Clinical Policy: Fondaparinux (Arixtra)

Reference Number: CP.PHAR.226
Effective Date: 05.01.16
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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.
- For the treatment of venous thromboembolism (VTE) in pediatric patients aged 1 year or older weighing at least 10 kg.

Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® 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. 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);
3. If request is for Arixtra, member must use generic fondaparinux, unless contraindicated or clinically significant adverse effects are experienced.

Approval duration:
Medicaid/HIM - 6 months
Commercial – 6 months or duration of request, whichever is less

**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 LMWH or heparin (e.g., HIT);
4. If request is for Arixtra, member must use generic fondaparinux unless contraindicated or clinically significant adverse effects are experienced.

Approval duration:
Medicaid/HIM – Antepartum (to estimated delivery date); postpartum (6 months)
Commercial – 6 months or duration of request, whichever is less

C. Other diagnoses/indications (must meet 1 or 2):
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Thrombosis/Thromboembolism (must meet all):

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
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/HIM - 6 months
Commercial – 6 months or duration of request, whichever is less

B. Anticoagulation in Pregnancy: Ante- and Postpartum (off-label) (must meet all):

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy;
3. See Section II.A for continued anticoagulation therapy 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/HIM – Antepartum (to estimated delivery date); postpartum (6 months)
Commercial – 6 months or duration of request, whichever is less

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, 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
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.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
enoxaparin (Lovenox®)	*Adults:* DVT prophylaxis in abdominal surgery • 40 mg SC once daily DVT prophylaxis in knee replacement surgery • 30 mg SC every 12 hours	Dose as specified; duration may vary.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	DVT prophylaxis in hip replacement surgery • 30 mg SC every 12 hours or 40 mg SC once daily DVT prophylaxis in medical patients • 40 mg SC once daily Inpatient treatment or acute DVT with or without PE • 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):
  - Severe renal impairment (creatinine clearance [CrCl] <30 mL/min) in prophylaxis or treatment of venous thromboembolism
  - 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 management of superficial vein thrombosis in cancer patients, management of chronic splanchnic vein thrombosis in cancer patients, management of acute splanchnic vein thrombosis in cancer patients, anticoagulation for acute DVT, acute catheter-related DVT, and/or acute pulmonary embolism in cancer patients with no contraindication to anticoagulation:
    - as monotherapy
    - for at least 5 days given currently with warfarin until transition to warfarin monotherapy
  - Anticoagulation for cancer patients following progression or new thrombosis on therapeutic anticoagulation: heparin sodium, low-molecular weight heparin, warfarin sodium, apixaban, dabigatran, edoxaban, or rivaroxaban
  - Venous thromboembolism prophylaxis for adult patients with cancer (excluding basal/squamous cell skin cancer) or those for whom a clinical suspicion of cancer

exists who are admitted for medical or surgical hospitalizations with no contraindication to anticoagulation
- 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
- Transition to alternative therapy for patents with heparin-induced thrombocytopenia who have been stabilized on initial treatment with a direct thrombin inhibitor and have no contraindications or invasive procedures planned

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
Pediatrics		
VTE treatment	SC based on body weight: 10 kg to 20 kg: 0.1 mg/kg per day	0.1 mg/kg per day

VI. Product Availability

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

VII. References

1. Arixtra Prescribing Information. Rockford, IL: Mylan Institutional, LLC. December 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/021345s052lbl.pdf. Accessed January 21, 2025.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2025. Available at: https://www.clinicalkey.com/pharmacology/. Accessed January 21, 2025.
3. 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 October 28, 2024.
4. Thromboembolism in pregnancy. Practice Bulletin No. 196. American College of Obstetrics and Gynecologists. *Obstet Gynecol.* July 2018; 132: e1-17.
5. National Comprehensive Cancer Network. Cancer-Associated Venous Thromboembolic Disease Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/vte.pdf. Accessed October 28, 2024.
6. Arixtra. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: nccn.org. Accessed October 28, 2024.

7. Kearon C, Akl EA, Omelas J, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. *Chest* 2016;149:315-352.
8. Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guidelines and Expert Panel Report. Chest 2021 Dec; 160 (6): e545- e608.
9. 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.
10. 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.
11. Douketis JD, Spyropoulos AC, Murad MH, et al. Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline. Chest. 2022 Nov;162(5):e207-e243. doi: 10.1016/j.chest.2022.07.025.

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.

HCPCS Codes	Description
J1652	Injection, fondaparinux sodium, 0.5 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: added criteria if request is for Arixtra, medical justification supports inability to use generic fondaparinux to initial and continuation criteria; reviewed and updated.	11.01.20	02.21
1Q 2022 annual review: no significant changes; changed "Medical justification" language to "Member must use"; references reviewed and updated.	11.23.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.05.22	
1Q 2023 annual review: no significant changes; updated appendix D with current NCCN compendium language; HIM-Medical benefit revised to HIM; references reviewed and updated.	09.26.22	02.23
Per health plan request, revised commercial approval duration language from "6 months or to member's renewal period, whichever is longer" to "6 months or duration of request, whichever is less."	03.29.23	
1Q 2024 annual review: updated appendix D with current NCCN compendium language; references reviewed and updated.	10.31.23	02.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2025 annual review: no significant changes; updated appendix D with current NCCN compendium language; references reviewed and updated. RT4: added newly approved indication for treatment of VTE in pediatric patients to criteria.	01.16.25	02.25

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.