This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the IEHP Pharmacy and Therapeutics Subcommittee.

**Drug:** dalteparin (Fragmin), enoxaparin (Lovenox), fondaparinux (Arixtra), unfractionated heparin, desirudin (Iprivask)
**Class:** Injectable anticoagulants
**Formulary Medications:** enoxaparin (Lovenox)
**Effective Date:** November 19, 2014
**Revision Date:** November 19, 2014

**Policy/Criteria:**

1. **Enoxaparin (Lovenox)**
   a. Limited 14 day supply will be approved without authorization, requests for longer duration must satisfy the criteria below:
      - Venous Thromboembolism (VTE) Prophylaxis in patients undergoing hip or knee replacement, or hip repair surgery; OR
      - Long-term therapy for DVT/PE in patients with cancer; OR
      - Failed or contraindicated to warfarin

2. **Dalteparin (Fragmin)**
   a. Must use formulary alternative enoxaparin
   b. OR provide medical justification for the use of Fragmin rather than enoxaparin

3. **Fondaparinux (Arixtra)**
   a. DVT/PE prophylaxis in patients undergoing hip or knee replacement, or hip fracture surgery
   b. Failed or contraindicated to enoxaparin or Fragmin

4. **Unfractionated Heparin**
   a. Postoperative bridging (days 0-5) until stable on warfarin

5. **Desirudin (Iprivask)**
   a. DVT/PE prophylaxis in patients undergoing hip replacement
   b. Failed or contraindicated to enoxaparin or Fragmin, then fondaparinux
**Clinical Justification:**

Comparison of FDA-Approved Indications

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<tr>
<th></th>
<th>Enoxaparin</th>
<th>Dalteparin</th>
<th>Fondaparinux</th>
<th>Desirudin</th>
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</thead>
<tbody>
<tr>
<td>Venous Thromboembolism (VTE)</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>VTE prophylaxis</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Acute MI</td>
<td>X</td>
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<td>Unstable Angina</td>
<td>X</td>
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<td>Coronary artery thrombosis prophylaxis</td>
<td>X</td>
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<tbody>
<tr>
<td>Usual Dosage</td>
<td>VTE/ACS: 1mg/kg SQ q12hr VTE ppx: 40mg SQ daily</td>
<td>VTE: 200 IU/kg SQ daily VTE ppx: 2500 IU SQ daily UA: 120 IU/kg SQ q12hr</td>
<td>VTE: 7.5 – 10mg SQ daily VTE ppx: 2.5mg SQ daily</td>
<td>VTE ppx: 15mg SQ q12hr</td>
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<tr>
<td>Mechanism of Action</td>
<td>LMWH, inhibit factor Xa and thrombin</td>
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<td>Synthetic pentasaccharide mediated inhibition of factor Xa</td>
<td>Direct thrombin inhibitor</td>
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<tr>
<td>Reversal agent</td>
<td>Protamine</td>
<td>Protamine</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Risk for HIT</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Half-Life</td>
<td>4.5 – 7 hours</td>
<td>2-5 hours; prolonged with renal impairment</td>
<td>17-21 hours; prolonged with renal impairment</td>
<td>2 hour; prolonged with renal impairment up to 12 hr</td>
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<tr>
<td>Renal Dosing Adjustment</td>
<td>Yes</td>
<td>Titrate dosage by anti-Xa level when CrCl &lt; 30mL/min</td>
<td>Use is contraindicated for CrCl &lt; 30mL/min</td>
<td>Yes</td>
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<tr>
<td>Costs/30 days (wgt 70kg)</td>
<td>VTE/ACS: $2747 VTE ppx: $660</td>
<td>VTE: $3190 VTE ppx: $656 UA: $4254</td>
<td>VTE: $3259 VTE ppx: $1312</td>
<td>VTE ppx: $9000</td>
</tr>
</tbody>
</table>

**VTE Treatment**

1. 2012 American College of Chest Physicians (ACCP) CHEST Guidelines: Recommend initial treatment with parenteral anticoagulation (LMWH, fondaparinux, IV UFH or SC UFH) in patients with acute DVT and PE.

2. In patients with pulmonary embolism (PE) or deep vein thrombosis (DVT) and no cancer, ACCP suggests warfarin over LMWH for long-term therapy. In patients with PE or DVT and cancer, ACCP suggests LMWH over warfarin. LMWH has lower risk of nonhemorrhagic side effects than LDUH.

**VTE Prophylaxis**
1. **2012 American College of Chest Physicians (ACCP) CHEST Guidelines:** Recommend a pharmacologic VTE prophylaxis with LWMH, LDUH or fondaparinux for moderate to high risk general surgery patients, or those with multiple risk factors for VTE.

2. In patients undergoing total hip arthroplasty (THA) or total knee arthroplasty (TKA), ACCP suggests the use of LMWH in preference to fondaparinux, dabigatran, rivaroxaban, or low-dose unfractionated heparin (LDUH). There may be increased bleeding risk with fondaparinux, rivaroxaban, and warfarin. There may be decreased efficacy with LDUH, warfarin, and aspirin. There is lack of long-term safety data with dabigatran and rivaroxaban. In patients undergoing hip fracture surgery (HFS), ACCP suggests the use of LMWH in preference to fondaparinux or LDUH.

3. Desirudin (Iprivask) is more effective than enoxaparin for preventing venous thromboembolism (VTE) due to hip replacement with a similar risk of bleeding, but is very expensive compared to low-molecular-weight heparin (LMWF) or fondaparinux.

4. Desirudin may be a potential alternative to argatroban. Further clinical studies in the setting of HIT are warranted.

**Acute Coronary Syndrome**

1. **ACC/AHA Guidelines:** Recommend enoxaparin, UFH and fondaparinux as Class I anticoagulants for the treatment of UA/NSTEMI for invasive or conservative interventions. In patients with STEMI requiring fibrinolytic therapy, UFH, enoxaparin or fondaparinux are recommended anticoagulants.

**References:**