Delegation Protocol Number: 134

Delegation Protocol Title:
Enoxaparin Dosing and Monitoring for Therapeutic Use - Pediatric - Inpatient

Delegation Protocol Applies To:
☒ Wisconsin ☐ N. Illinois
Inpatients

Target Patient Population:
Any pediatric patient (18 years old or younger) with an active order for treatment doses of enoxaparin

Delegation Protocol Champion:
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Purpose Statement:
To delegate the dosing and laboratory ordering for the adjustment of enoxaparin from the ordering provider to the pharmacist to achieve a defined therapeutic goal. Standardization of dosing, monitoring, and titration of enoxaparin can improve the time to a therapeutic concentration which can improve outcomes related to thromboembolic and bleeding events.

Who May Carry Out This Protocol:
Inpatient pharmacists

Guidelines for Implementation:
1. The protocol is initiated when the provider enters an order for enoxaparin at a treatment dose in a pediatric patient within the American Family Children's Hospital (AFCH) or University Hospital (UH)
   1.1. Enoxaparin orders for prevention of venous thromboembolism are excluded from the protocol
   1.2. Patients receiving renal replacement therapy are excluded from the protocol
2. Upon receipt of the order the pharmacist will complete an assessment of the patient's age, actual body weight, and renal function to determine if the ordered enoxaparin dose is correct. Pharmacist will also verify if the patient has any allergies.
   2.1. The pharmacist will use the recommendations provided in Table 1 to determine correct treatment dosing.
      2.1.1. Subcutaneous route of administration is preferred over intravenous route of administration due to potential for inconsistency in IV administration technique leading to variability in pharmacokinetic parameters, affecting medication therapy monitoring.
         2.1.1.1. Intravenous dosing and monitoring are extrapolated from subcutaneous dosing and this practice has been validated by small clinical trials.
   2.2. If an adjustment to the enoxaparin dose is needed, the pharmacist will discontinue the original enoxaparin order and enter a new order for enoxaparin with the corrected dose.
3. Pharmacists will order anti-Xa concentrations following initiation, with dose adjustment, and with continued maintenance as described in Table 2.
4. The pharmacist will adjust the enoxaparin dose as outlined in Table 3 until a therapeutic anti-Xa concentration has been achieved.
5. The pharmacist will also ensure appropriate maintenance monitoring for enoxaparin is completed
   5.1. Recommendations for maintenance monitoring is outlined in Table 4
   5.2. The pharmacist will order maintenance monitoring labs if not previously ordered

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6. Pharmacists will document anti-Xa concentrations, dose adjustments, and monitoring recommendations by writing a progress note in the electronic medical record utilizing a smartphrase (".ENOXAPARINNOTE")

Order Mode:
Medications - Protocol/Policy without Cosign
Laboratory Orders - Cosign Required Protocol/Policy

References:

1. Andrade-Campos MM, Montes-Limon AE, Fernandez-Mosteirin N, et al. Dosing and monitoring of enoxaparin therapy in children: experience in a tertiary care hospital. *Blood Coagul Fibrinolysis* 2013; 24(2):194-198.
2. Bauman ME, Belletrutti MJ, Bajzar L, et al. Evaluation of enoxaparin dosing requirements in infants and children: better dosing to achieve therapeutic levels. *Throm Haemost.* 2009;101(1):86-92.
3. Cies J, Santos L, and Chopra A. IV enoxaparin in pediatric and cardiac ICU patients. *Pediatr Crit Care Med.* 2014;15(2):e95-e103.
4. Chander A, Nagel K, Wiernikowski, et al. Evaluation of the use of low-molecular weight heparin in neonates: a retrospective, single center study. *Clin Appl Thromb Hemost.* 2013;19(5):488-493.
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6. Fung LS, Klockau C. Effects of age and weight-based dosing of enoxaparin on anti-factor Xa concentrations in pediatric patients. *J Pediatr Pharmacol Ther.* 2010;15(2):119-125.
7. Goldsmith R, Chan AK, Paes BA, et al. Feasibility and safety of enoxaparin whole milligram dosing in premature and term neonates. *J Perinatol.* 2015;35(10):852-854.
8. Ignjatovic V, Najid S, Newall F, et al. Dosing and monitoring of enoxaparin (low molecular weight heparin) therapy in children. *Br J Haematol.* 2010;149(5):734-738.
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10. Diab Y, Ramakrisnan K, Ferrell B, et al. IV Versus Subcutaneous Enoxaparin in Critically Ill Infants and Children: Comparison of Dosing, Anticoagulation Quality, Efficacy, and Safety Outcomes. *Pediatr Crit Care Med.* 2017;18(5):e207-e218.

Table 1: Treatment dosing of enoxaparin in neonatal and pediatric patients*

Patient Age	Standard Dosing	Renal Dosing (CrCl <30 mL/min/1.73 m^2)
<2 months	2 mg/kg every 12 hours	2 mg/kg every 24 hours
2 months to 10 years	1.5 mg/kg every 12 hours	1.5 mg/kg every 24 hours
>10 years	1 mg/kg every 12 hours	1 mg/kg every 24 hours

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Table 2: Monitoring Anti-Xa concentrations

Rationale for Anti-Xa Monitoring	Anti-Xa Monitoring Timing
Enoxaparin dose or with any change in enoxaparin dosing	4 hours after the second dose administered until therapeutic concentration is achieved
When first therapeutic concentration achieved	4 hours after next enoxaparin dose to confirm therapeutic range
When second therapeutic concentration achieved	Repeat in 7 days: • If therapeutic concentration ≤48 hours from initiating enoxaparin, then recheck anti-Xa concentration in another 48 hours. If therapeutic, then transition to maintenance monitoring • If therapeutic >48 hours from initiating enoxaparin, then transition to maintenance monitoring
Maintenance monitoring	Every 14 days
Renal insufficiency (CRCL <30 mL/min/1.73 m^2) and not on renal replacement therapy)	4 hours after each dose administered until therapeutic concentration is achieved, then check every 48-72 hours while patient remains hospitalized

Table 3. Enoxaparin dose adjustments based on the Anti-Xa concentration

Anti-Xa Concentration (international units/mL)	Hold Next Dose	Dosage Change	Next Anti-Xa Concentration
<0.35	No	Increase by 25%	4 hours after second dose
0.35 - 0.49	No	Increase by 10%	4 hours after second dose
0.50 - 1.1	No	No	See Table 2
1.11 - 1.5	No	Decrease by 20%	4 hours after second dose
1.51 - 2	Delay next dose by 3 hours from originally scheduled due time	Decrease by 30%	Before next dose & 4 hours after next dose
>2.01	Hold until anti-Xa <0.5 international units/mL	Contact MD and decrease by 40%	Every 12 hours until anti-Xa <0.5 international units/mL

Table 4. Monitoring low molecular weight heparin

Lab	Prior to Enoxaparin	Initial Phase	Maintenance Phase
Hemoglobin/ Hematocrit	Baseline	After 7 days	Every 2-4 weeks or as clinically indicated*
Platelet	Baseline	After 24 hours once, and after 7 days	Every 2-4 weeks or as clinically indicated*
Serum Creatinine	Baseline	After 7 days	Every 1-4 weeks or as clinically indicated*

*For abnormal values may monitor more frequently

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