Heparin-Induced Thrombocytopenia (HIT)

Overview
- Heparin-induced thrombocytopenia (HIT) is an immune-mediated reaction to heparin and platelet factor 4 (PF4) complexes resulting in a hypercoagulable state of platelet activation and thrombin generation.
- Low Molecular Weight Heparins (LMWHs) preferred over Unfractionated Heparin (UFH) for prophylaxis in orthopedic surgery patients because they are less frequently associated with HIT in that population.
- UFH is preferred over LMWH in the setting of renal insufficiency or fluctuating renal function, critical illness, body weight < 50 kg, when rapid reversal may be necessary, or when frequent monitoring of the intensity of anticoagulation is required.
- If left untreated, HIT carries a 30 – 50% risk of life or limb-threatening thromboembolic complications. For surveillance of this severe adverse drug reaction, platelet counts should be monitored while on heparin or LMWH therapy.
- As with all anticoagulation, therapy should be guided by consideration of bleeding risk versus coexisting thromboembolic risk.

Surveillance, Assessment and Treatment
- **Platelet Monitoring**
  - All patients on UFH or LMWH therapy should have a baseline platelet count
  - Subsequent platelet count monitoring for HIT surveillance should be considered as follows:

<table>
<thead>
<tr>
<th>If patients are receiving UFH or LMWH in populations with ≥ 1% risk of developing HIT:</th>
<th>In patient populations presumed to be at &lt;1% risk of developing HIT:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Platelet count monitoring should occur 24 hours after initiation (if able) and at least every 2-3 days between days 4 to 14 (or until UFH/LMWH is stopped, whichever occurs first). These populations include at least:</td>
<td>• Routine platelet count monitoring is not recommended for surveillance of HIT. Examples of such patient populations include:</td>
</tr>
<tr>
<td>▪ Postoperative patients</td>
<td>▪ Obstetric patients (other than those that are postoperative)</td>
</tr>
<tr>
<td>▪ Patients newly starting UFH or LMWH;</td>
<td>▪ Patients receiving heparin flushes</td>
</tr>
<tr>
<td>▪ Patients being initiated on UFH or LMWH and exposed to UFH in the last 100 days</td>
<td>▪ Outpatients on prolonged LMWH</td>
</tr>
<tr>
<td>▪ Patients being initiated on UFH or LMWH with unclear UFH exposure history</td>
<td>▪ Patients receiving fondaparinux</td>
</tr>
</tbody>
</table>

- **Other Considerations:**
  - While thrombocytopenia is the hallmark sign of HIT, evidence has demonstrated that thromboembolic complications may occur PRIOR to evidence of thrombocytopenia in up to 57% of HIT positive patients
  - In any patient where symptoms and signs develop (i.e. acute inflammatory, cardiorespiratory, neurologic symptoms, and/or abnormal skin reactions/lesions) within 30 min following an heparin product exposure, increased platelet count monitoring and HIT workup should be considered
  - If a patient meets suspicion based upon absolute thrombocytopenia (platelet count < 150,000 per mm^3) or relative thrombocytopenia (a decrease in the platelet count of > 50% from the highest count before the initiation of heparin therapy):
    - Use “Table 1. Recommendations based upon Pre-test HIT Risk and Probability” to guide testing and treatment considerations with the “Diagnostic Algorithm to Confirm or Rule Out Heparin–Induced Thrombocytopenia”
    - Consider use of a [pre-test probability score (click to go to calculator)](link) to determine likelihood of HIT based on various clinical factors available consider using the higher of the two scores if both are calculated and results are conflicting. Superiority has not been determined between these scoring systems.
      - Table 2. 4 T’s
      - Table 3. HIT Expert Probability (HEP) Score
  - **HIT is a CLINICAL DIAGNOSIS**
Diagnostic Algorithm to Confirm or Rule Out Heparin-Induced Thrombocytopenia (HIT)

Thrombocytopenia in a patient receiving:
- Unfractionated heparin (UFH)
- Low molecular weight heparin (LMWH), or
- Any heparin products (flushes, heparin-coated catheter, etc.)

High or intermediate clinical suspicion of HIT (See Table 1 for definition)

Discontinue ALL heparin or LMWH products and add “Heparin Allergy Pending” in patient allergy list

Low clinical suspicion of HIT (See Table 1 for definition)

Heparin or LMWH therapy may be continued. Continue to monitor platelets.

