Heparin Induced Thrombocytopenia (HIT) Treatment

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- **Estimate probability of HIT using the “Four T’s”**:  
  - Low  
  - Intermediate  
  - High

- **Monitor platelets and signs and symptoms of thrombosis and continue/restart heparin**

  - Consider Benign Hematology consult
  - Discontinue all heparin/heparin flushes, low molecular weight heparins, and warfarin
  - If patient on warfarin, consider reversing with vitamin K 10 mg PO or 5-10 mg IV
  - Check heparin antibody (Heparin Induced Ab)
  - Document diagnosis of HIT on the problem list and add heparin to the allergy list with a comment noting patient has HIT
  - Initiate therapeutic dose of a non-heparin anticoagulant
    - Critically ill patients or patients with high bleeding risk, potential for urgent procedures, life or limb threatening thrombosis present, or requiring dialysis: Argatroban or bivalirudin (see Appendix B)
    - Stable patients without a high risk for bleeding: Rivaroxaban, apixaban, dabigatran or fondaparinux (see Appendix C)
    - Moderate to severe hepatic dysfunction: AVOID argatroban, rivaroxaban, apixaban, and dabigatran
    - Moderate to severe renal dysfunction: AVOID fondaparinux and dabigatran

- **Heparin Induced Ab negative?**
  - Yes
    - Stop non-heparin anticoagulation
    - Monitor platelets and signs and symptoms of thrombosis and restart heparin as indicated
  - No
    - Intermediate  
      - Yes
        - Check serotonin release assay (SRA) to confirm diagnosis
      - No
        - Continue non-heparin anticoagulation
          - Bilateral lower extremity ultrasound to screen for deep vein thrombosis (DVT)
          - If non-femoral central venous access present, bilateral upper extremity ultrasound to screen for DVT
          - Transition anticoagulant when platelet count ≥ 150 K/microliter (see Appendix D)
          - Discontinue all heparin/heparin flushes and low molecular weight heparins from home medication list
          - Outpatient follow up as clinically indicated

  - No
    - Yes
      - Stop non-heparin anticoagulation
      - Monitor platelets and signs and symptoms of thrombosis and restart heparin as indicated
    - No
      - Intermediate  
        - Yes
          - Check serotonin release assay (SRA) to confirm diagnosis
        - No
          - Continue non-heparin anticoagulation
            - Bilateral lower extremity ultrasound to screen for deep vein thrombosis (DVT)
            - If non-femoral central venous access present, bilateral upper extremity ultrasound to screen for DVT
            - Transition anticoagulant when platelet count ≥ 150 K/microliter (see Appendix D)
            - Discontinue all heparin/heparin flushes and low molecular weight heparins from home medication list
            - Outpatient follow up as clinically indicated

1. See Appendix A: The Four T's
**APPENDIX A: The Four T’s**

To calculate the probability score, add the values from each “T” category based on presence of criteria

<table>
<thead>
<tr>
<th>Score 0-3: Low probability</th>
<th>Score 4-5: Intermediate probability</th>
<th>Score 6-8: High probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Platelet count fall  &gt; 50% and</td>
<td>Platelet count fall 30-50% (or platelet fall &gt; 50% due to surgery), or</td>
</tr>
<tr>
<td></td>
<td>Nadir ≥ 20 K/microliter</td>
<td>Nadir 10-19 K/microliter</td>
</tr>
<tr>
<td>Timing * of platelet</td>
<td>Onset between Days 5-10 or</td>
<td>Onset after Day 10 or timing unclear, or</td>
</tr>
<tr>
<td>fall onset</td>
<td>Platelet count fall ≤ Day 1 with recent heparin (past 30 days)</td>
<td>Platelet count fall ≤ Day 1 with recent heparin (past 31-100 days)</td>
</tr>
<tr>
<td>Thrombosis or other</td>
<td>Proven new thrombosis or skin necrosis; or</td>
<td>Progressive or recurrent thrombosis; erythematous skin lesions, suspected thrombosis (not proven); asymptomatic upper-limb deep vein thrombosis (DVT)</td>
</tr>
<tr>
<td>sequelae</td>
<td>Acute anaphylactoid reaction after IV heparin bolus</td>
<td></td>
</tr>
<tr>
<td>OTher causes   *</td>
<td>None</td>
<td>Possible</td>
</tr>
</tbody>
</table>

* First day of immunizing heparin exposure = Day 0

1 Examples of other causes include, but are not limited to: chemotherapy, drug-related, sepsis, disseminated intravascular coagulation (DIC)
## APPENDIX B: Direct Thrombin Inhibitor (DTI) Dosing and Monitoring

