Heparin Induced Thrombocytopenia (HIT) Treatment

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant women.

### Four T’s

- **Monitor platelets and signs and symptoms of thrombosis and continue heparin.**
- **If patient on warfarin, consider reversing with vitamin K 10 mg PO or 5-10 mg IV.**
- **Check heparin antibody (platelet heparin antibody).**
- **DO NOT use prophylactic platelet transfusions until HIT is ruled out.**

### HIT Algorithm

1. **Estimate probability of HIT using the “Four T’s”**
   - Low (score 0-3)
   - Intermediate (score 4-5) or
   - High (score 6-8)

2. **Document HIT in electronic health record (EHR) and in allergies.**
   - Place “NO HEPARIN – HIT” sign clearly visible above patient’s bed and
   - Patient with ACS with or without recent heparin

3. **Non-acute coronary syndrome (ACS)**
   - With normal liver function
   - Hepatic dysfunction
     - Total bilirubin greater than or equal to 1.5 mg/dL
     - Patient with ACS with or without percutaneous coronary intervention

4. **Check heparin antibody**
   - Discontinue all subcutaneous heparin
   - Discontinue direct oral anticoagulant (DOAC) medications
   - Discontinue all bivalirudin
   - Argatroban (see Appendix A for dosing)
   - Bivalirudin (see Appendix A for dosing)

5. **Patient’s platelet count recovered to at least 150 K/microliter?**
   - Yes: See Page 2 for transition to alternate anticoagulant
   - No: Continue current treatment and monitoring

### HIT Algorithm Table

<table>
<thead>
<tr>
<th>Four T’s</th>
<th>Low (score 0-3)</th>
<th>Intermediate (score 4-5) or High (score 6-8)</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>Platelet count fall &gt; 50% and Nadir ≥ 20 K/microliter</td>
<td>Platelet count fall 30-50% (or platelet fall &gt; 50% due to surgery), or Nadir 10-19 K/microliter</td>
<td>Platelet fall &lt; 30% or Nadir &lt; 10 K/microliter</td>
<td></td>
</tr>
<tr>
<td>Timing of platelet fall onset</td>
<td>Onset between Days 5-10 or Platelet count fall than or equal to Day 1 with recent heparin (past 30 days)</td>
<td>Onset after Day 10 or timing unclear, or Platelet count fall less than or equal to Day 1 with recent heparin (past 31-100 days)</td>
<td>Platelet count fall less than Day 4 without recent heparin</td>
<td></td>
</tr>
<tr>
<td>Thrombosis or other sequelae</td>
<td>Proven new thrombosis or skin necrosis; or Acute anaphylactoid reaction after IV heparin bolus</td>
<td>Progressive or recurrent thrombosis; erythematous skin lesions, suspected thrombosis (not proven); asymptomatic upper-limb deep vein thrombosis (DVT)</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Other causes</td>
<td>None evident</td>
<td>Possible</td>
<td>Definite</td>
<td></td>
</tr>
</tbody>
</table>

### Notes

- * First day of immunizing heparin exposure = Day 0
- 1 Use of bivalirudin for non-ACS is not an FDA approved indication
- 2 Examples of other causes include, but are not limited to: chemotherapy, drug-related, sepsis, disseminated intravascular coagulation (DIC)

*The Four T’s – add the values from each “T” category based on presence of criteria.*

Department of Clinical Effectiveness V8
Approved by the Executive Committee of Medical Staff on 11/19/2019
Begin warfarin $^1$ 2.5-5 mg PO daily
Turn argatroban infusion off and begin fondaparinux$^2$ at treatment doses
- Weight $< 50$ kg: 5 mg SQ
- Weight 50-100 kg: 7.5 mg SQ
- Weight $> 100$ kg: 10 mg SQ
After a minimum 5-day overlap of fondaparinux and warfarin, discontinue fondaparinux when the INR is between 2-3 and continue with warfarin monotherapy$^1$

Transition from argatroban to warfarin$^1$

Transition from bivalirudin to warfarin$^1$

Transition from bivalirudin or argatroban to DOAC or fondaparinux

Preferred

Alternative

• Begin warfarin$^1$ 2.5-5 mg PO daily and overlap with argatroban for a minimum of 5 days
• If argatroban rate $\leq 2$ mcg/kg/minute and INR $> 4$, stop infusion and obtain INR 4 hours after stopping infusion
  - INR 2-3: continue with warfarin monotherapy
  - INR $< 2$: restart argatroban and repeat above steps the following day
• If argatroban rate $> 2$ mcg/kg/minute, reduce dose to 2 mcg/kg/minute for 4 hours and obtain INR (infusion rate can return to baseline after INR drawn)
  - If INR $\leq 4$: continue concomitant therapy
  - If INR $> 4$: stop argatroban and obtain another INR 4 hours after stopping infusion
  - INR 2-3: continue with warfarin monotherapy
  - INR $< 2$: restart argatroban and repeat above steps the following day

Stop bivalirudin or argatroban infusion and begin DOAC or fondaparinux within 2 hours (see Appendix B for dosing)

$^1$ When initiating the transition to warfarin therapy DO NOT use a loading dose. The recommended maximum initial dose of warfarin is 5 mg. Overlap warfarin therapy with direct thrombin inhibitor (DTI) continuous infusion for at least 5 days.

$^2$ In patients with normal renal function (creatinine clearance $> 50$ mL/minute). Use caution in creatinine clearance 30-50 mL/minute and use is contraindicated in creatinine clearance $< 30$ mL/minute.