Consider alternative diagnosis. If clinical suspicion of HIT remains high, see high/intermediate risk algorithm.

Calculate Pre-Test Probability (See Table 2 and/or 3)

If warfarin therapy has been initiated, it should be reversed with Vitamin K. 2.5 to 5 mg IV/oral to avoid the additional prothrombotic state associated with warfarin initiation.

Activate HIT Order panel:
- Order HIT Screen with reflex to SRA (Heparin Platelet Factor 4 with reflex based on results to Serotonin Release Assay)
- Heparin products should be held at least 3 hours prior to drawing sample
- Pharmacy consult to screen medications and ensure pending allergy entered

Sample must arrive in lab Mon-Fri before 9 am to be processed on same day

Initiate a DTI while waiting for test results if no contraindication and consider risk of thrombosis vs bleeding

POSITIVE

What is HIT Screen result (Heparin PF4 ELISA Immunoassay)? See Table 4 for HIT test information

ABNORMAL or INDETERMINANT

- Sample will be reflexed to the SRA
- If not already started, consider initiation of DTI until further results unless absolute contraindication exists (Select agent based upon Table 5)
  - Argatroban
  - Bivalirudin
  - Pharmacy consult required

What is SRA result?

HIT confirmed

- Initiate DTI if not already started AND no absolute contraindication vs. bleeding
- Select agent based upon Table 5
  - Argatroban
  - Bivalirudin
  - Pharmacy consult required

Provider to remove “Heparin Allergy Pending” from allergy list and enter an allergy for heparin with HIT as the reaction.

Continue DTI until platelet count is >150,000 or return to baseline (if it was below 150,000) before initiating warfarin

NEGATIVE

INDETERMINANT

- HIT remains a CLINICAL DIAGNOSIS
  - Document diagnosis determination
  - Hematology consult is recommended (if not already completed) to evaluate patient’s clinical presentation and assist in the diagnosis of HIT

Consider alternative diagnosis

- Discontinue DTI (if started) and resume routine anticoagulation (if indicated)
- If clinical suspicion of HIT remains high consult hematology for further testing or work-up (if not already done)
- Provider to remove “Pending Heparin Allergy” once work-up confirmed as negative

Continue Warfarin for at least 4 weeks

- see Table 1
### Table 1. Recommendations based upon Pre-test HIT Risk and Probability

<table>
<thead>
<tr>
<th>4 Ts Score (Table 2)</th>
<th>HEP Score (Table 3)</th>
<th>Risk and Probability</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| 0-3                  | <2                  | **Low** (< 0.1%)     | • Continue platelet count monitoring and consider other causes of thrombocytopenia  
  • Continue UFH / LMWH if indicated  
  • See the Diagnostic Algorithm for additional recommendations |
| 4-5                  | Intermediat (0.1% - 1%) |                       | • Monitor platelet count at least every other day through day 14, or when UFH / LMWH is stopped  
  • Consider the following:  
    o Discontinue **ALL** heparin/LMWH products  
    o Order HIT Screen with reflex to SRA  
    o Initiate therapy with argatroban or bivalirudin, unless there are contraindications, i.e. high bleeding risk or platelet count < 20,000  
  • See the Diagnostic Algorithm for additional recommendations |
| ≥2                   | High (≥ 1%)         |                      | • Monitor platelet count daily at least through day 14  
  • Order “HIT Screen with reflex to SRA” and see the Diagnostic Algorithm for additional recommendations  
  • Discontinue **ALL** heparin/LMWH products  
  • If there is no active bleeding, then avoid platelet transfusion  
  • Strongly consider lower extremity ultrasound to rule out DVT  
  • **Initiate** therapy with argatroban or bivalirudin unless there are contraindications (i.e. high bleeding risk or platelet count < 20,000)  
  • See the Diagnostic Algorithm for further recommendations  
  • Warfarin therapy (for additional warfarin recommendations see the Pharmacy website):  
    o Restart warfarin only after anticoagulation has been established with a non-heparin agent  
    o Avoid warfarin until platelet count rises above 150,000 or returns to baseline if baseline is less than 150,000  
    o Unless there is another indication for warfarin, Warfarin therapy with INR goal of 2 - 3 for **at least 4 weeks for HIT without thrombosis**, and at least 3 months in those with HIT with thrombosis |

