

Prior Authorization DRUG Guidelines

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

Prevention of venous thromboembolism in adults for any of the following:

- Hip surgery including replacement and hip fracture
- Knee replacement surgery
- Abdominal surgery
- Other orthopedic surgery in patients at high-risk for thromboembolism.

Members who are acutely ill and are hospitalized for severe respiratory infection or congestive heart failure or who are non-ambulatory and over 65 years of age, have a history of VTE, have active cancer, have severe respiratory disease, or congestive heart failure

OR

Treatment of venous thrombosis and prophylaxis of extension of venous thrombosis when inpatient care can be diverted to an outpatient setting

OR

○ **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
 - Unstable angina (off-label)
 - Treatment of arterial thrombosis resulting in acute coronary syndrome
 - Acute ST-segment elevated myocardial infarction (STEMI) (off-label)
 - OR
 - Treatment of heparin-induced thrombocytopenia (see general information)

Coverage is Not Authorized for Non-FDA approved indications

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

CrCl 30-50 mL/minute: Use caution

CrCl <30 mL/minute: Contraindicated

Drug	<u>Dosing Regimen</u>	<u>Authorization Limit</u>
Hip fracture or replacement	<u>Arixtra:</u> 2.5 mg QD	<u>Arixtra:</u> 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 — 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 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 than 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.
- Drotrecogin alfa: May enhance the bleeding potential with drotrecogin alfa.
- NSAIDs: May enhance the anticoagulant effect of fondaparinux.
- Salicylates: May enhance the anticoagulant effect of fondaparinux.
- Thrombolytic agents: Increase the risk of hemorrhage.

ETHANOL / NUTRITION / HERB INTERACTIONS — Herb/Nutraceutical: 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 (all possess anticoagulant or antiplatelet activity and as such, may enhance the anticoagulant effects of fondaparinux).

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. There are no adequate and well-controlled studies in pregnant women; use only if clearly needed.

LACTATION — Excretion in breast milk unknown/use caution

PATIENT EDUCATION — This drug can only be administered by injection. You may have a tendency to bleed easily while taking this drug; brush teeth with soft brush, floss with waxed floss, use electric razor, avoid scissors or sharp knives, and potentially harmful activities. Report unusual bleeding or bruising (bleeding gums, nosebleed, blood in urine, dark stool); any falls or accidents; new joint pain or swelling, dizziness, severe headache, shortness of breath, weakness, fainting or passing out.

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