Heparin Induced Thrombocytopenia (HIT) Treatment

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### Low¹
(score 0-3)

- Monitor platelets and signs and symptoms of thrombosis and continue heparin
- Consider Benign Hematology consult
- Discontinue all subcutaneous heparin/heparin flushes, low molecular weight heparins, and warfarin
- Discontinue direct oral anticoagulant (DOAC) medications
- If patient on warfarin, consider reversing with vitamin K 10 mg PO or 5-10 mg IV
- Check heparin antibody (platelet heparin antibody)
  - For Intermediate (score 4-5) and positive heparin antibody, check serotonin release assay (SRA)²
  - **DO NOT use prophylactic platelet transfusions until HIT is ruled out**

### Intermediate¹,²
(score 4-5) or High¹ (score 6-8)

- Non-acute coronary syndrome (ACS)³ with normal liver function
- Hepatic dysfunction with total bilirubin > 1.5 mg/dL. or patient with ACS with/without percutaneous coronary intervention
- Argatroban (see Appendix A for dosing)
- Bivalirudin (see Appendix A for dosing)

### Thrombocytopenia

<table>
<thead>
<tr>
<th>Category</th>
<th>Platelet count fall</th>
<th>Nadir</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>≥ 50% and</td>
<td>≥ 20 K/microliter</td>
</tr>
<tr>
<td>1</td>
<td>30-50% (or platelet fall ≥ 50% due to surgery), and</td>
<td>10-19 K/microliter</td>
</tr>
<tr>
<td>0</td>
<td>&lt; 30% or</td>
<td>&lt; 10 K/microliter</td>
</tr>
</tbody>
</table>

### Timing

<table>
<thead>
<tr>
<th>Category</th>
<th>Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Between Days 5-10 and</td>
</tr>
<tr>
<td>1</td>
<td>Day 1 with recent heparin (past 30 days)</td>
</tr>
<tr>
<td>0</td>
<td>Day 10 or timing unclear, and</td>
</tr>
<tr>
<td></td>
<td>Day 1 with recent heparin (past 31-100 days)</td>
</tr>
</tbody>
</table>

### Thrombosis or other sequelae

- Proven new thrombosis or skin necrosis; or acute anaphylactoid reaction after IV heparin bolus
- Progressive or recurrent thrombosis; erythematous skin lesions, suspected thrombosis (not proven); asymptomatic upper-limb deep vein thrombosis (DVT)
- None

### Other causes

- None evident
- Possible
- Definite

¹ The Four T’s – add the values from each “T” category based on presence of criteria

² In patients with a Four T score of Intermediate (4-5) and a positive heparin antibody, a negative SRA rules out HIT and a positive SRA confirms HIT

³ Use of bivalirudin for non-ACS is not an FDA approved indication

Examples of other causes include, but are not limited to: chemotherapy, drug-related, sepsis, disseminated intravascular coagulation (DIC)

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Appendix A

See Page 2 for transition to alternate anticoagulant

Continue current treatment and monitoring

Department of Clinical Effectiveness
Approved by the Executive Committee of Medical Staff on 02/18/2020

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Heparin Induced Thrombocytopenia (HIT) Treatment

Transition from argatroban to warfarin¹
- **Preferred**
  - Begin warfarin¹ 2.5-5 mg PO daily
  - Turn argatroban infusion off and begin fondaparinux² 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 monotherapy³

- **Alternative**
  - Begin warfarin¹ 2.5-5 mg PO daily and overlap with argatroban for a minimum of 5 days
  - If argatroban rate ≤ 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 ≤ 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

Transition from bivalirudin to warfarin¹
- **Preferred**
  - Stop bivalirudin or argatroban infusion and begin DOAC or fondaparinux within 2 hours (see Appendix B for dosing)

Patient’s platelet count recovered to ≥ 150 K/microliter

Transition from bivalirudin or argatroban to DOAC or fondaparinux

¹When 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.
²In 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.
³Treat with warfarin for 4 weeks, unless there is an indication for long-term anticoagulation (e.g., active venous thromboembolism (VTE) or chronic atrial fibrillation)

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## 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 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>Dose for HIT:</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>Dose for ACS with or without percutaneous coronary intervention:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Normal renal function</td>
<td>Bolus dose 0.75 mg/kg,</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Creatinine clearance &lt; 30 mL/minute</td>
<td>followed by 1.75 mg/kg/hour</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Patient on dialysis</td>
<td>Bolus dose 0.75 mg/kg,</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>followed by 0.25 mg/kg/hour</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metabolized by proteolytic cleavage with 20% renal elimination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Note</strong>: Use of bivalirudin for non-ACS is not an FDA approved indication</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 See Appendix C for Child-Pugh Scoring System

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### 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>
</table>
| Fondaparinux | Indirect factor Xa inhibitor | Renal (17-24 hours)             | - Weight < 50 kg: 5 mg subcutaneously daily  
- Weight 50-100 kg: 7.5 mg subcutaneously daily  
- Weight > 100 kg: 10 mg subcutaneously daily | None                  |
| Apixaban     | Direct factor Xa inhibitor | Hepatic (8-15 hours)            | Heparin induced thrombocytopenia with thrombosis (HITT):  
- 10 mg PO twice daily for 1 week, then 5 mg PO twice daily  
Isolated HIT:  
- 5 mg PO twice daily until platelet recovery | None                  |
| Dabigatran   | Direct factor Xa inhibitor | Renal (12-17 hours)             | HITT:  
- 150 mg PO twice daily after ≥ 5 days of treatment with a parenteral non-heparin anticoagulant  
Isolated HIT:  
- 150 mg PO twice daily until platelet recovery | None                  |
| Rivaroxaban  | Direct factor Xa inhibitor | Renal (5-9 hours)               | HITT:  
- 15 mg PO twice daily for 3 weeks then, 20 mg PO daily thereafter  
Isolated HIT:  
- 15 mg PO twice daily until platelet recovery | None                  |
| Edoxaban     | No information available, therefore no recommendation can be made |                                   |                                                                       | None                  |

**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.
### 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</td>
<td>&lt; 2 mg/dL</td>
</tr>
<tr>
<td></td>
<td>1 - 4 mg/dL</td>
</tr>
<tr>
<td>Prothrombin time prolonged or</td>
<td>1 - 4 seconds</td>
</tr>
<tr>
<td>INR</td>
<td>&lt; 1.7</td>
</tr>
</tbody>
</table>

1. Child-Pugh score is obtained by adding the score for each parameter
2. Child-Pugh class:
   - Class A = 5 to 6 points
   - Class B = 7 to 9 points
   - Class C = 10 to 15 points
SUGGESTED READINGS


Heparin Induced Thrombocytopenia (HIT) Treatment

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:

Parvaneh Erfan, BS, AS (Core Lab)
Shuwei Gao, MD (General Internal Medicine)
Wendy Garcia, BS*
Xin Han, MD (Laboratory Medicine)
Cheryl F. Hirsch-Ginsberg, MD (Laboratory Medicine)
Sandra B. Horowitz, PharmD (Pharmacy)
Michael Kroll, MD (Benign Hematology)†
Amy Pai, PharmD*
Katy M. Toale, PharmD (Pharmacy)
Mary Lou Warren, DNP, RN, CNS-CC*
Ali Zalpour, PharmD (Pharmacy)

† Core Development Team Leads
* Clinical Effectiveness Development Team

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