LOS ANGELES COUNTY DEPARTMENT OF HEALTH SERVICES
HARBOR-UCLA MEDICAL CENTER

SUBJECT: ARGATROBAN CONTINUOUS INFUSION **POLICY NO.** 325P

CATEGORY: Provision of Care	**EFFECTIVE DATE:** 8/18
POLICY CONTACT: Julianne Joo, Pharm D.	**UPDATE/REVISION DATE:** 6/23
REVIEWED BY COMMITTEE(S): Pharmacy and Therapeutics Committee	

PURPOSE:
To provide guidelines for the prescribing, administration, and monitoring of argatroban continuous infusion for adult and pediatric patients, and to standardize practice for safety and efficacy.

POLICY:
Harbor-UCLA Medical Center's policy is designed to define an interdisciplinary approach involving providers, registered nurses (RNs), and pharmacists in providing argatroban continuous infusion for adult and pediatric patients.
RNs will administer argatroban continuous infusion to adult and pediatric patients according to this policy.
Pharmacists will monitor and adjust argatroban continuous infusion for adult patients.

PROCEDURE:
1. Provider must get an approval from Hematology Service to order argatroban.
2. In emergent/urgent situation if the patient must be rushed to the Operating Room (OR):
   a. Provider may order argatroban in the OR without obtaining hematology consult prior to Pharmacy dispensing argatroban.
   b. Appropriate baseline labs (CBC, PT/INR, aPTT, BMP, LFT) must be ordered before starting argatroban infusion.
   c. Hematology must be consulted immediately post-op.
   d. Pharmacist will NOT monitor/adjust argatroban infusion rate for the use in OR for procedures.
3. The hospital-approved argatroban form (**Appendix B** for adult patients or **Appendix C** for pediatric patients) must be printed/completed/affixed with patient information label and scanned to the Pharmacy for processing. The order forms are posted on the HUMC intranet website under Pre-Printed Forms. The form must include:
   a. Provider's contact information entered in the appropriate fields.
   b. Selection if patient has normal or impaired hepatic function.
   c. Selection if patient has thrombosis.

REVISED: 5/19, 7/19
REVIEWED: 8/18, 5/19, 7/19, 6/22, 6/23

APPROVED BY:

Nina J. Park Digitally signed by Nina J. Park Date: 2023.12.21 10:11:05 -08'00'

Nina J. Park, MD
Interim Chief Executive Officer

Griselda Gutierrez

Griselda Gutierrez, MD
Chief Medical Officer

Jason Black

Jason Black, MBA, DNP, RN
Chief Nursing Officer

4. An argatroban order must be placed into the Electronic Health Record (EHR) in addition to completing and scanning the order form to the Pharmacy.
5. Upon receiving a complete argatroban order via scanner and EHR, pharmacist will process argatroban order.
6. Argatroban Infusion Exclusion criteria include:
   a. Active major bleeding
   b. Hypersensitivity to argatroban or one of its components
7. Patient monitoring:
   a. It is the responsibility of all team members caring for the patient to monitor for signs of bleeding, thrombosis, or other complications and to notify the provider immediately if they should occur.
   b. The provider is responsible for monitoring the clinical response to therapy and for considering transition to oral anticoagulation soon as appropriate.
   c. Pharmacist will notify the provider if there is a significant decrease in the patient's hemoglobin.
8. If a custom titration scale is used instead of an approved argatroban protocol, the ordering provider is responsible for laboratory monitoring and subsequent titration orders.
9. It is the provider's responsibility to determine when a continuous argatroban infusion is no longer indicated and to discontinue the order in EHR.
10. Pharmacists will perform "Argatroban Per Pharmacy" for adult inpatients (see **ADULT PATIENTS** section below).
11. Pharmacists will **NOT** perform "Argatroban Per Pharmacy" for Pediatric patients (see **Appendix C** for physician order form).
12. For conversion from argatroban to other anticoagulants, see **Hospital Policy #325S,** Anticoagulant Management Guidelines.