$^3$ Treat with warfarin for 4 weeks, unless there is an indication for long-term anticoagulation (e.g., active venous thromboembolism (VTE) or chronic atrial fibrillation)
### APPENDIX A: Direct Thrombin Inhibitor (DTI) Dosing and Monitoring

<table>
<thead>
<tr>
<th>DTI</th>
<th>Special dosing parameters</th>
<th>Dose</th>
<th>Monitoring</th>
<th>Notes and special considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argatroban</td>
<td>Normal dosage</td>
<td>2 mcg/kg/minute</td>
<td>aPTT 2 hours after initiation and dose change</td>
<td>Use of this medication causes significant elevation of PT/INR results due to interference with testing</td>
</tr>
<tr>
<td></td>
<td>Consider dosage reduction with the following:</td>
<td></td>
<td></td>
<td>Do not discontinue this medication based on an elevated INR value</td>
</tr>
<tr>
<td></td>
<td>• Child-Pugh(^1) score &gt; 6.</td>
<td></td>
<td></td>
<td>Continue to monitor the patient for signs and symptoms of bleeding</td>
</tr>
<tr>
<td></td>
<td>• Total bilirubin &gt; 1.5 mg/dL.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Heart failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Multi-organ system failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Severe anasarca</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Status post cardiac surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bivalirudin</td>
<td><strong>Dose for HIT:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Normal renal function</td>
<td>0.15 mg/kg/hour</td>
<td>aPTT 2 hours after initiation and dose change</td>
<td>Use of this medication, causes mild elevation of PT/INR results due to interference with testing</td>
</tr>
<tr>
<td></td>
<td>Creatinine clearance &lt; 30 mL/minute</td>
<td>0.08 mg/kg/hour</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patient on dialysis</td>
<td>0.02 mg/kg/hour</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Dose for ACS with or without percutaneous coronary intervention:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Normal renal function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Creatinine clearance &lt; 30 mL/minute</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patient on dialysis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 See Appendix C for Child-Pugh Scoring System
## APPENDIX B: Non-heparin Anticoagulants Dosing and Monitoring

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Primary mechanism of elimination</th>
<th>Dosing</th>
<th>Laboratory monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fondaparinux</td>
<td>Indirect factor Xa inhibitor</td>
<td>Renal (17-24 hours)</td>
<td>● Weight &lt; 50 kg: 5 mg subcutaneously daily&lt;br&gt;● Weight 50-100 kg: 7.5 mg subcutaneously daily&lt;br&gt;● Weight &gt; 100 kg: 10 mg subcutaneously daily</td>
<td>None</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Direct factor Xa inhibitor</td>
<td>Hepatic (8-15 hours)</td>
<td>Heparin induced thrombocytopenia with thrombosis (HITT):&lt;br&gt;● 10 mg PO twice daily for 1 week then, 5 mg PO daily&lt;br&gt;Isolated HIT:&lt;br&gt;● 5 mg PO twice daily until platelet recovery</td>
<td>None</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>Direct factor Xa inhibitor</td>
<td>Renal (12-17 hours)</td>
<td>HITT:&lt;br&gt;● 150 mg PO twice daily after ≥ 5 days of treatment with a parenteral non-heparin anticoagulant&lt;br&gt;Isolated HIT:&lt;br&gt;● 150 mg PO twice daily until platelet recovery</td>
<td>None</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Direct factor Xa inhibitor</td>
<td>Renal (5-9 hours)</td>
<td>HITT:&lt;br&gt;● 15 mg PO twice daily for 3 weeks then, 20 mg PO daily thereafter&lt;br&gt;Isolated HIT:&lt;br&gt;● 15 mg PO twice daily until platelet recovery</td>
<td>None</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>No information available, therefore no recommendation can be made</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:**
- Considerations for transitioning to DOACs or fondaparinux:
  - Only if patient is clinically stable (hemodynamic stability, no dialysis, no liver failure, non-surgical) and at average risk of bleeding
  - No data exists for use in patients requiring dialysis
  - Not approved for treatment of acute HIT. Suggested dosing is extrapolated from venothromboembolism (VTE) trials and based on the limited published experience in HIT.
- The choice of agent maybe influenced by drug factors (cost, ability to monitor anticoagulants effects, route of administration, half-life, drug-drug interactions) and patient factors (kidney dysfunction, liver dysfunction, bleeding risk, clinical stability) and experience of the clinician.

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### APPENDIX C: Child-Pugh Scoring System

<table>
<thead>
<tr>
<th>Chemical and biochemical parameters</th>
<th>Scores (points) for increasing abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
</tr>
<tr>
<td>Albumin</td>
<td>&gt; 3.5 g/dL</td>
</tr>
<tr>
<td>Bilirubin in primary biliary cirrhosis</td>
<td>&lt; 2 mg/dL</td>
</tr>
<tr>
<td></td>
<td>1 - 4 mg/dL</td>
</tr>
<tr>
<td>Prothrombin time prolonged or INR</td>
<td>1 - 4 seconds</td>
</tr>
<tr>
<td></td>
<td>&lt; 1.7</td>
</tr>
</tbody>
</table>

1 Child-Pugh score is obtained by adding the score for each parameter.

Child-Pugh class:
- Class A = 5 to 6 points
- Class B = 7 to 9 points
- Class C = 10 to 15 points

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SUGGESTED READINGS


DEVELOPMENT CREDITS

This practice consensus statement is based on majority opinion of the anticoagulant experts at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

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