

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**

aPTT	Directions
< 45 seconds	Increase infusion rate in increments of 20% Recheck aPTT 2 hours after dosage change**
45 – 90 seconds	No change
> 90 seconds	Stop infusion for 1 hour and restart at 50% reduced infusion rate Recheck aPTT 2 hours after restart

**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/ μ L
- 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:

For doses \leq 2 mcg/kg/min	For doses $>$ 2 mcg/kg/min
<ul style="list-style-type: none">• Discontinue argatroban when the INR is $>$ 4 on combined therapy (& and least 5 days of overlap)• Check INR 4 to 6 hours after stopping argatroban to assure therapeutic goal (INR 2 - 3) is maintained• If repeat INR is below desired therapeutic range (2 - 3) resume argatroban & repeat procedure daily until desired therapeutic range on warfarin alone is reached	<ul style="list-style-type: none">• INR cannot be reliably predicted at argatroban doses $>$ 2 mcg/kg/min• Temporarily reduce dose of argatroban to 2 mcg/kg/min (in order to predict INR on warfarin alone)• Repeat INR 4 to 6 hours after reduction and follow the process outlined for doses up to 2 mcg/kg/min

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