### Other drugs commonly implicated in drug-induced thrombocytopenia

- Carbamazepine, Chemotherapeutic Agents, Glycoprotein IIb/IIIa Antagonists (Abciximab, Eptifibatide), Ibuprofen, Linezolid, Mirtazapine, Penicillins (Amoxicillin, Piperacillin, Nafcillin), Quinine, Quinidine, Oxaliplatin, Sulfamethoxazole/Trimethoprim, Vancomycin

- For more extensive list see: [http://moon.ouhsc.edu/rgorge/DITP.html](http://moon.ouhsc.edu/rgorge/DITP.html)
<table>
<thead>
<tr>
<th>Clinical Parameter</th>
<th>Score</th>
<th>Clinical Description of Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thrombocytopenia</strong></td>
<td></td>
<td>Compare the highest platelet count within the sequence of declining platelet counts with the lowest count to determine the % of platelet fall (Select only 1 option)</td>
</tr>
<tr>
<td>2 Points</td>
<td></td>
<td>Platelet count fall &gt; 50%, but lowest platelet count ≥ 20,000 mm³ and no surgery within preceding 3 days</td>
</tr>
<tr>
<td>1 Point</td>
<td></td>
<td>&gt;50% platelet fall but surgery within preceding 3 days OR any combination of platelet fall and nadir that does not fit criteria for Score 2 or 0 (eg 30-50% platelet fall or nadir 10-19,000/ mm³)</td>
</tr>
<tr>
<td>0 Points</td>
<td></td>
<td>Platelet count fall &lt; 30%, OR lowest platelet count &lt; 10,000/mm³</td>
</tr>
<tr>
<td><strong>Day 0= first day of most recent heparin exposure (Select only 1 option)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Points</td>
<td></td>
<td>Platelet count fall 5-10 days after start of heparin/LMWH treatment, or Platelet fall within 1 day of start of heparin within 5-30 days</td>
</tr>
<tr>
<td>1 Point</td>
<td></td>
<td>Consistent with 5-10 day period, but uncertain (e.g., missing platelet counts), OR platelet fall within 1 day of start of heparin or LMWH WITH heparin exposure in past 31-100 days, OR platelet fall after day 10</td>
</tr>
<tr>
<td>0 Points</td>
<td></td>
<td>Platelet count fall ≤ 4 days after starting heparin treatment without prior heparin or LMWH exposure in the prior 100 days.</td>
</tr>
<tr>
<td><strong>(Select only 1 option)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thrombosis (or other clinical sequelae)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Points</td>
<td></td>
<td>New thrombosis (confirmed), skin necrosis, or acute systemic reaction after an intravenous bolus of heparin or adrenal hemorrhage</td>
</tr>
<tr>
<td>1 Point</td>
<td></td>
<td>Progressive or recurrent thrombosis, non-necrotizing (erythematous) skin lesions at injection sites, or suspected (not proven) thrombosis</td>
</tr>
<tr>
<td>0 Points</td>
<td></td>
<td>Thrombosis suspected</td>
</tr>
<tr>
<td><strong>Other cause of platelet decline</strong></td>
<td></td>
<td>Such as mechanical devices, mechanical circulatory support, CRRT, intra-aortic balloon pump (IABP), other medications, sepsis, etc.</td>
</tr>
<tr>
<td>2 Points</td>
<td></td>
<td>No alternative explanation for platelet fall is evident</td>
</tr>
<tr>
<td>1 Point</td>
<td></td>
<td>Other possible cause evident:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May include Sepsis without proven microbial source, thrombocytopenia associated with initiation of ventilator, or other</td>
</tr>
<tr>
<td>0 Points</td>
<td></td>
<td>Other probable cause present</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May include such scenarios as within 3 days of surgery, confirmed bacteremia or fungemia, chemotherapy or radiation within past 20 days, DIC, post-transfusion purpura, platelet count &lt;20,000 AND exposure to drug implicated in causing drug-induced immune thrombocytopenia</td>
</tr>
</tbody>
</table>

