PRESCRIBING INFORMATION

ARIXTRA (fondaparinux sodium) 1.5 mg/0.3 ml, 2.5 mg/0.5 ml solution for injection, pre-filled syringe

Please refer to Summary of Product Characteristics (SmPC) before prescribing.

Indications (Common): Prevention of Venous Thromboembolic Events (VTE) in adults undergoing major orthopaedic surgery of the lower limbs such as hip fracture, major knee surgery or hip replacement surgery. Prevention of VTE in adults undergoing abdominal surgery who are judged to be at high risk of thromboembolic complications, such as patients undergoing abdominal cancer surgery. Prevention of VTE in adult medical patients who are judged to be at high risk for VTE and who are immobilised due to acute illness such as cardiac insufficiency and/or acute respiratory disorders, and/or acute infectious or inflammatory disease. Treatment of adults with acute symptomatic spontaneous superficial-vein thrombosis of the lower limbs without concomitant deep-vein thrombosis.

Indications (2.5 mg/0.5 ml specific): Treatment of unstable angina or non-ST segment elevation myocardial infarction (UA/NSTEMI) in adults for whom urgent (< 120 mins) invasive management (PCI) is not indicated. Treatment of ST segment elevation myocardial infarction (STEMI) in adults who are managed with thrombolytics or who initially are to receive no other form of reperfusion therapy.

Presentation: Solution for injection. The solution is a clear and colourless liquid. Arixtra 1.5mg/0.3ml: Each pre-filled syringe (0.3 ml) contains 1.5 mg of fondaparinux sodium. Arixtra 2.5mg/0.5ml: Each pre-filled syringe (0.5 ml) contains 2.5 mg of fondaparinux sodium.

Dosage and administration (Common): *Patients undergoing major orthopaedic or abdominal surgery:* The recommended dose of fondaparinux is 2.5 mg once daily administered post-operatively by subcutaneous injection. The initial dose should be given 6 hours following surgical closure provided that haemostasis has been established. Treatment should be continued until the risk of venous thrombo-embolism has diminished, usually until the patient is ambulant, at least 5 to 9 days after surgery. In patients undergoing hip fracture surgery, the risk of VTE continues beyond 9 days after surgery. In these patients the use of prolonged prophylaxis with fondaparinux should be considered for up to an additional 24 days. *Medical patients who are at high risk for thromboembolic complications based on an individual risk assessment:* The recommended dose of fondaparinux is 2.5 mg once daily administered by subcutaneous injection. *Treatment of superficial-vein thrombosis:* The recommended dose of fondaparinux is 2.5 mg once daily, administered by subcutaneous injection. Patients eligible for fondaparinux 2.5 mg treatment should have acute, symptomatic, isolated, spontaneous superficial-vein thrombosis of the lower limbs, at least 5 cm long and documented by ultrasonographic investigation or other objective methods. Treatment should be initiated as soon as possible following diagnosis and after exclusion of concomitant DVT or superficial-vein thrombosis within 3 cm from the sapheno-femoral junction. Treatment should be continued for a minimum of 30 days and up to a maximum of 45 days in patients at high risk of thromboembolic complications. *Patients who are to undergo surgery or other invasive procedures:* In superficial vein thrombosis patients who are to undergo surgery or other invasive procedures, fondaparinux, where possible, should not be given during the 24 hours before surgery. Fondaparinux may be restarted at least 6 hours post-operatively provided haemostasis has been achieved. *Special populations:* In patients undergoing surgery, timing of the first fondaparinux injection requires strict adherence in patients ≥75 years, and/or with body weight <50 kg and/or with renal impairment with creatinine clearance ranging between 20 to 50 ml/min. The first fondaparinux administration should be given not earlier than 6 hours following surgical closure. The injection should not be given unless haemostasis has been established. *Renal impairment:* Fondaparinux should not be used in patients with creatinine clearance <20 ml/min. For VTE prophylaxis and treatment of superficial venous thrombosis, the dose should be reduced to 1.5 mg once daily in patients with creatinine clearance in the range of 20 to 50 ml/min. No dosage reduction is required for patients with mild renal impairment (creatinine clearance >50 ml/min). *Treatment of superficial-vein thrombosis:* The safety and efficacy of Arixtra 1.5 mg/0.3ml has not been studied. *Hepatic impairment:* No dosing adjustment is necessary in patients with either mild or moderate hepatic impairment. In patients with severe hepatic impairment, fondaparinux should be used with care and is not recommended in the treatment of superficial-vein thrombosis. *Paediatric population:* Fondaparinux is not recommended for use in children below 17 years of age due to a lack of data on safety and efficacy. *Low body weight:* Fondaparinux should be used with caution in these patients for the prevention of VTE, UA/NSTEMI and STEMI. Fondaparinux is not recommended for treatment of superficial-vein thrombosis in these patients. *Method of administration:* Fondaparinux is administered by deep subcutaneous injection while the patient is lying down. Sites of administration should alternate between the left and the right anterolateral and left and right posterolateral abdominal wall.

Dosage and administration (2.5 mg/0.5 ml specific): *Treatment of unstable angina/non- ST segment elevation myocardial infarction (UA/NSTEMI):* The recommended dose of fondaparinux is 2.5 mg once daily, administered by subcutaneous injection. Treatment should be initiated as soon as possible following diagnosis and continued for up to a maximum of 8 days or until hospital discharge if that occurs earlier. *Treatment of ST segment elevation myocardial infarction (STEMI):* The recommended dose of fondaparinux is 2.5 mg once daily. The first dose of fondaparinux is administered intravenously and subsequent doses are administered by subcutaneous injection. Treatment should be initiated as soon as possible following diagnosis and continued for up to a maximum of 8 days or until hospital discharge if that occurs earlier. *Renal impairment in treatment of UA/NSTEMI and STEMI:* Fondaparinux should not be used in patients with creatinine clearance <20 ml/min. No dosage reduction is required for patients with creatinine clearance > 20 ml/min. *Intravenous administration (first dose in patients with STEMI only):* Intravenous administration should be through an existing intravenous line either directly or using a small volume (25 or 50ml) 0.9% saline minibag.

