ± 0.02
IHD	0.07 ± 0.03
SLEDD	0.09 ± 0.03
CRRT	0.07 ± 0.02

IHD: Intermittent Hemodialysis
SLEDD: Sustained Low Efficiency Daily Diafiltration
CRRT: Continuous Renal Replacement Therapy

Bivalirudin dosing weight is based on total body weight (TBW) minus any excess fluid weight from anasarca.
CrCL is based on a stable serum creatinine using total body weight (TBW) for calculations.

Dose Adjustments:

- CrCL > 30 ml/min
  - aPTT values 1-15 seconds outside of target→ adjust by 1mg/hr of the initial infusion rate
  - aPTT values 16-30 seconds outside of target→ adjust by 2mg/hr of the initial infusion rate
- CrCL <30 ml/min, IHD, SLEDD, CRRT
  - aPTT values 1-15 seconds outside of target→ adjust by 0.5mg/hr of the initial infusion rate
  - aPTT values 16-30 seconds outside of target→ adjust by 1 mg/hr of the initial infusion rate
- Low weight <50 kg
  - aPTT values 1-15 seconds outside of target→ adjust by 0.5mg/hr of the initial infusion rate
  - aPTT values 16-30 seconds outside of target→ adjust by 1 mg/hr of the initial infusion rate

Monitoring:

- Request aPTT 4 hours post starting the infusion. Target aPTT is 1.5-2.5 times baseline value (see below for select populations).
  - In high bleeding risk patients, a Q2 hour aPTT x3 draws is suggested to evaluate response
- INR every day with (morning) aPTT
- CBC/Platelets/aPTT 4 hours post each rate adjustment and every morning

- Do not stop the DTI infusion simply because the INR increases (no warfarin); If the INR exceeds baseline INR by 0.5 with an aPTT that is not excessively elevated, call the pharmacy for further assessment. DTI including Bivalirudin can cause a false positive increase in the INR.

Populations of importance:

- **Critically Ill:** Patients often have renal and/or hepatic dysfunction, anasarca, and are thought to be of high-bleeding risk. The risk for bleeding versus thrombosis must be evaluated to determine goal aPTT levels that are safe and effective for treatment. Consider the following:
  - **High risk of bleeding:** adjust aPTT to 1.5-2.0x normal
  - **High risk of clotting or active HITTS:** adjust aPTT to 2.0-2.5x normal
- **Renal dysfunction:** Patients are already at a higher risk of bleeding due to some accumulation of drug and if they require renal replacement therapy, conservative dosing should be considered. Bivalirudin can partially be removed during dialysis.
  - **Dosing:** use the above dosing guide and titrate to goal aPTT
- **Hepatic dysfunction:** Similar to renal dysfunction patients, clearance of the drug as well as coagulation factors are impaired, conservative dosing should be considered
  - **Dosing:** Call the Anticoagulation Service for dosing assistance
- **Transitioning from another agent to Bivalirudin**
  - Currently receiving another long acting anticoagulant (dalteparin, dabigatran, enoxaparin, rivaroxaban, apixaban):
    - Initiate Bivalirudin infusion initiation, monitor aPTT, signs and symptoms of bleeding
    - Discontinue the long acting anticoagulant
  - Transferred from OSH on Argatroban:
    - Obtain baseline aPTT from OSH, or if unable to obtain, use mean hospital baseline aPTT (30 seconds)
    - Start Bivalirudin infusion with the above dosing guide at time of stopping other long acting anticoagulant
  - Warfarin
    - Stop warfarin therapy
    - Call the Anticoagulation Service for additional suggestions
    - Vitamin K may be considered to reverse INR
  - Fondaparinux
    - In selected situations in consultation with the Anticoagulation Service or Heme-Onc Consult Services.
    - Fondaparinux may be an alternative anticoagulation option

References:

1. Tsu LV and Dager WE. Bivalirudin dosing adjustments for reduced renal function with or without hemodialysis in the management of heparin induced thrombocytopenia. Ann Pharmacother 2011;45:1185-1192.
2. Kiser TH and Fish DN. Evaluation of Bivalirudin treatment for heparin-induced thrombocytopenia in critically ill patients with hepatic and/or renal dysfunction. Pharmacotherapy 2006;26(4);452-460.

Approved by UCDHS P&T Committee 5/2014.