<table>
<thead>
<tr>
<th>DTI</th>
<th>Special dosing parameters</th>
<th>Dose</th>
<th>Monitoring¹</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>• Baseline: Hgb/Hct, platelet count, aPTT/PT, serum creatinine, and hepatic function tests</td>
<td></td>
</tr>
<tr>
<td>Plasma half-life = 39-51 minutes (in healthy subjects)</td>
<td>AVOID or consider dosage reduction with the following:</td>
<td>0.5 mcg/kg/minute</td>
<td>• Therapeutic monitoring: aPTT 2 hours after initiation and dose changes to achieve specified</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Child-Turcotte-Pugh² score &gt; 6,</td>
<td></td>
<td>target range per protocol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Total bilirubin &gt; 1.5 mg/dL,</td>
<td></td>
<td>• Adverse effects monitoring: Hgb/Hct and platelet count daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Heart failure</td>
<td></td>
<td>• Use of this medication causes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Multi-organ system failure</td>
<td></td>
<td>significant elevation of PT/INR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Severe anasarca</td>
<td></td>
<td>results due to interference with testing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Status post cardiac surgery</td>
<td></td>
<td>• Do not discontinue this medication</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>based on an elevated INR value</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Continue to monitor the patient for</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>signs and symptoms of bleeding</td>
<td></td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>Normal renal function</td>
<td>0.15 mg/kg/hour</td>
<td>• Baseline: Hgb/Hct, platelet count, aPTT/PT, serum creatinine, and hepatic function tests</td>
<td></td>
</tr>
<tr>
<td>Plasma half-life = 25 minutes (in healthy subjects)</td>
<td>Creatinine clearance &lt; 30 mL/minute</td>
<td>0.08 mg/kg/hour</td>
<td>• Therapeutic monitoring: aPTT 2 hours after initiation and dose changes to achieve specified</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>target range per protocol</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Adverse effects monitoring: Hgb/Hct and platelet count daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metabolized by proteolytic cleavage with 20% renal elimination</td>
<td>Patient on dialysis</td>
<td>0.02 mg/kg/hour</td>
<td>Use of this medication causes mild elevation of PT/INR results due to interference with testing</td>
</tr>
</tbody>
</table>

¹ See the Anticoagulant Management and Required Laboratory Monitoring Policy (MD Anderson Institutional Policy #CLN0984)
² See Appendix E for Child-Turcotte-Pugh (CTP) Scoring System
Heparin Induced Thrombocytopenia (HIT) Treatment

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APPENDIX C: Non-heparin Anticoagulants Dosing and Monitoring

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing</th>
<th>Monitoring</th>
<th>Dose Adjustments/Considerations</th>
</tr>
</thead>
</table>
| Fondaparinux (Aniftra®) | Actual Body Weight:  
- < 50 kg: 5 mg subcutaneously daily  
- 50-100 kg: 7.5 mg subcutaneously daily  
- > 100 kg: 10 mg subcutaneously daily | Baseline: Hgb/Hct, platelet count, aPTT/PT, and SCr  
Therapeutic laboratory tests: Routine monitoring not required.  
However, antifactor Xa levels may be useful in certain high-risk patients (e.g., obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis)  
Inpatient: Hgb/Hct, platelet count, and SCr at least once weekly  
Outpatient: Hgb/Hct, platelet count, SCr, and hepatic function tests at least once yearly  
- If CrCl 30-60 mL/minute, SCr every 6 months  
- If CrCl < 30 mL/minute, SCr every 3 months | Use in liver disease:  
If CTP class C: use with caution  
Renal:  
If CrCl is between 30-50 mL/minute: use with caution  
If CrCl is < 30 mL/minute: contraindicated  
Weight:  
For BMI ≥ 40 kg/m²: no dose adjustment necessary  
Elderly:  
For age > 75 years: may have reduced clearance, use with caution |
| Apixaban (Eliquis®) | Heparin Induced Thrombotic Thrombocytopenia (HITT):  
5 mg PO twice daily until platelet recovery | Baseline: Hgb/Hct, platelet count, aPTT/PT, SCr, and hepatic function tests  
Therapeutic laboratory tests: Routine monitoring not required.  
Apixaban and rivaroxaban: Antifactor Xa levels may be useful in certain high-risk patients (e.g., obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis)  
Dabigatran: Thrombin time (TT) may be useful in certain high-risk patients (e.g., obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis)  
Inpatient: Hgb/Hct, platelet count, and SCr at least once weekly  
Outpatient: Hgb/Hct, platelet count, SCr, and hepatic function tests at least once yearly  
- If CrCl 30-60 mL/minute, SCr every 6 months  
- If CrCl < 30 mL/minute, SCr every 3 months | Use in liver disease:  
Apixaban: use in CTP class C not recommended and there is limited experience for use in class B  
Rivaroxaban: CTP class B or C: NOT recommended  
Dabigatran: No manufacturer recommendations  
Renal:  
Dabigatran: If CrCl is < 30 mL/minute: avoid use  
Significant drug-drug interactions:  
- Apixaban and rivaroxaban  
- P-glycoprotein  
- CYP 3A4  
Dabigatran  
- P-glycoprotein  
Class specific contraindications: moderate to severe mitral stenosis or mechanical heart valve |
| Rivaroxaban (Xarelto®) | HITT:  
15 mg PO twice daily for 3 weeks, then 20 mg PO daily  
Isolated HIT:  
15 mg PO twice daily until platelet recovery | No information available, therefore no recommendation can be made |
| Edoxaban | 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 | No information available, therefore no recommendation can be made |