ADULT PATIENTS:

1. Follow all the ordering requirement in the procedure section above.
2. The hospital-approved argatroban form (**Appendix B)** Section A must be completed.
3. Provider orders "Argatroban dosing per Pharmacy" in EHR.
4. Provider orders baseline tests (unless tests performed within 24 hours prior to argatroban infusion initiation):
   a. CBC – to be ordered before starting argatroban infusion and once daily while the argatroban infusion is continued
   b. PT, INR, and aPTT
   c. BMP
   d. LFT
   e. Argatroban infusion may be initiated **before** baseline tests are resulted.
   f. Baseline tests do not need to be repeated if performed within 24 hours prior to initiating argatroban infusion unless there is a change in patient's status.
5. Provider and pharmacist are responsible for reviewing the results of the baseline labs (CBC, PT/INR, PTT, Anti-Xa if applicable) when available.
6. Provider discontinues all other prophylactic or therapeutic anticoagulants except oral antiplatelet agents and warfarin overlap therapy.
7. Pharmacist will determine and place argatroban infusion rate/order according to protocol.

Pharmacy Procedures – Initiation of Argatroban

1. Pharmacist reviews order for appropriateness.
   a. Pharmacist reviews the clinical indication for argatroban.

   b. If pharmacist has questions or concerns, contact ordering provider for clarification.
2. Pharmacist may order any baseline blood tests that are missing, including:
   a. CBC – prior to starting heparin infusion and once daily while the heparin infusion is continued.
   b. PT, INR, and Anti-Xa, UFH, or aPTT
   c. BMP
   d. LFT
3. Pharmacist may discontinue a duplicate aPTT order placed by provider.
4. Review of laboratory results:
   a. Prior to dispensing initial argatroban infusion, pharmacist will review any ***available*** results for CBC, PT/INR, aPTT, and Anti-Xa. Pharmacist will notify provider if:
      1) INR > 2
      2) Platelet count < 100,000 mm^3
      3) PT or aPTT > 1.5 x upper level of normal
      4) Anti-Xa > 0.30 IU/mL
   b. While argatroban infusion is ongoing, pharmacist will review available values for CBC and INR on a daily basis. Notify provider if:
      1) INR > 4
      2) Platelet count < 100,000 mm^3
5. Pharmacist reviews the dosing weight according to **Appendix D**.
6. Pharmacist determines the initial argatroban infusion rate (mcg/kg/min) and enters the order in EHR.
7. Pharmacist will discontinue other parenteral and oral anticoagulants if not discontinued by the provider, with the exception of antiplatelet agents and warfarin for bridge therapy. Pharmacist will notify provider of the change.
8. Pharmacist orders “aPTT” level to be drawn according to the approved protocol after starting the argatroban infusion.
9. Pharmacist calls nurse to communicate infusion instructions.
10. Argatroban will be dispensed from the Pharmacy.
11. Details of infusion rate are automatically captured in the order information.
12. Documentation is required when argatroban infusion is initiated.

Pharmacy Procedures – Adjustment and Monitoring of Argatroban

1. Pharmacist will titrate the argatroban infusion and order aPTT according to protocol (**Appendix B**).
2. Order entry and communication details are outlined in **Appendices E and F**.
3. Documentation is required when the argatroban infusion is titrated (**Appendix G**).
4. All aPTT checks will be ordered/processed as timed STAT. Details of aPTT timing can be found in **Appendix H**.
5. aPTT, PT/INR, CBC, BMP are checked daily after 2 consecutive therapeutic aPTT values.
6. Liver panel is checked every 3 days or more frequently, if indicated.
7. The provider will be contacted if aPTT is not drawn according to protocol or if the titration guideline cannot be followed.

Nursing Procedures

1. Obtain patient weight:
   a. Weigh patient as soon as possible after receiving order.
   b. Enter weight in “measured weight” field in EHR and also in the “dosing weight” field.
   c. If patient can’t be weighed, nurse will enter reported or estimated patient weight instead.

