



Guidelines for Use Fondaparinux (Arixtra®)

Background

Fondaparinux (Arixtra®) is a synthetic and specific inhibitor of activated Factor X (Xa). It selectively binds to antithrombin III (ATIII) and potentiates (by about 300 times) the neutralization of Factor Xa by ATIII. Neutralization of Factor Xa interrupts the blood coagulation cascade and thus inhibits thrombin formation and thrombus development. By comparison, heparin also binds with ATIII, but neutralizes thrombin in addition to factor Xa.

In March 2008, the Anticoagulation Safety Committee sought P&T approval to lift restrictions on fondaparinux (Arixtra®). The P&T committee approved the request and recommended that the Anticoagulation Safety Committee provide guidelines for the use of fondaparinux. The following is a description of indications, dosing and monitoring recommendations, contraindications, and pregnancy information.

FDA-approved Indications

- Prophylaxis of deep vein thrombosis (DVT) in:
 - Hip fracture surgery; including extended prophylaxis
 - Hip replacement surgery
 - Knee replacement surgery
 - Abdominal surgery patients at risk for thromboembolic complications
- Treatment of acute DVT in conjunction with warfarin sodium
- Treatment of acute pulmonary embolism (PE) in conjunction with warfarin sodium when initial therapy is administered in the hospital

Off-label uses

- DVT prophylaxis in medically ill (including cancer patients)
- DVT prophylaxis in patients with a history of heparin-induced thrombocytopenia (HIT)
- Treatment of HIT
- Anti-coagulation during a non-ST-segment-elevation myocardial infarction (non-STEMI)

Dosing Recommendations

- **Prophylaxis** of DVT: 2.5 mg subcutaneous once daily
 - Administer 6-8 hours after hip fracture, hip replacement, knee replacement, or abdominal surgery (administration within 6 hours after surgery is associated with increased risk of bleeding)
- **Treatment** of DVT and acute PE:
 - < 50 kg → 5 mg SC once daily
 - 50-100 kg → 7.5 mg SC once daily
 - > 100 kg → 10 mg SC once daily

PLUS

 - Warfarin sodium therapy (to be started ASAP, usually within 72 hrs)
 - Fondaparinux and warfarin should overlap for at least 5 days and until therapeutic INR of 2 - 3 is reached

Monitoring

- CBC, SCr (baseline, then daily until stable, then periodically as clinically indicated)
- Anti-Xa monitoring may be useful in high-risk patients. (available as a “send out” lab)
- Signs and symptoms of bleeding

Contraindications

- Severe renal impairment (Creatinine clearance < 30 mL/min)
- DVT prophylaxis in patient with body weight < 50 kg
- Active major bleeding
- Bacterial endocarditis

Warnings

- Not intended for intramuscular administration
- Use caution in conditions with increased risk of hemorrhage
- Spinal/epidural anesthesia or spinal puncture increases risk of developing an epidural or spinal hematoma which can result in paralysis
- If platelet count falls below 100 K/ μ L fondaparinux should be discontinued

Pregnancy Category B

- No well-controlled studies in pregnant women
- Should only be used during pregnancy if clearly indicated
- Reproductive studies in pregnant rats and rabbits at subcutaneous doses up to 10 mg/kg/day have not shown evidence of harm to fetus