<p>| <strong>Composite Score</strong> |       |                                                                                                                                                                                                                                           |</p>
<table>
<thead>
<tr>
<th>Clinical Parameter</th>
<th>Patient Score</th>
<th>Corresponding Score</th>
<th>Clinical factor and presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Magnitude of fall in platelet count (from peak to nadir since initial heparin exposure)</td>
<td>-1</td>
<td>&lt;30%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>30 - 50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>&gt;50%</td>
<td></td>
</tr>
<tr>
<td>A. If Suspected typical onset</td>
<td>-2</td>
<td>Begins &lt;4 days after exposure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Begins 4 days after exposure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Begins 5-10 days after exposure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Begins 11-14 days after exposure</td>
<td></td>
</tr>
<tr>
<td>B. Previous heparin exposure in last 100 days in whom rapid onset HIT could be expected</td>
<td>2</td>
<td>Begins &lt;48 hr after re-exposure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-1</td>
<td>Begins &gt;48 hr after re-exposure</td>
<td></td>
</tr>
<tr>
<td>2. Timing of fall in platelet count (select appropriate category under only &quot;A&quot; OR &quot;B&quot;)</td>
<td>-2</td>
<td>≤20,000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>&gt;20,000</td>
<td></td>
</tr>
<tr>
<td>3. Nadir platelet count</td>
<td>3</td>
<td>New VTE or ATE ≥ 4 days after exposure</td>
<td></td>
</tr>
<tr>
<td>4. Thrombosis</td>
<td>2</td>
<td>Progression of pre-existing arterial or venous thrombosis while on heparin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>5. Skin necrosis</td>
<td>3</td>
<td>Skin necrosis at subQ heparin administration sites</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>6. Acute systemic reaction</td>
<td>2</td>
<td>Acute systemic reaction after heparin bolus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>7. Bleeding</td>
<td>-1</td>
<td>Presence of bleeding, petechiae or extensive bruising</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>8. Other causes of thrombocytopenia present (select all that apply)</td>
<td>-1</td>
<td>Presence of a chronic thrombocytopenic disorder</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-2</td>
<td>Newly added medication known to cause thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-2</td>
<td>Severe infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-2</td>
<td>Severe DIC (Fibrinogen &lt;100 mg/dl and D-dimer&gt;5 mcg/ml)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-2</td>
<td>Mechanical Circulatory device (IABP, LVAD, ECMO)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-1</td>
<td>Cardiopulmonary bypass within 96 hr</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>No other apparent cause</td>
<td></td>
</tr>
<tr>
<td>Composite Score</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 4. HIT Laboratory Testing* (Reminder: HIT is a CLINICAL DIAGNOSIS supported in-part by laboratory assays)

<table>
<thead>
<tr>
<th>Test</th>
<th>About test</th>
<th>Pearls:</th>
</tr>
</thead>
</table>
| HIT Screen (Heparin PF4 IgG ELISA Immunoassay) | - First line screening test  
- Detects heparin-dependent IgG antibody binds to Heparin-PF4 complexes associated with HIT  
- Not a Diagnostic test – if abnormal or indeterminate, should validate by using a functional assay (i.e. SRA)  
- Potential of false positives | - Performed in-house, Mon-Friday.  
- Degree of optical density elevation and/or >50% heparin inhibition on confirmatory step, increase the positive predictive value of this test |

<table>
<thead>
<tr>
<th>Optical Density (O.D.)</th>
<th>% Probability of Clinical HIT</th>
<th>If heparin inhibition &lt; 50%</th>
<th>If heparin inhibition ≥ 50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.40</td>
<td>0%</td>
<td>NA – HIT negative</td>
<td>NA – HIT negative</td>
</tr>
<tr>
<td>0.40 - &lt;1.00</td>
<td>1.4%</td>
<td>Inconclusive</td>
<td>Likely Increased probability</td>
</tr>
<tr>
<td>1.00 - &lt;1.40</td>
<td>22.2%</td>
<td>Inconclusive</td>
<td>Likely Increased probability</td>
</tr>
<tr>
<td>1.40 - &lt;2.00</td>
<td>53.3%</td>
<td>Inconclusive</td>
<td>Likely Increased probability</td>
</tr>
<tr>
<td>≥2.00</td>
<td>&gt;99%</td>
<td>Inconclusive</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Serotonin Release Assay (SRA)  
Not usually ordered independently without Hematology direction

- Validation test  
- Functional assay used to detect release of radioactive carbon-14 labeled serotonin from donor platelets.  
- These donor platelets are placed in patient plasma and when HIT positive the platelets are activated in the presence of heparin releasing radiolabeled serotonin

| Send out test Mon-Friday  
| Performed by Reference Laboratory on all HIT Screen samples resulting as abnormal or indeterminate  
| Heparin must be held at least 3 hours prior to performing assay to minimize risk of false negative results (interferes with confirmatory heparin inhibition step)  
| Detects actual pathologic response in active HIT.  
| Has low clinical utility if patient has not had recent heparin exposure |

