Clinical Policy: Fondaparinux (Arixtra)
Reference Number: PA.CP.PHAR.226
Effective Date: 01/18
Last Review Date: 01/19

Description
Fondaparinux (Arixtra®) is a synthetic factor Xa inhibitor.

FDA Approved Indication(s)
Arixtra is indicated:
- For prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE) in patients undergoing:
  - Hip fracture surgery, including extended prophylaxis;
  - Hip replacement surgery;
  - Knee replacement surgery;
  - Abdominal surgery who are at risk for thromboembolic complications.
- For treatment of acute DVT when administered in conjunction with warfarin sodium.
- For treatment of acute PE when administered in conjunction with warfarin sodium when initial therapy is administered in the hospital.

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness® that fondaparinux 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. Major surgery - orthopedic and non-orthopedic;
            iv. Critical illness related to ICU admissions or events;
            v. Restricted mobility associated with acute illnesses or conditions;
            vi. 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;
      2. Failure of a trial of enoxaparin unless (a, b or c):
         a. Enoxaparin is contraindicated;
         b. History of clinically significant adverse effects or allergy to low molecular weight heparin (LMWH; enoxaparin or dalteparin) or heparin (e.g., history of heparin-induced thrombocytopenia [HIT]);
         c. The requested use is FDA labeled for fondaparinux but not for enoxaparin (i.e., hip fracture surgery prophylaxis; PE treatment).
*Includes off-label use for adults and pediatrics.

**Approval duration: 6 months**

### 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 (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;
3. History of clinically significant adverse effects or allergy to LMWH or heparin (e.g. HIT);

**Approval duration:**

- **Antepartum:** to estimated delivery date (EDD)
- **Postpartum:** to 6 months postpartum (3 month approvals)

### C. Other diagnoses/indications:
Refer to PA.CP.PMN.53

---

### II. Continued Approval

#### A. Thrombosis/Thromboembolism (must meet all):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria, and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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 warfarin;
   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: 6 months**

#### B. Anticoagulation in Pregnancy: Ante- and Postpartum (off-label) (must meet all):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria, and documentation supports
positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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 (1 or 2):
1. Currently, receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   
   **Approval duration:** Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

**Background**

**Description/Mechanism of Action:**
Arixtra (fondaparinux sodium) Injection is a sterile solution containing fondaparinux sodium. It is a synthetic and specific inhibitor of activated Factor X (Xa). The antithrombotic activity of fondaparinux sodium is the result of antithrombin III (ATIII)-mediated selective inhibition of Factor Xa. By selectively binding to ATIII, fondaparinux sodium potentiates (about 300 times) the innate neutralization of Factor Xa by ATIII. Neutralization of Factor Xa interrupts the blood coagulation cascade and thus inhibits thrombin formation and thrombus development. Fondaparinux sodium does not inactivate thrombin (activated Factor II) and has no known effect on platelet function. At the recommended dose, fondaparinux sodium does not affect fibrinolytic activity or bleeding time.

**III. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

- **DVT**: deep vein thrombosis
- **HIT**: heparin-induced thrombocytopenia
- **LMWH**: low molecular weight heparin
- **PE**: pulmonary embolism

*Appendix B: Therapeutic Alternatives*

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>enoxaparin</td>
<td>DVT prophylaxis in abdominal surgery 40 mg SC once daily</td>
<td>Dose as specified; duration may vary.</td>
</tr>
<tr>
<td>(Lovenox®)</td>
<td>DVT prophylaxis in knee replacement surgery 30 mg SC every 12 hours</td>
<td></td>
</tr>
<tr>
<td>- Adults</td>
<td>DVT prophylaxis in hip replacement surgery 30 mg SC every 12 hours or 40 mg SC once daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DVT prophylaxis in medical patients 40 mg SC once daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inpatient treatment or acute DVT with or without PE</td>
<td></td>
</tr>
</tbody>
</table>
**Drug Name** | **Dosing Regimen** | **Dose Limit/Maximum Dose**  
--- | --- | ---  
 | 1 mg/kg SC every 12 hours or 1.5 mg/kg SC once daily |  
Outpatient treatment of acute DVT without PI |  
1 mg/kg SC every 12 hours |  
Unstable angina and non-Q wave MI |  
1 mg/Kg SC every 12 hours (with aspirin) |  

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

**Appendix C: Contraindications/Boxed Warnings**

- **Contraindication(s):** Arixtra is contraindicated in the following conditions:
  - Severe renal impairment (creatinine clearance [CrCl] <30 mL/min)
  - Active major bleeding
  - Bacterial endocarditis
  - Thrombocytopenia associated with a positive in vitro test for anti-platelet antibody in the presence of fondaparinux sodium.
  - Body weight <50 kg (venous thromboembolism [VTE] prophylaxis only)
  - History of serious hypersensitivity reaction (e.g., angioedema, anaphylactoid/anaphylactic reactions) to Arixtra
- **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>Adults</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DVT prophylaxis following hip fracture, hip replacement, and knee replacement surgery and abdominal surgery</td>
<td>2.5 mg SC per day</td>
<td>2.5 mg per day</td>
</tr>
</tbody>
</table>
| Acute DVT/PE treatment | SC based on body weight:  
< 50 kg: 5 mg per day  
50 to 100 kg: 7.5 mg per day  
> 100 kg: 10 mg per day | 10 mg per day |

**V. Product Availability**

Single-dose, prefilled syringes: 2.5 mg, 5 mg, 7.5 mg, or 10 mg

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.
CLINICAL POLICY
Fondaparinux

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J1652</td>
<td>Injection, fondaparinux sodium, 0.5 mg</td>
</tr>
</tbody>
</table>

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>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 LMWH policies. Per specialist recommendation an additional indication is added for short-term prophylaxis to or from oral anticoagulation. Continuation criteria added for pregnancy. References reviewed and updated.</td>
<td></td>
<td>01/19</td>
</tr>
<tr>
<td>1Q 2019 annual review: references reviewed and updated.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References