   d. Patient weight details can be found in **Appendix D**.
2. Review of laboratory results:
   a. Prior to administering initial argatroban infusion, nurse will review any ***available*** results for CBC, INR, aPTT, and Anti-Xa. Nurse will notify provider if:
      1) INR > 2
      2) Platelet count < 100,000 mm^3
      3) PT or aPTT > 1.5 x upper level of normal
      4) Anti-Xa > 0.30 IU/mL
   b. While argatroban infusion is ongoing, nurse will review available values for CBC and INR on a daily basis. Nurse will notify provider if:
      1) INR > 4
      2) Platelet count < 100,000 mm^3
3. Critical aPTT results:
   Critically high aPTT values will be reported according **to HUMC Policy #393B** (Notification of Critical Diagnostic Results) for notification of critical results.
4. Administration of Argatroban:
   a. Registered Nurse (RN) will draw baseline labs including PT/INR, aPTT, CMP, and CBC before starting argatroban, unless instructed by provider.
   b. Argatroban is a high alert medication. RNs will follow HUMC policy (Hospital Policy #396: Handling High-alert Medications) for administering high alert medications.
   c. Start argatroban infusion immediately after the baseline aPTT drawn. Argatroban infusion will be delivered via continuous infusion pump according to HUMC policy (Hospital Policy #331: Smart Pump).
   d. Nurse will document initiation of continuous infusion and any subsequent rate changes in the Medication Administration Record (eMAR).
5. The nurse will draw any “stat” or “timed-stat” orders related to the argatroban infusion.
6. Argatroban patients must be continuously monitored for signs and symptoms of bleeding and thromboembolism.
   a. Provider and pharmacist will be contacted immediately for any of the following: drop in blood pressure, tachycardia, the development of hematoma, drop in hemoglobin of greater than 1 g/dL, or any signs of bleeding or gross hematuria.

Laboratory Procedures

1. aPTT samples must be processed within one (1) hour of collection.
2. In the event that an acceptable specimen cannot be obtained, provider will be contacted.
3. The laboratory will check validity of aPTT and report to the ordering provider any abnormalities per laboratory protocols.
4. Critical aPTT results will be reported according **to HUMC Policy #393B** (Notification of Critical Diagnostic Results).

Special Situations

1. When ***short-term*** discontinuation of argatroban is required:
   a. To discontinue infusion:
      1) To immediately stop argatroban infusion: Provider selects “discontinue” on argatroban infusion orderable.
      2) To stop argatroban infusion at a specific future time: Provider selects “modify” on argatroban infusion orderable and indicates the desired end-time.

3) When provider modifies argatroban infusion order, this will result in electronic communication to pharmacist.
4) Provider will not discontinue or change the "argatroban dosing per pharmacy" orderable.
5) Provider will contact nurse to verbally communicate plan to discontinue argatroban infusion.

b. To resume infusion:
   a) Provider will order a new argatroban order.
   2) Pharmacist selects new infusion rate based on patient's previous aPTT levels and previous infusion rate.
   3) Pharmacist orders aPTT according to protocol.

2. Deviation from protocol:
   The pharmacist shall NOT accept any deviation from the approved protocols. If the provider determines, according to clinical judgement, that it would be beneficial to deviate from the approved protocols, the pharmacist must sign off.
   a. Pharmacist must communicate to provider prior to signing off and document the name of provider along with reason for deviation.
   b. After communicating to the provider, the pharmacist shall discontinue the "Argatroban Per Pharmacy" entry.
   c. Pharmacist must verbally notify the nurse to obtain further argatroban titration orders from the provider.

3. Discontinuation of argatroban:
   a. When the provider determines that argatroban infusion is no longer clinically indicated, provider will discontinue the infusion order.
   b. Provider will discontinue "argatroban dosing per pharmacy" orderable.
   c. Pharmacist must verbally communicate with nurse to ensure argatroban drip is discontinued.

Reviewed and approved by:
Medical Executive Committee 06/2023

Beverley A. Petrie, M.D.
President, Professional Staff Association

Appendix A: Inpatient Pharmacy Anticoagulation Service Contact Numbers

7am to 11pm: (310) 222-8009 or (424) 306-7456, 7458, or 7499
11pm to 7am: (310) 222-2363 or (424) 306-7477, 7479, 7481, or 7483

SUBJECT: ARGATROBAN CONTINUOUS INFUSION **POLICY NO.** 325P

Appendix B: ARGATROBAN CONTINUOUS INFUSION PROTOCOL (ADULT)

SECTION A—To be completed by provider

Exclusion Criteria: Do not initiate protocol if one of the following criteria is present	Yes	*No*
1. Active bleeding	❑	❑
2. Hypersensitivity to Argatroban or one of its components	❑	❑

Indications: Confirmed or suspected Heparin Induced Thrombocytopenia	
Recommended Dosage	❑ Normal Hepatic function: Initiate at **2 mcg/kg/min** ❑ Impaired Hepatic Function (total bilirubin > 1.5 mg/dL), patients with heart failure, multiple organ system failure, severe anasarca, or during early post-cardiac surgery period: Initiate at **0.5 mcg/kg/min**
Does patient have thrombosis?	❑ NO THROMBOSIS—if patient on warfarin when HIT is suspected, discontinue warfarin, then start argatroban ❑ THROMBOSIS PRESENT—if patient on warfarin when HIT is suspected, discontinue warfarin, reverse warfarin with vitamin K 5mg PO x1, then start argatroban

