General Information

These guidelines apply to the use of enoxaparin for the prevention and treatment of thromboembolic disorders. We have organized the information by phase of care: Initiation of therapy & inpatient management and Discharge & follow-up planning.

Low Molecular Weight Heparin (LMWH) has become the anticoagulant agents of choice in many pediatric patients, both for primary prophylaxis and treatment of thromboembolism. At CHOP Enoxaparin is the LMWH that is on formulary. The potential advantages of LMWH for pediatric patients include the need for minimal monitoring, lack of interference by other drugs or diet (unlike warfarin), reduced risk of Heparin-induced thrombocytopenia (HIT), and reduced risk of osteoporosis with long-term use compared to that with the use of heparin.

Baseline Monitoring (To be completed prior (< 48 hrs) to or upon initiation of enoxaparin)

Baseline labs are to be completed to ensure patient has a normal baseline coagulation state:
- CBC
  - Thrombocytopenia is a relative contraindication to anticoagulant therapy and should be corrected to ≥75,000/mL before use.
- PT
- PTT
- Creatinine (Cr)

If the patient has abnormal coagulation studies, thrombocytopenia, or an elevated Cr, the hematology team should be consulted for further recommendations.

Dosing Considerations:
- The half-life of enoxaparin is 4 hours.
- Peak enoxaparin levels occur 3 to 5 hours following a subcutaneous injection.
- Enoxaparin is renally cleared and adjustments to dosage may be required if calculated CrCl is <30 mL/minute. Consult hematology or pharmacy for dose adjustments or consider alternative therapy (unfractionated heparin or warfarin) in patients with decreased renal function.
- Infants < 3 months of age or weight < 5 kg have increased requirements per kilogram, which likely is due to a large volume of distribution and low antithrombin levels. Prior published enoxaparin dosing recommendations are often inadequate for neonates. The doses...
Initiation and Maintenance of Enoxaparin (Lovenox)

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Recommended in this document have been updated to reflect current practice and are more likely to achieve the therapeutic range.

- Obese patients: (BMI > 30) should receive lower dose ~ 0.8 mg/kg
- DOSES SHOULD BE ROUNDED UP TO THE NEAREST WHOLE MILLIGRAM

Initial Dose:
- < 3 months: 1.7 mg/kg Sub-Q q 12 hours
- 3 months - 2 years: 1.2 mg/kg Sub-Q q 12 hours
- > 2 years: 1 mg/kg Sub-Q q 12 hours
- Obese patients ~ 0.8 mg/kg Sub-Q q12 hours - **Maximum dose 170 mg**

Monitoring

- Enoxaparin is monitored by a heparin anti-Xa level using an assay for LMWH. It should be sent 4 hours (range 3-5 hours) after 2nd or 3rd dose upon initiation, after any dose change, and when there is concern that the patient may be bleeding
  - Neonates and infants (< 1 yr): weekly while inpatient - if two anti-Xa levels are within therapeutic range, then go to a schedule of every other week or more frequent with concerns about deteriorating renal function
  - Children (1-17 yrs): every other week while inpatient or more frequent with concerns about deteriorating renal function
  - Adults (≥ 18 yrs): monitoring of anti-Xa level is not required if the patient has normal renal function and non-obese (< 100 kg or BMI < 30 kg/m2) or non-malnourished (weight > 45 kg)
- Enoxaparin dose may accumulate over the first few weeks, therefore anti-Xa levels should be monitored accordingly

Therapeutic Range: A guideline for therapeutic enoxaparin is a heparin anti-Xa level of 0.5 to 1 units/mL in a sample taken 4 hours (range 3-5 hours) following a subcutaneous injection. Anti-Xa levels up to 1.2 unit/mL have been targeted for patients with high risk of thrombosis. Closer monitoring is needed (at least weekly anti-Xa).
**CLINICAL PRACTICE GUIDELINES**