**HIT Laboratory Testing FAQ**

- **Brief Operational Fundamentals**
  - Collect sample in a RED TOP TUBE as a soon as indicated below (Serum separator tubes that contain gel are NOT accepted):  
  - No sooner than 3 hours after last dose of unfractionated heparin (UFH)  
  - At least 6 hours after last dose of a low molecular weight heparin (LMWH)  
  - Call Pharmacy for assistance with the timing of a blood draw whenever additional assistance is required

- **Detailed Questions:**
  - **1. Why doesn’t the lab call for the draw with the new “PF4 IgG HIT Screen with reflex to SRA”?**
    - **The sample type and storage requirements have changed and the sample may potentially be drawn the same day that heparin is stopped; therefore a fresh specimen is no longer necessary as was the case in the past.**
  - **2. Do I have to wait for the lab to call me before I draw the sample for this test?**
    - **No.**
  - **3. Why does my patient have to be off heparin before I can draw for the Platelet Factor 4 (PF4) HIT Screen?**
    - **All abnormal or inconclusive PF4 HIT tests are “reflexed” and sent to an outside lab to perform a confirmatory functional assay known as the Serotonin Release Assay (SRA). If heparin products are present in the blood sample, the SRA testing cannot be performed.**
  - **4. What is the sample type for the new HIT Screen test (“PF4 IgG HIT Screen with reflex to SRA”) and what does “reflex” mean?**
    - **The sample is 1 red top tube, completely full. Serum separator tubes (any tube containing a gel separator) are NOT acceptable.**
    - **Reflex means that only a single blood sample is drawn for all of the testing – including the PF4 HIT Screen and, if needed, the SRA confirmatory HIT test.**
  - **5. What is the method of the new PF4 IgG HIT Screen and how does it differ from the previous test for HIT?**
    - **The PF4 IgG HIT Screen is an immunologic test performed at the OSUWMC Clinical Lab by ELISA method to detect IgG antibodies that may be associated with HIT. The old test was a functional assay performed using a method known as platelet aggregation.**
  - **6. When will results be available for the PF4 IgG HIT Screen?**
    - **Results will usually be available by 5 pm on days the test is performed unless there is a problem with the sample or with testing.**

- **7. How is the PF4 IgG HIT Screen used to diagnose HIT?**
  - **The PF4 IgG HIT Screen is only one part of a complex diagnosis. All positive HIT Screens automatically reflex to the confirmatory SRA. However, all results should be interpreted within the context of the patient’s clinical symptoms to make the final diagnosis.**

- **8. What do the results from the PF4 IgG HIT Screen Mean?**
  - **The Optical Density (OD) measures amounts of IgG antibodies heparin-PF4 associated with HIT. Normal values are <0.40 OD Units.**
  - **All samples testing 0.400 and above will also be tested in the presence of “high dose” heparin to determine heparin dependence (Heparin Inhibition)**

- **9. Is the OD value significant when determining the risk of HIT for my patient?**
  - **Yes. The probability of HIT has been established and published by experts in the field. For the test performed here at OSUWMC, the probability of HIT can be found above or in Table 4 of the Guidelines. For more information you can call the lab or see the following references:  

- **10. If the SRA must be sent out, when can I expect the results to be available?**
  - **All abnormal or inconclusive HIT PF4 IgG results will automatically reflex to send out a SRA. Since most samples are already in the lab, the specimen will ship out the same afternoon that the PF4 is performed. Once the sample is received at the referring lab (usually the afternoon of the next day), it will be placed on the next run (this will be – 2 days after the PF4 is performed) and the result will generally be available the following day (this equates approximately to a 3 day turnaround time from PF4 IgG HIT Screen testing). If there is a need to repeat the testing, this time may be extended.**
### Table 5. OSUMC Direct Thrombin Inhibitors for the Management of Heparin-Induced Thrombocytopenia