☑ **Discontinue all heparin products (including flushes, dialysis, heparin-coated catheters), low molecular weight heparin, factor Xa inhibitor (rivaroxaban, apixaban, edoxaban, betrixaban), fondaparinux or dabigatran**
☑ **Add Heparin allergy to patient's profile and update according to final test results**

Argatroban Dosage: **Infusion rate = _____ mcg/kg/min x_____kg = _____ mcg/min**
Argatroban concentration: 250 mg/250 mL D5W (1 mg/mL)

Hematology approval by Dr._____ ☐ **New Order** ☐ **Ongoing Therapy**

SECTION B—FOR PHARMACY USE ONLY

❑ **Normal Hepatic function:**
Initiate at 2 mcg/kg/min (Not to Exceed 10 mcg/kg/min)

aPTT (seconds)	Action	Next aPTT (STAT)
< 58	Increase infusion rate BY 1 mcg/kg/min	2 hours (post rate change)
58-74.9	Increase infusion rate BY 0.5 mcg/kg/min	2 hours (post rate change)
75-100 (Goal)	No change	2 hours until 2 consecutive therapeutic aPTT, then daily
100.1-116	Decrease infusion rate BY 0.5 mcg/kg/min	2 hours (post rate change)
116.1-141	Decrease infusion rate BY 1 mcg/kg/min	2 hours (post rate change)
>141	Stop infusion until aPTT<100 seconds, then resume at decreased rate by 1 mcg/kg/min	Every 2 hours until aPTT<100 seconds, then 2 hours post rate change. contact provider

❑ **Impaired Hepatic function (total bilirubin > 1.5 mg/dL), patients with heart failure, multiple organ system failure, severe anasarca, or during the early post-cardiac surgery period: Initiate at 0.5 mcg/kg/min (Not To Exceed 10 mcg/kg/min)**

aPTT (seconds)	Action	Next aPTT (STAT)
< 58	Increase infusion rate BY 0.2 mcg/kg/min	4 hours (post rate change)
58-74.9	Increase infusion rate BY 0.1 mcg/kg/min	4 hours (post rate change)
75-100 (Goal)	No change	2 hours until 2 consecutive therapeutic aPTT, then daily
100.1-116	Decrease infusion rate BY 0.1 mcg/kg/min	4 hours (post rate change)
116.1-141	Decrease infusion rate BY 0.2 mcg/kg/min	4 hours (post rate change)
>141	Stop infusion until aPTT<100 seconds, then resume at decreased rate by 0.2 mcg/kg/min	Every 4 hours until aPTT<100 seconds, then 4 hours post rate change

Provider Printed Last Name:	
Provider Signature	**ID:**
Date: __ __ – __ __ – __ __ __ __	**Time:** __ __ : __ __
RN Printed Last Name:	
RN Signature:	
Date: __ __ – __ __ – __ __ __ __	**Time:** __ __ : __ __
Clerk/LVN Signature:	
Date: __ __ – __ __ – __ __ __ __	**Time:** __ __ : __ __

SUBJECT: ARGATROBAN CONTINUOUS INFUSION **POLICY NO.** 325P

Appendix C: ARGATROBAN CONTINUOUS INFUSION PROTOCOL (PEDIATRIC)—NOT PER PHARMACY
PHYSICIAN ORDER FORM

Exclusion Criteria: Do not initiate protocol if one of the following criteria is present	Yes	*No*
1. Active bleeding	❑	❑
2. Hypersensitivity to Argatroban or one of its components	❑	❑

Indications: confirmed or suspected Heparin Induced Thrombocytopenia	
Recommended Dosage	❑ Normal Hepatic function: Initiate at **0.75 mcg/kg/min** ❑ Impaired Hepatic Function (total bilirubin > 1.5 mg/dL), patients with heart failure, multiple organ system failure, severe anasarca, or during early post-cardiac surgery period: Initiate at **0.2 mcg/kg/min**
Does patient have thrombosis?	❑ NO THROMBOSIS—if patient on warfarin when HIT is suspected, discontinue warfarin, then start argatroban ❑ THROMBOSIS PRESENT—if patient on warfarin when HIT is suspected, discontinue warfarin, reverse warfarin with vitamin K 5mg PO x1, then start argatroban

