Clinical Policy: Enoxaparin (Lovenox)
Reference Number: ERX.SPA.208
Effective Date: 01.11.17
Last Review Date: 02.19

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Enoxaparin (Lovenox®) is a low molecular weight heparin (LMWH).

FDA Approved Indication(s)
Lovenox is indicated:
- For prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism pulmonary embolism (PE):
  - In patients undergoing:
    - Abdominal surgery who are at risk for thromboembolic complications;
    - Hip replacement surgery, during and following hospitalization;
    - Knee replacement surgery;
  - In medical patients who are at risk for thromboembolic complications due to severely restricted mobility during acute illness.
- For treatment of acute DVT:
  - Inpatient treatment of acute DVT with or without PE, when administered in conjunction with warfarin sodium.
  - Outpatient treatment of acute DVT without pulmonary embolism when administered in conjunction with warfarin sodium.
- For prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction, when concurrently administered with aspirin.
- For treatment of acute ST-elevation myocardial infarction (STEMI).

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Lovenox is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Thrombosis/Thromboembolism* (must meet all):
      1. Any of the following indications (a, b, or c):
         a. Thrombosis or thromboembolism prevention associated with any of the following conditions:
            i. Cancer;
            ii. Unstable angina or myocardial infarction;
            iii. Atrial fibrillation or prosthetic heart valve;
            iv. Major surgery - orthopedic or non-orthopedic;
            v. Critical illness related to ICU admissions or events;
            vi. Restricted mobility associated with acute illnesses or conditions;
            vii. Implanted devices-vascular (e.g., central venous access device, umbilical venous catheter, devices/fistulas related to hemodialysis, ventricular assist devices);
         b. Thrombosis or thromboembolism treatment;
         c. Short-term prophylaxis for transition to or from oral anticoagulation.
Approval duration: Length of Benefit

*Includes off-label use for adults and pediatrics.

B. Anticoagulation in Pregnancy: Ante- and Postpartum (off-label) (must meet all):
   1. Any of the following indications:
      a. Acute venous thrombosis during current pregnancy;
      b. Prior venous thrombosis;
      c. Receiving long-term therapy with a vitamin K antagonist (VKA) (e.g., warfarin);
      d. Prosthetic heart valve;
      e. Inherited thrombophilia;
      f. Antiphospholipid antibody syndrome;
      g. Development of severe ovarian hyperstimulation syndrome post assisted reproduction;
      h. Cesarean section – current pregnancy and request is for the postpartum period;
      i. Any other indication not listed here that is listed in section I.A.;
   2. Member is pregnant or < 6 months postpartum.
   Approval duration: Antepartum (to estimated delivery date); postpartum (6 months)

C. Other diagnoses/indications
   1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III
      (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
   A. Thrombosis/Thromboembolism (must meet all):
      1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or
         member has previously met initial approval criteria;
      2. Member is responding positively to therapy;
      3. Continued use is limited to any of the following indications (a, b, or c):
         a. Venous thrombosis prophylaxis or treatment in the presence of cancer;
         b. Past history of failed anticoagulation therapy (clot development) on a non-LMWH* (e.g.,
            failed therapy on heparin, fondaparinux, warfarin, apixaban, dabigatran, edoxaban, rivaroxaban);
         c. Any other indication in section I.A where bridging to warfarin is inappropriate or member
            has a contraindication to warfarin and extended (indefinite duration) anticoagulation
            therapy is required.
   Approval duration: Length of Benefit

*LMWHs include enoxaparin and dalteparin.

B. Anticoagulation in Pregnancy: Ante- and Postpartum (off-label) (must meet all):
   1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or
      member has previously met initial approval criteria;
   2. Member is responding positively to therapy;
   3. See Section II.A for continued anticoagulation therapy beyond 6 months postpartum.
   Approval duration: Antepartum (to estimated delivery date); postpartum (6 months)

C. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions
      and documentation supports positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III
      (Diagnoses/Indications for which coverage is NOT authorized).
II. Diagnoses/Indications for which coverage is NOT authorized:
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DVT: deep vein thrombosis
LMWH: low molecular weight heparin
PE: pulmonary embolism
STEMI: ST-elevation myocardial infarction

