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.

<table>
<thead>
<tr>
<th>CrCL (ml/min)</th>
<th>Bivalirudin Initial Dose (mg/kg/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>0.13 ± 0.1</td>
</tr>
<tr>
<td>30-60</td>
<td>0.08 ± 0.04</td>
</tr>
<tr>
<td>&lt;30</td>
<td>0.05 ± 0.02</td>
</tr>
<tr>
<td>IHD</td>
<td>0.07 ± 0.03</td>
</tr>
<tr>
<td>SLEDD</td>
<td>0.09 ± 0.03</td>
</tr>
<tr>
<td>CRRT</td>
<td>0.07 ± 0.02</td>
</tr>
</tbody>
</table>

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:


Approved by UCDHS P&T Committee 5/2014.