☑ **Discontinue all heparin products (including flushes, dialysis, heparin-coated catheters), low molecular weight heparin, factor Xa inhibitor (rivaroxaban, apixaban, edoxaban, betrixaban), fondaparinux or dabigatran**
☑ **Add Heparin allergy to patient's profile and update according to final test results**

Argatroban Dosage: **Infusion rate = _____ mcg/kg/min x_____kg = _____ mcg/min**
Argatroban concentration: 250 mg/250 mL D5W (1 mg/mL)

Hematology approval by Dr. ☐ **New Order** ☐ **Ongoing Therapy**

❑ **Normal Hepatic function:**
Initiate at 0.75 mcg/kg/min (Not To Exceed 10 mcg/kg/min)

aPTT (seconds)	Action	Next aPTT (STAT)
< 50	Increase infusion rate BY **0.2** mcg/kg/min	2 hours (post rate change)
51-69	Increase infusion rate BY **0.1** mcg/kg/min	2 hours (post rate change)
70-90 (Goal)	No change	2 hours until 2 consecutive therapeutic aPTT, then daily
91-110	Decrease infusion rate BY **0.1** mcg/kg/min	2 hours (post rate change)
111-120	Decrease infusion rate BY **0.2** mcg/kg/min	2 hours (post rate change)
>121	Stop infusion until aPTT<100 seconds, then resume at decreased rate by **0.25** mcg/kg/min	Every 2 hours until aPTT<100 seconds, then 2 hours post rate change

❑ **Impaired Hepatic function (total bilirubin > 1.5 mg/dL), patients with heart failure, multiple organ system failure, severe anasarca, or during the early post-cardiac surgery period: Initiate at 0.2 mcg/kg/min (Not To Exceed 10 mcg/kg/min)**

aPTT (seconds)	Action	Next aPTT (STAT)
< 50	Increase infusion rate BY **0.05** mcg/kg/min	**3** hours (post rate change)
50-69	Increase infusion rate BY **0.03** mcg/kg/min	**3** hours (post rate change)
70-90 (Goal)	No change	**2** hours until 2 consecutive therapeutic aPTT, then daily
91-110	Decrease infusion rate BY **0.03** mcg/kg/min	3 hours (post rate change)
111-120	Decrease infusion rate BY **0.05** mcg/kg/min	**3** hours (post rate change)
>121	Stop infusion until aPTT<100 seconds, then resume at decreased rate by **0.1** mcg/kg/min	Every **3** hours until aPTT<100 seconds, then 4 hours post rate change

Provider Printed Last Name:	
Provider Signature	**ID:**
Date: – –	**Time:** :
RN Printed Last Name:	
RN Signature:	
Date: – –	**Time:** :
Clerk/LVN Signature:	
Date: – –	**Time:** :

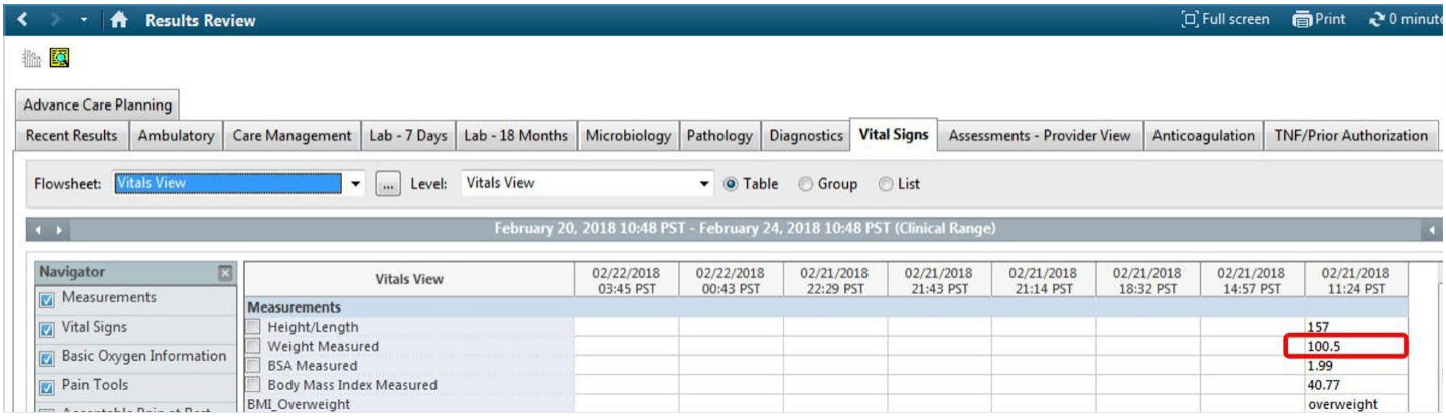
SUBJECT: ARGATROBAN CONTINUOUS INFUSION **POLICY NO.** 325P

Appendix D: Dosing Weight

Definitions:

