Argatroban Dosing Guidelines

For Prevention & Treatment of Thrombosis in Heparin-Induced Thrombocytopenia (HIT)

1. Before starting Argatroban:
   - Stop all heparin (including catheter flushes), enoxaparin or dalteparin, and warfarin
   - Obtain baselines labs (if none in past 24 hours)- CBC, PTT, PT/INR, Basic Metabolic Profile, LFTs
   - If aPTT is > 65 seconds, do not start DTI
     - Recheck aPTT every 2 hours until < 65 seconds, then start DTI
   - Monitor a CBC and aPTT at least daily during treatment
   - Consider consulting Hematology

2. If the patient has a baseline aPTT of 25 – 37 seconds (UHS reference interval):
   - The target aPTT is 45 - 90 seconds.
   - Target is based on the prescribing information for argatroban which recommends targeting a steady state aPTT of 1.5 to 3 times the baseline.
   - This is lower than heparin anticoagulation goals and approximately 2 X UHS normal range
   - If the baseline aPTT is > 40 seconds, Hematology consult is recommended

3. Argatroban dosing recommendations:
   - Initiate dose at 1 mcg/kg/min (Note: this is lower than FDA-approved initial dosing)
   - Check aPTT every 2 hours until consecutive values are in range, and at least daily thereafter
     - In patients with hepatic impairment
       - Initiate dose at 0.5 mcg/kg/min
       - Half-life can be extended up to 180 minutes (3 x normal half-life of 39-51 minutes)
     - In patients with renal impairment
       - Argatroban is not renally eliminated, and does not require initial dosage adjustments

**Clinical conditions which may warrant dosing as low as 0.1 or 0.2 mcg/kg/min:
- High risk of bleeding
- Coagulopathy
- Severe liver disease
- Severe kidney disease

- Adjusting argatroban dose based on aPTT: Revised August 2016

<table>
<thead>
<tr>
<th>aPTT</th>
<th>Directions</th>
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</thead>
<tbody>
<tr>
<td>&lt; 45 seconds</td>
<td>Increase infusion rate in increments of 20%</td>
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<tr>
<td></td>
<td>Recheck aPTT 2 hours after dosage change**</td>
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<tr>
<td>45 – 90 seconds</td>
<td>No change</td>
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<tr>
<td>&gt; 90 seconds</td>
<td>Stop infusion for 1 hour and restart at 50% reduced infusion rate</td>
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<tr>
<td></td>
<td>Recheck aPTT 2 hours after restart</td>
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**For clinical condition listed above, consider more intense monitoring to assure the patient has reached steady-state before doses are increased (ex. aPTT every 2 hrs X 4, then increase dose if aPTT < 30 sec)
4. Conversion to Warfarin

If the decision is made to continue anticoagulation with oral therapy (warfarin) after argatroban infusion, several steps should be taken to avoid the pro-thrombotic effects of warfarin:

- Do not use warfarin as monotherapy in acute HIT
- Do not initiate warfarin until the platelet count has rebounded to >100 K/µL
- Do not use a loading dose of warfarin; initiate therapy with expected maintenance dose
- **Overlap** warfarin and argatroban therapy for at least 5 days – to allow for the half–lives of all the clotting factors
- Measure INR daily; INR will be significantly affected by argatroban as well as by warfarin; however increased INR may not correspond to an increased risk of bleeding
- To stop argatroban infusion, see table below:

<table>
<thead>
<tr>
<th>For doses ≤ 2 mcg/kg/min</th>
<th>For doses &gt; 2 mcg/kg/min</th>
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</thead>
<tbody>
<tr>
<td>• Discontinue argatroban when the INR is &gt; 4 on combined therapy (&amp; at least 5 days of overlap)</td>
<td>• INR cannot be reliably predicted at argatroban doses &gt; 2 mcg/kg/min</td>
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<tr>
<td>• Check INR 4 to 6 hours after stopping argatroban to assure therapeutic goal (INR 2 - 3) is maintained</td>
<td>• Temporarily reduce dose of argatroban to 2 mcg/kg/min (in order to predict INR on warfarin alone)</td>
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<tr>
<td>• If repeat INR is below desired therapeutic range (2 - 3) resume argatroban &amp; repeat procedure daily until desired therapeutic range on warfarin alone is reached</td>
<td>• Repeat INR 4 to 6 hours after reduction and follow the process outlined for doses up to 2 mcg/kg/min</td>
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</tbody>
</table>

This is to be used as a guide and should not supersede clinical judgment. For questions call pharmacy or consider consulting Hematology.