VENTURA COUNTY
HEALTH CARE PLAN

ARIXTRA® (Fondaparinux) PA Guidelines

Effective Date: 7/28/05

Date Developed: 7/28/05 by C. Wilhelmy MD

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Arixtra is a Factor Xa Inhibitor. It is a synthetic pentasaccharide that causes an antithrombin III-mediated selective inhibition of factor Xa. Neutralization of factor Xa interrupts the blood coagulation cascade and inhibits thrombin formation and thrombus development.

Authorization Criteria: prophylaxis of deep vein thrombosis (DVT) in selected surgical patients (hip or knee replacement; hip fracture; abdominal surgery in at-risk patients); acute pulmonary embolism (PE); acute DVT without PE

Off-Label: venous thromboembolism prophylaxis in general surgery; acute symptomatic superficial lower extremity venous thrombosis (≥5 cm in length); acute coronary syndromes [unstable angina; non-ST elevation myocardial infarction (UA/NSTEMI); ST elevation myocardial infarction (STEMI)]

Pre-Authorization Criteria:

Coverage of Arixtra is recommended for those who meet the following criteria:
FDA-Approved Indications

Deep vein thrombosis: Treatment of acute deep vein thrombosis.
Pulmonary embolism: Treatment of acute pulmonary embolism.
Venous thromboembolism prophylaxis in surgical patients: Prophylaxis of venous thromboembolism in patients undergoing surgery for hip replacement, knee replacement, hip fracture (including extended prophylaxis following hip fracture surgery), or abdominal surgery (in patients at risk for thromboembolic complications)

Use: Off-Label: Adult
Acute coronary syndrome; Heparin-induced thrombocytopenia treatment; Superficial vein thrombosis, acute symptomatic; Venous thromboembolism prophylaxis in medical patients with acute illness; Venous thromboembolism prophylaxis in patients undergoing major surgery for cancer

MONITORING PARAMETERS — Periodic monitoring of CBC, serum creatinine, occult blood testing of stools recommended. Antifactor Xa activity of fondaparinux can be measured by the assay if fondaparinux is used as the calibrator. PT and aPTT are insensitive measures of fondaparinux activity.

DOSING: ADULTS
DVT prophylaxis: SubQ: Adults 50 kg: 2.5 mg once daily. Note: Initiate dose after hemostasis has been established, 6-8 hours postoperatively.
Usual duration: 5-9 days (up to 11 days) following hip replacement or knee replacement.
Extended prophylaxis is recommended following hip fracture surgery (has been tolerated for up

to 32 days).

Acute DVT/PE treatment: SubQ: Adults:
<50 kg: 5 mg once daily
50-100 kg: 7.5 mg once daily
>100 kg: 10 mg once daily

DOSING: ELDERLY — Refer to adult dosing.

DOSING: RENAL IMPAIRMENT
ClCr 30-50 mL/minute: Use caution
ClCr<30 mL/minute: Contraindicated

Drug	Dosing Regimen	Authorization Limit
Hip fracture or replacement	:	Arixra: 30 days
Abdominal surgery	Arixtra: 2.5 mg QD	Arixtra: 5-10 days
Knee replacement	Arixtra: 2.5 mg QD	Arixtra: 14 days
Acute medical illness	Arixtra: 2.5 mg QD	Arixtra: 7-14 days until illness resolves and/or ambulatory
Treatment of VTE	Arixtra: Weight based: 5 mg, 7.5	Arixtra: 5 days until INR 2-3 achieved with warfarin mg, 10 mg

PRODUCT AVAILABILITY: Solution for injection, prefilled syringe: 2.5 mg/0.5 ml, 5 mg/0.4 ml, 7.5 mg/0.6 ml, 10 mg/0.8 ml.

ADMINISTRATION — Do not administer I.M.; for SubQ administration only. Do not mix with other injections or infusions. Do not expel air bubble from syringe before injection. Administer according to recommended regimen; early initiation (before 6 hours after surgery) has been associated with increased bleeding.

ADVERSE REACTIONS SIGNIFICANT — As with all anticoagulants, bleeding is the major adverse effect. Hemorrhage may occur at any site. Risk appears increased by a number of factors including renal dysfunction, age (>75 years), and weight (<50 kg).

CONTRAINDICATIONS — Hypersensitivity to fondaparinux or any component of the formulation; severe renal impairment (Clcr<30 mL/minute); body weight <50 kg (prophylaxis); active major bleeding; bacterial endocarditis; thrombocytopenia associated with a positive in vitro test for antiplatelet antibody in the presence of fondaparinux

WARNINGS / PRECAUTIONS —
Boxed Warning: Patients with recent or anticipated neuraxial anesthesia (epidural or spinal anesthesia) are at risk of spinal or epidural hematoma and subsequent paralysis. Consider risk versus benefit prior to neuraxial anesthesia; risk is increased by concomitant agents which may alter hemostasis, as well as traumatic or repeated epidural or spinal puncture. Patient should be observed closely for bleeding and/or signs and symptoms of neurologic impairment if administered during or immediately following diagnostic lumbar puncture, epidural anesthesia, or spinal anesthesia.