**Initiation and Maintenance of Enoxaparin (Lovenox)**

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<table>
<thead>
<tr>
<th>Anti-Xa Level</th>
<th>Hold Next Dose?</th>
<th>Dose Change?</th>
<th>Repeat Anti-Xa Level?</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.35 units/mL</td>
<td>No</td>
<td>Increase by 25%</td>
<td>4 h after 2nd dose</td>
</tr>
<tr>
<td>0.35-0.49 units/mL</td>
<td>No</td>
<td>Increase by 10%</td>
<td>4 h after 2nd dose</td>
</tr>
<tr>
<td>0.5-1.0 units/mL</td>
<td>No</td>
<td>None</td>
<td>See “Monitoring” section</td>
</tr>
<tr>
<td>1.1-1.5 units/mL</td>
<td>Decrease by 20%</td>
<td>4 h after 2nd dose</td>
<td></td>
</tr>
<tr>
<td>1.6-2.0 units/mL</td>
<td>Decrease by 30%</td>
<td>4 h after 2nd dose</td>
<td></td>
</tr>
<tr>
<td>&gt; 2.0 units/mL</td>
<td>For these patients, all further doses should be held, and the anti-factor Xa level measured q 12 h until the anti-factor Xa level is &lt; 0.5 units/mL. Check for decreased renal function (rising creatinine). Enoxaparin can then restarted at a dose 40% less than was originally prescribed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Ideally, blood samples for the heparin anti-Xa level should be drawn by venipuncture. Heparin contamination in the central line or IV may affect the level. In the case where a level is drawn from a line through which heparin has been administered, ensure that an adequate amount of “waste” is withdrawn from the line before drawing the lab [at least twice the volume of the catheter].

**Administration**

- Administer by subcutaneous injection to the anterolateral/posterolateral abdominal wall, upper arm, or thigh. (an illustration of potential sites can be found in the enoxaparin educational booklet and the nursing procedure for administration of subcutaneous injections)
- Do NOT administer IM or IV.
- Insuflon™ catheters may be used to administer enoxaparin in children ≥5kg.

**Safety**

- Bleeding! The major adverse event related to enoxaparin is bleeding. If a patient on enoxaparin develops bleeding, stop enoxaparin and urgently seek a Hematology consult.
- Heparin Induced Thrombocytopenia (HIT) - Though rare, HIT does occur in children. This should be suspected in any patient on heparin, uFH or LMWH, with unexplained drop in platelet count > 50% from baseline or with thrombocytopenia. **Hematology should be consulted immediately if HIT is suspected.**
- Long term use (≥1 year) of heparin or LMWH may increase the risk of osteoporosis. Consider obtaining a baseline dexa scan in patients > 5 years of age.
Avoid IM injections and arterial punctures during anticoagulant therapy. When such procedures are clinically necessary, ensure that adequate external pressure is applied post-procedure.

Other invasive procedures that may result in bleeding in a patient who is anticoagulated and should be carefully considered include NG tube insertions, intubation, and rectal temps.

Avoid drugs that affect platelet function (eg, aspirin, NSAIDs, dipyridamole) as they may potentiate the risk of hemorrhage.

**Enoxaparin Reversal**

- Protamine sulfate can be used – However, it does not fully reverse LWMH – (about 70% reversal).
- Protamine combines with the strongly acidic heparin to form a stable salt complex neutralizing the anticoagulant activity.
- Protamine requires a high level of caution when being prescribed and administered Protamine should be administered intravenously in a concentration of 10 mg/mL at a rate not to exceed 5 mg/minute. If administered too quickly it may cause cardiovascular collapse. Patients with known hypersensitivity reactions to fish, and those who have received protamine containing insulin or previous protamine therapy may be at risk of hypersensitivity reactions to protamine sulfate.
- The dosage of protamine sulfate is based on both the amount of enoxaparin and the time since the last dose, as follows:

  **Table 2. Nomogram for Enoxaparin Reversal**

<table>
<thead>
<tr>
<th>Time Since Last Enoxaparin Dose</th>
<th>Protamine Dose per 1 mg Enoxaparin Received</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4 hours</td>
<td>1 mg per 1 mg enoxaparin received</td>
</tr>
<tr>
<td>4-8 hours</td>
<td>0.5-0.75 mg per 1 mg enoxaparin received</td>
</tr>
<tr>
<td>8-12 hours</td>
<td>0.25-0.5 mg per 1 mg enoxaparin received</td>
</tr>
<tr>
<td>&gt; 12 hours</td>
<td>Do not give protamine</td>
</tr>
</tbody>
</table>

Max dose: 50 mg

**Converting from LMWH to uFH:**

- Begin unfractionated heparin (uFH) no earlier than 8 hours after the last dose of LMWH.
  - If starting within 8-12 hours, do not use bolus dose of uFH.
  - After 12 hours, consider bolus dose of uFH followed by maintenance dose per protocol.

**CLINICAL PRACTICE GUIDELINES**

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Elective Procedures

- Consult the provider conducting the procedure for specific direction of holding anticoagulation.
  In general, hold at least 1 LMWH dose for minor procedure and 2 LMWH doses prior to major procedure such as invasive surgical procedure or lumbar puncture (list not all inclusive).