1. Anticoagulant should continue if indication for long-term anticoagulation present.
2. See the Anticoagulant Management and Required Laboratory Monitoring Policy (MD Anderson Institutional Policy #CLN0984)
3. For concerns regarding affordability, consider submitting a test claim 48 hours prior to discharge via the Pharmacy Test Claim and Pre-Authorization Reports (PECON) (for inpatient use only)
4. Fondaparinux, apixaban, and rivaroxaban anti-Xa levels may be ordered as a send out lab using a miscellaneous test order and adding a note for Anti-Xa fondaparinux, Anti-Xa apixaban or Anti-Xa rivaroxaban assay as indicated
5. See Appendix E for Child-Turcotte-Pugh (CTP) Scoring System
6. Assessing for drug-drug interactions: Lexicomp® or Micromedex®
7. Dabigatran capsules should be swallowed whole and NOT opened, broken, crushed, or chewed
8. Not currently on MD Anderson Formulary

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Department of Clinical Effectiveness V10
Approved by the Executive Committee of Medical Staff on 01/18/2022
APPENDIX D: Transitioning Anticoagulants

- For patients with isolated HIT and no thrombosis continue anticoagulation at least until platelet count recovery
- Continue anticoagulation long-term if thrombosis present or other indication for anticoagulation (e.g., active deep vein thrombosis or chronic atrial fibrillation)
  - For patients on DOAC who require long-term therapy, DOAC may be continued
  - For patients on argatroban or bivalirudin, see table below on how to transition to warfarin or DOAC or fondaparinux
  - For patients on fondaparinux, may continue therapy for 3-6 months or see table below on how to transition to DOAC or warfarin

<table>
<thead>
<tr>
<th>Transitioning Anticoagulants</th>
<th>Preferred:</th>
</tr>
</thead>
</table>
| Argatroban to warfarin        | Begin warfarin 2.5-5 mg PO daily (maximum initial dose = 5 mg). Do not use loading dose.  
  - Turn argatroban infusion off and begin fondaparinux 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  
  Alternate:  
  - Begin warfarin 2.5-5 mg PO daily (maximum initial dose = 5 mg). Do not use loading dose. Overlap with argatroban for a minimum of 5 days.  
  - If argatroban dose ≤ 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 dose > 2 mcg/kg/minute, reduce dose to 2 mcg/kg/minute for 4 hours and obtain INR (infusion dose 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 |
| Bivalirudin to warfarin        | Begin warfarin 2.5-5 mg PO daily and overlap with bivalirudin for a minimum of 5 days  
  - Stop bivalirudin infusion and obtain INR 4 hours after stopping infusion  
    - INR 2-3: continue with warfarin monotherapy  
    - INR < 2: restart bivalirudin and repeat above steps the following day |
| Fondaparinux to warfarin      | Overlap fondaparinux with warfarin for at least 5 days and discontinue fondaparinux when INR is in therapeutic range for 24 hours |
| Bivalirudin or argatroban to  | Stop bivalirudin or argatroban infusion and begin apixaban, rivaroxaban, or fondaparinux within 2 hours (see Appendix B for dosing) |
| DOAC or fondaparinux          | N/A |
| Fondaparinux to DOAC          | Discontinue fondaparinux and start apixaban or rivaroxaban when the next dose of fondaparinux was to be administered |

**WARFARIN MONITORING**

- General INR goal: 2-3
- Mechanical aortic valve:  
  - INR goal: 2-3
- Mechanical mitral valve:  
  - INR goal: 2.5-3.5
- Baseline: Hgb/Hct, platelet count, PT/INR, and hepatic function tests
- Therapeutic laboratory tests:  
  - INR to achieve specified target range  
  - Inpatient: Hgb/Hct, platelet count, and INR at least once weekly  
  - Outpatient: INR every 3 months at a minimum; Hgb/Hct, platelet count, serum creatinine, and hepatic function tests at least once year

1 See the Anticoagulant Management and Required Laboratory Monitoring Policy (MD Anderson Institutional Policy #CLN0984)
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**APPENDIX E: Child-Turcotte-Pugh (CTP) Scoring System**

<table>
<thead>
<tr>
<th>Chemical and Biochemical Parameters</th>
<th>Points for Increasing Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>None</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>&gt; 3.5 g/dL</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>&lt; 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>&lt; 4 seconds</td>
</tr>
<tr>
<td></td>
<td>&lt; 1.7</td>
</tr>
</tbody>
</table>

1 CTP score is obtained by adding the score for each parameter.

CTP 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**


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:

- 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 Clinical Programs)
- Michael Kroll, MD (Benign Hematology)†
- Katy M. Toale, PharmD (Pharmacy Quality-Regulatory)†
- Mary Lou Warren, DNP, APRN, CNS-CC*
- Ali Zalpour, PharmD (Pharmacy Clinical Programs)

† Core Development Team Leads
* Clinical Effectiveness Development Team