Clinical Policy: Fondaparinux (Arixtra)

Reference Number: CP.PHAR.226
Effective Date: 05.01.16
Last Review Date: 02.19 Coding Implications
Line of Business: Commercial, HIM-Medical Benefit, 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 (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;
      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).

Approval duration:
Medicaid/HIM - 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

_____
**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).

Approval duration:
Medicaid/HIM - Antepartum (to estimated delivery date); postpartum (6 months)
Commercial – Antepartum (to estimated delivery date); postpartum (6 months)

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

II. Continued Therapy

A. Thrombosis/Thromboembolism (must meet all):
1. Currently receiving medication via Centene benefit 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.

Approval duration:
Medicaid/HIM - 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Anticoagulation in Pregnancy: Ante- and Postpartum (off-label) (must meet all)**:**
1. Currently receiving medication via Centene benefit 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:
Medicaid - Antepartum (to estimated delivery date); postpartum (6 months)
Commercial – Antepartum (to estimated delivery date); postpartum (6 months)

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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 and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

IV. 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.

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	Dose as specified;

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	30 mg SC every 12 hours 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)	duration may vary.

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

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 2017. Available at https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed November 7, 2018.
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 7, 2018. *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. 123. American College of Obstetrics and Gynecologists. *Obstet Gynecol.* July 2018; 132: e1-17.
4. Fondaparinux. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed November 7, 2018.
5. Cancer-associated venous thromboembolic disease (Version 2.2018). National Comprehensive Cancer Network Clinical Practice Guidelines. Available at nccn.org.

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
Arixtra information is split from CP.PHAR.04.LMWH policy. Added bridge to or contraindication to warfarin for DVT and PE. Added continuation criteria for VTE in presence of cancer.	04.16	05.16
Section I.A. Criteria are edited to follow CHEST 2012 and 2016 guidelines (which for the most part include NCCN and ACOG guidelines) in addition to labeled indications. Major additions include 1) prophylaxis: major orthopedic, general surgery; critical illness; restricted mobility due to acute illness; 2) treatment: SVT, splanchnic thrombosis without cancer. HIT is added to bypass enoxaparin preferencing. Warfarin bridging criteria are moved to renewal criteria. Safety information is removed; safety information is limited to black box warnings and contraindications that instruct a test be conducted to rule out a condition before starting therapy. Dosing is not added given the extent of off-label use in the policy.	04.17	05.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Section I.B. Pregnancy criteria are added for cases of HIT. Section II. Criteria are edited to follow CHEST 2016 guidelines. Major additions include 1) 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.		
1Q18 annual review: - Combined policies for Medicaid and commercial lines of business - 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. Continuation criteria added for pregnancy. - References reviewed and updated.	12.01.17	02.18
1Q 2019 annual review; HIM-Medical Benefit line of business added; no significant changes; references reviewed and updated.	11.13.18	02.19

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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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.