

Argatroban for the Treatment of HIT

The use of argatroban should be limited to Heparin Induced Thrombocytopenia (HIT) or Heparin Induced Thrombocytopenia and Thrombosis Syndrome (HITTS)

I. GUIDELINES

1. Draw baseline aPTT prior to initiation of argatroban.
2. If patient is currently on
 - Heparin, discontinue heparin, wait one hour before starting argatroban
 - Fondaparinux: wait for 8 hrs before starting argatroban
 - Enoxaparin: wait for 6 hrs before starting argatroban
3. Remove all sources of heparin (flushes and others)
4. Initiate argatroban (concentration 1mg/ml) at a dose of 2 mcg/kg/min (actual body weight). For patients with moderate to severe hepatic dysfunction, initiate argatroban at 0.5 mcg/kg/min.

II. MONITORING OF THERAPY

1. Draw aPTT 2 hours after initiation of argatroban. Target aPTT is 1.5 to 3 times the baseline value (not to exceed 120 seconds).
2. Adjust the argatroban dose as follows to maintain aPTT 70-125 seconds (1.5 to 3 times control, not to exceed 10 mcg/kg/min*):
2 mcg/kg/min:
 - If aPTT < or = 55 seconds: increase dose by 1 mcg/kg/min
 - If aPTT > 55 and < or = 75 seconds: increase dose by 0.5 mcg/kg/min
 - If aPTT 75-125 seconds: **no change**
 - If aPTT > 125 and < or = 140 seconds: decrease dose by 0.5 mcg/kg/min
 - If aPTT > 140 seconds (3.5 times baseline): decrease dose by 1 mcg/kg/min**0.5 mcg/kg/min (moderate hepatic dysfunction)**
 - If aPTT < or = 55 seconds: increase dose by 0.2 mcg/kg/min
 - If aPTT > 55 and < or = 75 seconds: increase dose by 0.1 mcg/kg/min
 - If aPTT 75-125 seconds: **no change**
 - If aPTT > 125 and < or = 140 seconds: decrease dose by 0.1 mcg/kg/min
 - If aPTT > 140 seconds (3.5 times baseline): decrease dose by 0.2 mcg/kg/min
3. Draw aPTT 2 hours after each dosage adjustment. Adjust as above.
4. Once the therapeutic range has been reached, repeat the aPTT daily.
5. Initiate warfarin as appropriate. Argatroban has a synergistic effect with warfarin on the INR so the INR is unreliable as a guide to management warfarin therapy. There are three options:
 - All of these options assume that the platelets have return to normal and the patient is clinically stable.
 - Option 1:** Change to therapeutic fondaparinux and start warfarin. Fondaparinux does not affect the INR and does not interact with the HIT antibodies. However, fondaparinux **should not** be in patients with significant renal insufficiency.
 - Option 2:** Use the chromogenic factor X assay. Factor X being a vitamin K dependent protein will reflect the warfarin effect – lower factor X = higher INR. Therapeutic factor X levels are 15-35%. Given its longer half-life, factor X will lag behind the change in INR (which reflects the shorter half-life of factor VII).
 - Option 3:** The relationship between INR on co-therapy and on warfarin alone is dependent on the dose of argatroban and the thromboplastin reagent used. The INR on warfarin alone can be estimated from the INR obtained on the combination therapy (warfarin and argatroban) using the following equation: $INR_{\text{warfarin alone}} = 0.19 + 0.57(INR_{\text{from cotherapy}})$. (ex: INR on co-therapy is 4. Estimated INR on warfarin alone = 2.47.) This equation can only be used for argatroban doses of 2 mcg/kg/min or less.
 1. Draw INR daily. Estimate of the INR on warfarin alone may be calculated with the above equation. For patients receiving argatroban at a dose > than 2 mcg/kg/min, temporarily reduce the dose to 2 mcg/kg/min. Draw an INR 4 hours after the dosage reduction. Return the argatroban dose to the previous rate once the INR has been drawn. Estimate the INR on warfarin alone using the above equation.
 2. When the estimated INR is within the goal INR range, temporarily discontinue the argatroban infusion. Draw a repeat INR in 4 hours. If INR is within the goal INR range, argatroban can be discontinued. If the INR is below the goal range, resume the argatroban at the previous rate and repeat the procedure daily until the desired INR range with warfarin is achieved.

*Lower aPTT for Cardiac/Stroke/RO Stroke/TIA Protocol