Not to be used interchangeably (unit-for-unit) with heparin, low molecular weight heparins (LMWHs), or heparinoids. Use caution in patients with moderate renal dysfunction (Clcr 30-50 mL/minute). Patients with serum creatinine >2 mg/dL were excluded from clinical trials. Periodically monitor renal function; discontinue if severe dysfunction or labile function develops.Use caution in conditions with increased risk of hemorrhage such as congenital or acquired bleeding disorders; active ulcerative or angiodysplastic gastrointestinal disease; hemorrhagic stroke; shortly after brain, spinal, or ophthalmologic surgery; or in patients taking platelet inhibitors. Risk of major bleeding may be increased if initial dose is administered earlier then recommended (initiation recommended at 6-8 hours following surgery). Discontinue agents that may enhance the risk of hemorrhage if possible. If thrombocytopenia occurs, discontinue fondaparinux. Use caution in the elderly, patients with a history of heparin-induced thrombocytopenia, patients with a bleeding diathesis, uncontrolled hypertension, recent gastrointestinal ulceration, diabetic retinopathy, and hemorrhage. Use caution in patients <50 kg who are being treated for DVT/PE; fondaparinux clearance may be decreased. Safety and efficacy in pediatric patients have not been established.

DRUG INTERACTIONS
- Anticoagulants: May enhance the effects of other anticoagulants.
- Antiplatelet agents (including abciximab, anagrelide, cilostazol, clopidogrel, dipyridamole, eptifibatide, ticlopidine, tirofiban): May enhance the anticoagulant effect of fondaparinux.
- NSAIDs: May enhance the anticoagulant effect of fondaparinux.
- Salicylates: May enhance the anticoagulant effect of fondaparinux.
- Thrombolytic agents: Increase the risk of hemorrhage.

HERB INTERACTIONS (all possess anticoagulant or antiplatelet activity and as such, may enhance the anticoagulant effects of fondaparinux):
Avoid alfalfa, anise, bilberry, bladderwrack, bromelain, cat's claw, celery, coleus, cordyceps, dong quai, evening primrose oil, fenugreek, feverfew, garlic, ginger, ginkgo biloba, ginseng (American/Panax/Siberian), grape seed, green tea, guggul, horse chestnut seed, horseradish, licorice, prickly ash, red clover, reishi, sweet clover, turmeric, white willow.

PREGNANCY RISK FACTOR — B

PREGNANCY IMPLICATIONS — Reproductive animal studies have not shown fetal harm. Based on case reports, small amounts of fondaparinux have been detected in the umbilical cord following multiple doses during pregnancy. Use should be limited to those women who have severe allergic reactions to heparin, including heparin-induced thrombocytopenia, and who

cannot receive danaparoid

LACTATION — Excretion in breast milk unknown/use caution

fainting or passing out.

REFERENCES

1. Bauer, KA, Eriksson, BI, Lassen, MR, et al. Fondaparinux Compared With Enoxaparin for the Prevention of Venous Thromboembolism After Elective Major Knee Surgery. N Engl J Med 2001; 345: 1305-10.
2. Bauer, KA. Fondaparinux Sodium: A Selective Inhibitor of Factor Xa. Am J Health Syst Pharm 2001; 58(Suppl 2):14.
3. Buller, HR, Davidson, BL, Decousus, H, et al. Fondaparinux or Enoxaparin for the Initial Treatment of Symptomatic Deep Venous Thrombosis: A Randomized Trial. Ann Intern Med 2004; 140:867.
4. Buller, HR, Davidson, BL, Decousus, H, et al. Subcutaneous Fondaparinux Versus Intravenous Unfractionated Heparin in the Initial Treatment of Pulmonary Embolism. N Engl J Med 2003; 349:1695.
5. Dempfle, CE. Minor Transplacental Passage of Fondaparinux in vivo. N Engl J Med 2004; 350:1914.
6. Eriksson, BI, Bauer, KA, Lassen, MR, et al. Fondaparinux Compared With Enoxaparin for the Prevention of Venous Thromboembolism After Hip-Fracture Surgery. N Engl J Med 2001; 345: 1298-304.
7. Arixtra (fondaparinux) [prescribing information]. Morgantown, WV: Mylan Institutional LLC; August 2020.
8. Douketis JD, Mithoowani S. Prevention of venous thromboembolism in adults undergoing hip fracture repair or hip or knee replacement. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed December 21, 2022.
9. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. J Am Coll Cardiol. 2022;79(2):e21-e129.
10. Key NS, Khorana AA, Kuderer NM, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO clinical practice guideline update. J Clin Oncol. 2020;38(5):496-520. doi:10.1200/JCO.19.01461
11. Cuker A, Arepally GM, Chong BH, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia. Blood Adv. 2018;2(22):3360-3392. doi:10.1182/bloodadvances.2018

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1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
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1/31/23	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
2/13/24	No	Howard Taekman, MD; Robert Sterling, MD	Annual review
2/18/25	Yes	Howard Taekman, MD; Robert Sterling, MD	Updated preauthorization criteria, Warnings/Precautions, Herb interactions and pregnancy implications