Argatroban protocol

- Usual presentation is a **MULTI-DOSE** vial of Argatroban containing 250mg in 2.5ml. [Exembol Multidose 100 mg/ml concentrate for solution for infusion]
- For infusion rates ***less than 9.0ml/hr:*** Withdraw 0.5ml (50mg) and dilute in 50ml of cystalloid in a 50ml syringe to make a solution with a concentration of 1mg/ml. ***YELLOW***
- Place the opened vial in the drug fridge having written on the box the date first opened. Storage for 28 days is allowed.
- For infusion rates ***greater than 9.0ml/hr:*** Dilute 250mg (2.5mL) with 250mL NS or D5W (1mg/mL). ***BLUE***

Argatroban 250mg in 2.5ml multi use vial	***Syringe***	**Default:** 0.5mcg/kg/min **Maximum:** 10mcg/kg/min	Dilute 50mg (0.5mL) with 50mL NS, D5W or Hartmanns (1mg/mL)	Use only the multidose vial. Once opened, store in the fridge up to 28 days.
Argatroban 250mg in 2.5ml multi use vial	***Volumatic pump required***	**Default:** 0.5mcg/kg/min **Maximum:** 10mcg/kg/min	Dilute 250mg (2.5mL) with 250mL NS or D5W (1mg/mL)	Use Uncommon Volumat Pump Make a bag only if more than 10mL/hour is required See protocol for dosing guidelines If no uncommon pump, MUST calculate rate in mL/hr Give via Drug X

- Initial Infusion Rate 2mcg/kg/min. Dose titration table shown below and should be guided by aPTTr

aPTTr	Infusion Rate change	Next aPTTr
< 1.5	***INCREASE*** by 0.5mcg/kg/min	2 hours
1.5-3.0	***NO CHANGE***	2 hours After 2 consecutive aPTTr within target range, check with daily bloods
> 3.0 **ON RRT**	***HALF*** of the previous infusion rate	2 hours
> 3.0 **NOT ON RRT**	***STOP*** infusion until the aPTTr is 1.5-3.0; ***RESUME*** at half of the previous infusion rate	2 hours

- Conversion table showing ml/hr infusion rate for dose range and patient weight

DOSE (mcg/kg/min)	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0
Actual body weight (kg)	***Infusion Rate (ml/hr) using dilution of 1mg/ml***							
50	1.5	3.0	4.5	6.0	7.5	9.0	10.5	12.0
60	1.8	3.6	5.4	7.2	9.0	10.8	12.6	14.4
70	2.1	4.2	6.3	8.4	10.5	12.6	14.7	16.8
80	2.4	4.8	7.2	9.6	12.0	14.4	16.8	19.2
90	2.7	5.4	8.1	10.8	13.5	16.2	18.9	21.6
100	3.0	6.0	9.0	12.0	15.0	18.0	21.0	24.0
110	3.3	6.6	9.9	13.2	16.5	19.8	23.1	26.4
120	3.6	7.2	10.8	14.4	18.0	21.6	25.2	28.8
130	3.9	7.8	11.7	15.6	19.5	23.4	27.3	31.2
140	4.2	8.4	12.6	16.8	21.0	25.2	29.4	33.6
150	4.5	9.0	13.5	18.0	22.5	27.0	31.5	36.0

- ***USE CONTINUOUS*** IV Argatroban ***UNTIL*** off RRT for >48 hours with decision ***NOT*** to restart in the next 24-48 hours.
- ***ONCE OFF RRT RE-COMMENCE*** UFH subcutaneous regime.
- **Pharmacodynamics:** Argatroban, a synthetic L-arginine derivative, is a direct thrombin inhibitor that binds reversibly to thrombin. Argatroban exerts its anticoagulant effect independently of antithrombin III and inhibits fibrin formation; activation of coagulation factors V, VIII and XIII; activation of protein C; and platelet aggregation.
- **Pharmacokinetics:**
    - Steady-state levels typically achieved within 1-3 hours following initiation.
    - Anticoagulation parameters return to baseline generally within 2 to 4 hours after discontinuation of infusion. There is no reversal agent.
    - Predominantly inactivated by hepatic metabolism. Use with caution / dose reduce in severe hepatic impairment.
    - No significant clearance on RRT
- **NOTE:**
    - Argatroban will result in an elevated INR but this should not be used to titrate therapy.
    - Argatroban interferes with the Fibrinogen lab assay resulting in falsely low levels. If assessment of Fibrinogen required during therapy perform a TEG as the functional fibrinogen (CFF) assay should not be affected.

This guideline has been peer reviewed by: James Uprichard, Steve Austin, Pamala Kanagasabapathy, Paul Grayston and Joanne Peh.

References

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