Clinical Policy: Fondaparinux (Arixtra)

Reference Number: ERX.SPA.206
Effective Date: 01.11.17
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

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

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
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 Arixtra 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 (*see Appendix D*);
      ii. Unstable angina or myocardial infarction;
      iii. Major surgery - orthopedic or 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. If request is for Arixtra, member must use generic fondaparinux, unless contraindicated or clinically significant adverse effects are experienced.

Approval duration:
Medicaid – 6 months
Commercial – 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 (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 low molecular weight heparin (LMWH; e.g., enoxaparin) or heparin (e.g., heparin-induced thrombocytopenia [HIT]);
4. If request is for Arixtra, member must use generic fondaparinux unless contraindicated or clinically significant adverse effects are experienced.

Approval duration:
Medicaid – Antepartum (to estimated delivery date); postpartum (6 months)
Commercial – Length of Benefit

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 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;
4. If request is for Arixtra, member must use generic fondaparinux, unless contraindicated or clinically significant adverse effects are experienced.

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

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 beyond 6 months postpartum;
4. If request is for Arixtra, member must use generic fondaparinux, unless contraindicated or clinically significant adverse effects are experienced.

Approval duration:
Medicaid – Antepartum (to estimated delivery date); postpartum (6 months)
Commercial – Length of Benefit

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).

III. 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.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DVT: deep vein thrombosis
HIT: heparin-induced thrombocytopenia
LMWH: low molecular weight heparin
NCCN: National Comprehensive Cancer Network
PE: pulmonary embolism

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - 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

Appendix D: General information

- Per National Comprehensive Cancer Network (NCCN) guidelines for cancer-associated venous thromboembolic disease, fondaparinux is recommended for:
  - Anticoagulation for acute and chronic management of acute superficial vein thrombosis, management of chronic splanchnic vein thrombosis in cancer patients, management of acute splanchnic vein thrombosis, anticoagulation for acute DVT, acute catheter-related DVT, and/or acute pulmonary embolism in cancer patients with no contraindication to anticoagulation:
    - as monotherapy
    - for 5 - 10 days given concurrently with warfarin monotherapy
  - Anticoagulation for cancer patients following therapeutic anticoagulation failure with: heparin sodium, low-molecular weight heparin, warfarin sodium, apixaban, dabigatran, edoxaban, or rivaroxaban
  - Venous thromboembolism prophylaxis for adult patients with no contraindication to anticoagulation
    - for inpatient medical and/or surgical patients with cancer or those for whom a clinical suspicion of cancer exists
    - for outpatient surgical patients with cancer for up to 4 weeks following high-risk surgery (e.g., abdominal/pelvic)
  - Initial treatment for suspected or confirmed heparin-induced thrombocytopenia following discontinuation of heparin-based products in clinically stable patients with no contraindications and without hemodynamically unstable pulmonary embolism, limb-threatening thrombosis, or planned invasive procedures

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Adults		
DVT prophylaxis following hip fracture, hip replacement, and knee replacement surgery and abdominal surgery	2.5 mg SC per day	2.5 mg per day
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

VI. Product Availability

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

VII. References

1. Arixtra Prescribing Information. Rockford, IL: Mylan Institutional, LLC. August 2020. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021345s037lbl.pdf. Accessed November 23, 2021.
2. Executive summary: Antithrombotic therapy and prevention of thrombosis: CHEST guidelines and expert panel reports. Available at http://www.chestnet.org/Guidelines-and-Resources/CHEST-Guideline-Topic-Areas/Pulmonary-Vascular. Accessed November 6, 2020. *The CHEST guideline series presents recommendations for the prevention, diagnosis, and treatment of thrombosis, addressing a comprehensive list of clinical conditions, including medical, surgery, orthopedic surgery, atrial fibrillation, stroke, cardiovascular disease, pregnancy, and neonates and children*.
3. Thromboembolism in pregnancy. Practice Bulletin No. 196. American College of Obstetrics and Gynecologists. *Obstet Gynecol.* July 2018; 132: e1-17.
4. National Comprehensive Cancer Network. Cancer-Associated Venous Thromboembolic Disease Version 3.2021. Available at: http://www.nccn.org. Accessed November 23, 2021.
5. Arixtra. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed November 23, 2021.
6. Kearon C, Akl EA, Omelas J, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. Chest 2016;149:315-352.
7. Ortel TL, Neumann I, Ageno W, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood Adv. 2020 Oct 13;4(19):4693-38.
8. Mehta LS, Warnes CA, Bradley E, et al. Cardiovascular considerations in caring for pregnant patients – a scientific statement from the American Heart Association. *Circulation*. June 2020;141:e884–e903. DOI: 10.1161/CIR.0000000000000772.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: 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.	12.01.17	02.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	11.13.18	02.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2020 annual review: no significant changes; added Medicaid line of business with 6 month approval durations for thrombosis/thromboembolism; modified pregnancy anticoagulation approval durations from length of benefit to antepartum or 6 months postpartum to align with other injectable anticoagulant policies; references reviewed and updated.	11.01.19	02.20
1Q 2021 annual review: added criteria if request is for Arixtra, medical justification supports inability to use generic fondaparinux to initial and continuation criteria; added Appendix D; references reviewed and updated.	11.01.20	02.21
1Q 2022 annual review: no significant changes; removed the requirement for a prior trial of enoxaparin for thrombosis/thromboembolism since fondaparinux and enoxaparin are both preferred formulary agents; changed "Medical justification" language to "Member must use"; references reviewed and updated.	11.23.21	02.22

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.