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Optimal amount of time required between procedure and previous dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial line</td>
<td>12 hours</td>
</tr>
<tr>
<td>Biopsy (all)</td>
<td>24 hours</td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>24 hours</td>
</tr>
<tr>
<td>Broviac</td>
<td>24 hours</td>
</tr>
<tr>
<td>Chest tube</td>
<td>24 hours</td>
</tr>
<tr>
<td>Circumcision</td>
<td>24 hours</td>
</tr>
<tr>
<td>Dental (minor)</td>
<td>12 hours</td>
</tr>
<tr>
<td>Dental (major – extraction)</td>
<td>24 hours</td>
</tr>
<tr>
<td>Immunization Administration</td>
<td>12 hours</td>
</tr>
<tr>
<td>Epidural procedure</td>
<td>24 hours</td>
</tr>
<tr>
<td>Foley Placement</td>
<td>12 hours</td>
</tr>
<tr>
<td>Hernia repair</td>
<td>24 hours</td>
</tr>
<tr>
<td>Lumbar puncture</td>
<td>24 hours</td>
</tr>
<tr>
<td>NG/ND/NJ Placement</td>
<td>12 hours</td>
</tr>
<tr>
<td>Paracentesis</td>
<td>24 hours</td>
</tr>
<tr>
<td>PICC</td>
<td>24 hours</td>
</tr>
</tbody>
</table>

Complications

- The attending of record or the attending defined responsible for outpatient management will be responsible for the diagnosis and management of any potential complications (i.e. bleeding, etc) in consultation with the division of hematology as deemed appropriate.
- Reporting of complications, including bleeding requiring transfusion, intracranial hemorrhage, and over-anticoagulation requiring reversal with protamine, into the electronic reporting system, Safety Net, is highly recommended.

Discharge & Follow-Up Planning

**ALERT:** Prescription insurance plans often require prior authorization of enoxaparin (Lovenox) as a condition of covering the drug. This process may take up to 3 days to complete. Case Management facilitates this process and should be alerted to help with enoxaparin arrangements in ample time as not to delay discharge.
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Ordering Drug:
When writing discharge orders/instructions) appreciate that for standard therapy, injections are given every 12 hours. Needle gauge and length are important considerations.

- Doses should be rounded up to the nearest WHOLE MILLIGRAM
- Enoxaparin (Lovenox®) can be ordered as a multidose vial 300 mg (3ml). Most patients prefer to use an insulin syringe with a 31 gauge, 5/16” needle with the dose drawn from the multiple dose vial.
  - Insulin syringes are marked in units and were made for use with insulin. Enoxaparin is given in mg, not units. However, because 1 mg of enoxaparin is the same volume as 1 unit of insulin, the insulin syringe can be used. A 1 unit measurement in an insulin syringe is equivalent to 1 mg of enoxaparin.
    - Outpatient anticoagulation management service usually request/prefers the multidose vial with insulin syringes
    - You must order a syringe if ordering a multiple dose vial. Either choose the insulin syringe (30 units/0.3mL, 50 units/0.5 mL or 100 units/1 mL) or a standard needle. Be sure the family is educated prior to discharge to use the needle you prescribe for home use.
    - Some pharmacies prepare syringes (referred to as pre-drawn syringes)

- Manufacturer’s pre-filled syringes. The concentration is 100 mg/1 mL. The needle is 27 gauge, ½ inch length and is attached to the syringe.
  - 30 mg and 40 mg syringes have NO graduation marks on the syringe barrel. They are ordered specifically for a dose that is fixed/not changing.
  - 60 mg, 80 mg and 100 mg syringes – all are graduated; consequently some drug can be squirted out to achieve the ordered dose i.e. using a 60 mg prefilled syringe, for ordered dose of 48 mg, a patient could squirt out 12 mg prior to administering the injection.
  - Rarely to never used in pediatric patients are Manufacturer’s pre-filled syringes at a concentration of 150 mg/1 mL. This information is included here for completeness and in the event that a morbidly obese patient requires an enoxaparin dose > 100 mg.
    - 120 mg and 150 mg syringes both have 27 gauge, ½ inch needles attached

Ordering Patient/Family Education:
Prior to discharge, all patients and their families should receive education regarding the safe use of enoxaparin. There are educational booklets on enoxaparin available through hematology, cardiology, and the Connelly Center and as a PDF file through the CHOP intranet under Patient Family Education (PFE)
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Arranging Follow up Planning:

All patients discharged on enoxaparin should have a follow-up appointment with the service responsible for managing the patient’s enoxaparin therapy (i.e. hematology or cardiology),

- Including date, time scheduled, and location for outpatient follow-up in written discharge instructions
- An anti-Xa level should be ordered/arranged for within 1-2 weeks of discharge (within one week in patients < 20 kg)
  - Then every 4 to 6 weeks or sooner if bleeding symptoms or significant changes in weight or renal function occur in the interim
- The attending physician who will be responsible for outpatient management of the enoxaparin will be identified and documented.