"**Dosing weight**" The value contained within the "Dosing Weight" field in the EHR, located in the banner bar of the patient's chart.

"**Measured weight**" The value contained within the "Weight Measured" field in eHR, located in the results section of the patient's chart.



How to identify correct weight for argatroban infusion protocol:

1. Nurse weighs patient and updates the "measured weight" and the "dosing weight".
2. If measured weight is unavailable:
   a. Pharmacist will contact nurse to measure patient's current weight and enters the value as the "measured weight."
   b. If weight cannot be measured, nurse will obtain patient's stated or estimated weight, which will be entered as the "dosing weight"
   c. In any situation in which measuring the patient's weight will significantly delay the administration of the argatroban infusion, it is acceptable to use the patient's stated or estimated weight.

Appendix E: Pharmacist order entry details

1. General instructions:
    a. Adjustments to the rate of argatroban infusion will be ordered via Pharmnet.
    b. aPTT levels will be ordered in eHR .
        i. Collection priority for future orders is “Timed Stat”.
        ii. Collection type is “nurse draw”.
2. Specific procedure, based on aPTT value:
    a. aPTT value below target level.
        i. Modify order for argatroban infusion and enter new rate.
        ii. Order aPTT to be drawn according to protocol.
        iii. Call nurse to communicate infusion instructions.
    b. aPTT value within target range
        i. Order aPTT to be drawn according to protocol.
        ii. If aPTT within target range on two consecutive measurements, order next aPTT to be drawn daily thereafter (see **Appendix G** for details).
    c. aPTT above target level
        i. If protocol calls for infusion to be temporarily stopped, pharmacist will discontinue argatroban infusion order.
        ii. Call nurse to stop infusion
        iii. Enter a new order for argatroban infusion (with a lower rate, according to protocol) with an appropriate new start date and time
        iv. Order next aPTT to be drawn according to protocol
    d. aPTT critically high
        i. If aPTT is critically high (value depends on nomogram) on two consecutive measurements, provider must be notified
        ii. Place order to discontinue argatroban infusion
        iii. Call nurse to stop infusion
        iv. Contact provider for new instructions

Appendix F: Required communication between pharmacist and nurse
In the following situations, the nurse must give verbal report to the pharmacist:

1. Patient’s weight cannot be measured
2. Patient shows signs of bleeding, thrombosis, or other clinical complications (nurse must also notify provider)
3. Patient has an upcoming procedure that might require discontinuation of argatroban infusion

In the following situations, the pharmacist must give verbal report to the nurse. If the primary nurse is not available, the instructions may be given to the charge nurse or another RN on the patient’s unit. Initial infusion and infusion rate changes should occur within 15 minutes of notification.

1. Initial argatroban infusion have been made available by pharmacy
2. Argatroban infusion needs to be discontinued or temporarily stopped
3. Rate of argatroban infusion needs to be changed

Appendix G: Pharmacy documentation

1. Pharmacist will document using “Notes” for required written documentation.
2. Pharmacist documentation is required in the following situations:
   a. Argatroban infusion initiation
   b. Any time the argatroban infusion rate is modified
   c. Any time protocol provider is contacted
      1) Required information includes:
         a) Name of provider
         b) Reason for notification

Appendix H: aPTT Timing

Pharmacist will order aPTT according to protocol (2 hrs. or 4 hrs.) after any change to rate of argatroban infusion.

If the argatroban infusion is interrupted and restarted according to protocol, the 2-hr or 4-hr period begins when the argatroban infusion is restarted.

If the aPTT is at goal on two consecutive measurements, recheck aPTT daily as long as the value remains therapeutic. The next aPTT (after two consecutive therapeutic values) should be checked no sooner than 2 hours and no later than 24 hours after the second consecutive therapeutic value.