Heparin Induced Thrombocytopenia (HIT) Treatment

This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant women.

Documentation:
- Place “NO HEPARIN – HIT” sign clearly visible above patient’s bed and
- Document HIT in medical record and in allergies

Non-acute coronary syndrome (ACS)²
- with normal liver function
- Hepatic dysfunction with total bilirubin greater than 1.5 mg/dL² or
- patient with ACS with/without percutaneous coronary intervention

Monitor platelets and signs and symptoms of thrombosis and continue heparin

Consult benign hematology
- Discontinue all subcutaneous heparin/heparin flushes, low molecular weight heparins, and warfarin
- Discontinue the following direct oral anticoagulant (DOAC) medications: dabigatran, edoxaban, rivaroxaban, and apixaban
- 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

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The Four ‘T’s’
- Thrombocytopenia
- Timing
- Thrombosis or other sequelae
- Other causes

<table>
<thead>
<tr>
<th>2</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>Greater than 50% platelet fall and nadir greater than or equal to 20 K/microliter</td>
<td>30-50% platelet fall (or greater than 50% platelet fall due to surgery), or nadir 10-19 K/microliter</td>
</tr>
<tr>
<td>Timing* of onset of platelet fall</td>
<td>Days 5-10 or less than or equal to Day 1 with recent heparin (past 30 days)</td>
<td>Greater than Day 10 or timing unclear, or less than Day 1 with recent heparin (past 31-100 days)</td>
</tr>
<tr>
<td>Thrombosis or other sequelae</td>
<td>Proven new thrombosis, 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 DVT</td>
</tr>
<tr>
<td>Other causes</td>
<td>None evident</td>
<td>Possible</td>
</tr>
</tbody>
</table>

* First day of immunizing heparin exposure = Day 0

² 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)

Documentation:
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- Document HIT in medical record and in allergies

Intermediate¹
- (score 4-5) or
- High¹ (score 6-8)

Low¹
- (score 0-3)

Patient’s platelet count recovered to at least 150 K/microliter?

Bivalirudin (Angiomax®) (see Appendix A for dosing)

Argatroban (see Appendix A for dosing)

Yes → See Page 2 for transition to warfarin

No → Continue current treatment and monitoring

1 The Four ‘T’s’ – add the values from each “T” category based on presence of criteria
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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 greater than 50 mL/minute). Use caution in creatinine clearance 30-50 mL/minute and use is contraindicated in creatinine clearance less than 30 mL/minute.

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

4. See Adult Venous Thromboembolism (VTE) Treatment for Cancer Patients Algorithm for standard dosing for DOAC: apixaban, dabigatran, edoxaban, and rivaroxaban.

Patient’s platelet count recovered to at least 150 K/microliter

Method to transition from argatroban to warfarin

- Begin warfarin 2.5-5 mg PO daily
- Turn argatroban infusion off and begin fondaparinux at treatment doses
  - Less than 50 kg: 5 mg SQ; between 50-100 kg: 7.5 mg SQ; greater than 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

Preferred

Alternative

Transition from bivalirudin

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

Transition from bivalirudin (Angiomax®) to warfarin

- Stop bivalirudin infusion and obtain INR 4 hours after stopping infusion
  - INR 2-3: continue with warfarin monotherapy
  - INR less than 2: restart bivalirudin and repeat above steps the following day

Transition from bivalirudin (Angiomax®) or argatroban to DOAC

- Stop bivalirudin or argatroban infusion and begin DOAC (apixaban, dabigatran, edoxaban, and rivaroxaban) after 2 hours

1, 3

Applies to patients with normal renal function

2
**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>Reduced dosage</td>
<td>0.5 mcg/kg/minute</td>
<td></td>
<td>- Do not discontinue this medication based on an elevated INR value. Continue to monitor the patient for signs and symptoms of bleeding</td>
</tr>
<tr>
<td></td>
<td>Child-Pugh score greater than 6, total bilirubin greater than 1.5 mg/dL, heart failure, multiple organ system failure, severe anasarca, or status post cardiac surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bivalirudin (Angiomax®)</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></td>
</tr>
<tr>
<td></td>
<td>- Creatinine clearance less than 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, followed by 1.75 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>
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<tr>
<td></td>
<td>- Creatinine clearance less than 30 mL/minute</td>
<td>Bolus dose 0.75 mg/kg, followed by 1 mg/kg/hour</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>- Patient on dialysis</td>
<td>Bolus dose 0.75 mg/kg, followed by 0.25 mg/kg/hour</td>
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</table>

1See Appendix B for Child-Pugh Scoring System
APPENDIX B: 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>Greater than 3.5 g/dL</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>1 – 2 mg/dL</td>
</tr>
<tr>
<td>For primary biliary cirrhosis</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>Less than 1.7</td>
</tr>
</tbody>
</table>

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
SUGGESTED READINGS


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
- Shuwei Gao, MD
- Wendy Garcia, BS
- Xin Han, MD
- Wendy D. Heck, PharmD
- Cheryl F. Hirsch-Ginsberg, MD
- Sandra B. Horowitz, PharmD
- Michael Kröll, MD
- Laura L. Michaud, PharmD
- Amy Pai, PharmD
- Katy M. Toale, PharmD
- Mary Lou Warren, DNP, RN, CNS-CC, CCNS
- Ali Zalpour, PharmD

† Core Development Team Leads
* Clinical Effectiveness Development Team

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