<table>
<thead>
<tr>
<th>Agent</th>
<th>Argatroban</th>
<th>Bivalirudin (Angiomax®)</th>
</tr>
</thead>
</table>
| **Recommended Population of Use** | • In patients with no end organ dysfunction or isolated renal dysfunction (minimal other end organ dysfunction)  
  • Patients not requiring invasive procedures (e.g. surgery)  
  • Avoid in patients with acute or chronic hepatic failure | • Patients requiring invasive procedures or are at high risk of post-operative bleeding  
  • Patients with multi-organ dysfunction (particularly those with hepatic or hepatorenal failure) |
| **Labeled Indications** | • FDA approved for prophylaxis or treatment of thrombosis in patients with HIT  
  • FDA approved for patients with suspected or confirmed HIT who are undergoing percutaneous coronary intervention (PCI) | • FDA approved for patients with suspected or confirmed HIT who are undergoing PCI |
| **Off-label Indications** | • Has been investigated for use in anticoagulation during cardiopulmonary bypass (CPB) in patients with confirmed or suspected HIT(not recommended agent for this use) | • Has been investigated for prophylaxis or treatment of thrombosis in patients with HIT using considerably decreased dosing relative to PCI dosing for selected populations with HIT  
  • Has been investigated for use in anticoagulation during cardiopulmonary bypass (CPB) in patients with confirmed or suspected HIT |
| **Half-Life** | • Normal Organ function: 39-51 min  
  • Critically Ill and/or Child-Pugh Score ≥ 6: > 3 hours (often unpredictable) | • Normal Organ function: 25 min  
  • If CrCl 10-29 mL/min: 57 min  
  • Intermittent HD (Off Dialysis): 3.5 hours |
| **Clearance** | • Hepatobiliary (86%)  
  • Renal (14%)  
  • Non-dialyzable | • Renal (20%)  
  • Proteolytic cleavage independent of organ function (80%)  
  • Dialyzable |
| **Therapeutic Dose** | • Recommended dosing available on OSUMC Pharmacy website | • Recommended dosing available on OSUMC Pharmacy website  
  • Dosing for HIT/TS management is much lower than that used in PCI or O.R. setting |
| **Monitoring** | • Recommended aPTT monitoring available on OSUMC Pharmacy website | • Recommended aPTT monitoring available on OSUMC Pharmacy website |
| **Adverse Effects** | • Major bleeding with therapeutic dose in 5.3 to 11.1% of patients  
  • No reversal agent available | • Bleeding with therapeutic dose in 5-9% of patients  
  • No reversal agent available |

All DTIs can increase the INR value (Argatroban influences INR more than Bivalirudin); however, this is NOT a reflection of the patient’s true INR and is at least partly laboratory artifact.

Elevated INRs solely due to argatroban or bivalirudin do NOT respond to FFP or vitamin K, because the direct thrombin inhibitors do not work via vitamin K inhibition. Vitamin K should be used judiciously, because it can cause warfarin resistance, and many of these patients must be transitioned to warfarin prior to discharge.

**Other agents**: Due to a lack of evidence, a hematology consult is recommended if any of these agents are considered for treatment.

**Desirudin (Iprivask®)**:
- Subcutaneous DTI injection that is FDA approved for the prophylaxis of deep vein thrombosis, which may lead to pulmonary embolism, in patients undergoing elective hip replacement surgery  
  • Has been studied in comparison to argatroban for the for prophylaxis or treatment of thrombosis in patients with suspected or confirmed HIT

**Fondaparinux (Arixtra®)**:
- Subcutaneous anti-Xa inhibitor that is FDA approved for treatment of acute DVT/PE and for prophylaxis of DVT in patients undergoing major hip surgery, knee replacement surgery, or abdominal surgery.  
  • Very limited data in HIT therefore is NOT advocated or FDA approved for management of acute HIT.  
  • Has been identified to induce HIT, albeit with a much lower incidence than heparin or LMWHs.

**Dabigatran (Pradaxa®)**:
- Oral DTI that has only been FDA approved to reduce the risk of stroke and systemic thromboembolism in patients with non-valvular atrial fibrillation without any active thrombus  
  • Has not been studied in patients with HIT

**Rivaroxaban (Xarelto®) or Apixiban (Eliquis®)**:
- Oral anti-Xa inhibitor FDA approved to reduce the risk of stroke and systemic thromboembolism in patients with non-valvular atrial fibrillation without any active thrombus (Rivaroxaban also approved for postoperative thromboprophylaxis after knee or hip replacement and DVT/pulmonary embolism acute treatment and/or secondary prophylaxis).  
  • Neither have been studied in patients with HIT.
Order Panels

- Bivalirudin HIT order panels (2)
- Argatroban HIT order panels (2)
- HIT screen order panel

References


Quality Measures

Percentage of patients that:
- Underwent HIT laboratory testing (Heparin PF4 ELISA Immunoassay and or SRA)
- Were HIT positive by laboratory or clinical diagnosis
- Were started on argatroban or bivalirudin

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Disclaimer

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