Contraindications: Hypersensitivity to the active substance, sodium chloride, hydrochloric acid or sodium hydroxide. Active clinically significant bleeding. Acute bacterial endocarditis. Severe renal impairment defined by creatinine clearance < 20 ml/min.

Warnings and precautions (Common): Do not administer intramuscularly. Fondaparinux should be used with caution in patients who have an increased risk of haemorrhage. Agents that may enhance the risk of haemorrhage should not be administered concomitantly with fondaparinux. If co-administration is essential, close monitoring is necessary. Presence of superficial-vein thrombosis greater than 3 cm from the sapheno-femoral junction should be confirmed and concomitant DVT should be excluded by compression ultrasound or objective methods prior to initiating treatment with fondaparinux. In patients undergoing major orthopaedic surgery, epidural or spinal haematomas that may result in long-term or permanent paralysis cannot be excluded with the concurrent use of fondaparinux and spinal/epidural anaesthesia or spinal puncture. Fondaparinux should be used with caution in elderly patients and patients with body weight <50 kg due to increased risk of bleeding. Patients with creatinine clearance <50 ml/min are at increased risk of bleeding and VTE and should be treated with caution. Fondaparinux should not be used in patients with creatinine clearance <20 ml/min. Fondaparinux is not recommended for the treatment of superficial-vein thrombosis in patients with severe hepatic impairment. Fondaparinux should be used with caution in patients with a history of HIT.

The needle shield of the pre-filled syringe contains dry natural latex rubber that has the potential to cause allergic reactions in latex sensitive individuals.

Warnings and precautions (2.5 mg/0.5 ml specific): For treatment of UA/NSTEMI and STEMI, Fondaparinux should be used with caution in patients who are being treated concomitantly with other agents that increase the risk of haemorrhage (such as GPIIb/IIIa inhibitors or thrombolytics). In STEMI patients undergoing primary PCI, the use of fondaparinux prior to and during PCI is not recommended. Similarly, in UA/NSTEMI patients with life threatening conditions that require urgent revascularisation, the use of fondaparinux prior to and during PCI is not recommended. These are patients with refractory or recurrent angina associated with dynamic ST deviation, heart failure, life-threatening arrhythmias or haemodynamic instability. In UA/NSTEMI and STEMI patients undergoing non-primary PCI, the use of fondaparinux as the sole anticoagulant during PCI is not recommended due to an increased risk of guiding catheter thrombus therefore adjunctive UHF should be used.

Interaction with other medicinal products: Bleeding risk is increased with concomitant administration of fondaparinux and agents that may enhance the risk of haemorrhage. Oral anticoagulants (warfarin), platelet inhibitors (acetylsalicylic acid), NSAIDs (piroxicam) and digoxin did not interact with the pharmacokinetics of fondaparinux. Fondaparinux neither influenced the INR activity of warfarin, nor the bleeding time under acetylsalicylic acid or piroxicam treatment, nor the pharmacokinetics of digoxin at steady state. If follow-up treatment is to be initiated with heparin or LMWH, the first injection should, as a general rule, be given one day after the last fondaparinux injection. If follow up treatment with a Vitamin K antagonist is required, treatment with fondaparinux should be continued until the target INR value has been reached.

Pregnancy and lactation: There are no adequate data from the use of fondaparinux in pregnant women. Fondaparinux should not be prescribed to pregnant women unless clearly necessary. Breast-feeding is not recommended during treatment with fondaparinux. There are no data available on the effect of fondaparinux on human fertility.

Effects on ability to drive and use machines: No studies on the effect on the ability to drive and to use machines have been performed.

Undesirable effects: The most commonly reported serious adverse reactions reported with fondaparinux are bleeding complications (various sites including rare cases of intracranial/ intracerebral and retroperitoneal bleedings) and anaemia. Fondaparinux should be used with caution in patients who have an increased risk of haemorrhage. Common (≥1/100 to <1/10): post-operative haemorrhage, anaemia, bleeding (haematoma, haematuria, haemoptysis, gingival bleeding). *Other Adverse Effects:* For uncommon, rare, very rare and unknown undesirable effects, please refer to SmPC.

Legal Category: POM Marketing Authorisation Number: **PLGB 46302/0230, PLGB 46302/0231, MAH: Mylan Products Limited NHS Price: 1.5 mg/0.3ml x 10 - £62.79, 2.5 mg/0.5 ml x 10 - £62.79, Date of Revision of Prescribing Information: June 2022. ARX-2022-0003**

The SmPC for this product, including adverse reactions, precautions, contra-indications, and method of use can be found at: http://www.mhra.gov.uk/Safetyinformation/Medicinesinformation/SPCandPILs/index.htm and from Mylan Medical Information, Building 4, Trident Place, Hatfield Business Park, Mosquito Way, Hatfield, Hertfordshire, AL10 9UL, phone no. 01707 853000, Email: info.uk@viatris.com

Please continue to report suspected adverse drug reactions and device failures with any medicine or vaccine to the MHRA through the Yellow Card Scheme. It is easiest and quickest to report adverse drug reactions and device failures online via the Yellow Card website: https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Alternatively, you can report via some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) or by calling the Commission on Human Medicines (CHM) free phone line: 0800-731-6789. Adverse reactions/events and device failures should also be reported to MAH at e-mail address: pv.uk@viatris.com.