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Active major bleeding
  - History of immune-mediated heparin-induced thrombocytopenia (HIT) within the past 100 days or in the presence of circulating antibodies
  - Known hypersensitivity to enoxaparin sodium (e.g., pruritus, urticaria, anaphylactic/anaphylactoid reactions)
  - Known hypersensitivity to heparin or pork products
  - Known hypersensitivity to benzyl alcohol (which is in only the multidose formulation of Lovenox)

- Boxed warning(s): spinal/epidural hematomas

IV. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT prophylaxis in abdominal surgery</td>
<td>40 mg SC once daily</td>
<td>Dose as specified; duration may vary.</td>
</tr>
<tr>
<td>DVT prophylaxis in knee replacement</td>
<td>30 mg SC every 12 hours</td>
<td></td>
</tr>
<tr>
<td>surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DVT prophylaxis in hip replacement</td>
<td>30 mg SC every 12 hours or 40 mg SC</td>
<td></td>
</tr>
<tr>
<td>surgery</td>
<td>once daily</td>
<td></td>
</tr>
<tr>
<td>DVT prophylaxis in medical patients</td>
<td>40 mg SC once daily</td>
<td></td>
</tr>
<tr>
<td>Inpatient treatment or acute DVT with or</td>
<td>1 mg/kg SC every 12 hours or 1.5 mg</td>
<td></td>
</tr>
<tr>
<td>without PE</td>
<td>kg SC once daily</td>
<td></td>
</tr>
<tr>
<td>Outpatient treatment of acute DVT</td>
<td>1 mg/kg SC every 12 hours</td>
<td></td>
</tr>
<tr>
<td>without PI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unstable angina and non-Q wave MI</td>
<td>1 mg/kg SC every 12 hours (with aspirin)</td>
<td></td>
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<tr>
<td>Acute STEMI in patient &lt; 75 years of</td>
<td>30 mg single IV bolus plus a 1 mg/kg</td>
<td></td>
</tr>
<tr>
<td>age</td>
<td>SC dose followed by 1 mg/kg SC every</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 hours (with aspirin)</td>
<td></td>
</tr>
<tr>
<td>Acute STEMI in patient ≥ 75 years of</td>
<td>0.75 mg/kg SC every 12 hours (no bolus)</td>
<td></td>
</tr>
<tr>
<td>age</td>
<td>(with aspirin)</td>
<td></td>
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</tbody>
</table>

V. Product Availability

- Prefilled syringes: 30 mg/0.3 mL, 40 mg/0.4 mL
- Graduated prefilled syringes: 60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/1 mL, 120 mg/0.8 mL, 150 mg/1 mL
- Multiple-dose vial: 300 mg/3 mL

VI. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created.</td>
<td>12.01.16</td>
<td></td>
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<tr>
<td>4Q17 Annual Review</td>
<td>09.28.17</td>
<td>11.17</td>
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<tr>
<td>Converted to new template.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Section I.A. Criteria are edited to follow CHEST 2016 in addition to labeled indications. Major additions include 1) prophylaxis: hip fracture, major orthopedic, general, cardiac, thoracic surgery, craniotomy; traumatic injury; critical illness; restricted mobility due to intracerebral hemorrhage, STEMI; a-fib, prosthetic heart valve; 2) treatment: PE; SVT; CVST; splanchnic thrombosis without cancer; nonbacterial thrombotic endocarditis. Warfarin bridging criteria are moved to renewal criteria. Section I.B. Removed required risk factors. Section II. Criteria are edited to follow CHEST 2016 guidelines. Major additions include 1) recurrent venous thrombosis on a non-low molecular weight heparin, 2) any other indication in section I.A. where bridging to warfarin is inappropriate or member has a contraindication to warfarin and extended (indefinite) anticoagulation therapy is required.</td>
<td>12.01.17</td>
<td>02.18</td>
</tr>
<tr>
<td>Section I.A., Venous Thrombosis, is changed to “Thrombosis and Thromboembolism” so as not to restrict to venous thrombi. Section I.A criteria are edited to encompass CHEST guidelines for neonates and children (seen primarily under implantable devices), and the criteria is collapsed to maximize consistency across the Lovenox, Fragmin and Arixtra policies. Per specialist recommendation an additional indication is added for short-term prophylaxis to or from oral anticoagulation. Duration changed to length of benefit. Continuation criteria added for pregnancy. References updated.</td>
<td>11.13.18</td>
<td>02.19</td>
</tr>
</tbody>
</table>

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.
This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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