Xarelto® (rivaroxaban) – New indications, new formulation approval

- On December 20, 2021, the FDA approved Janssen's Xarelto (rivaroxaban), for:
    - Treatment of venous thromboembolism (VTE) and the reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years after at least 5 days of initial parenteral anticoagulant treatment; and
    - Thromboprophylaxis in pediatric patients aged 2 years and older with congenital heart disease who have undergone the Fontan procedure.

- Xarelto is also approved for:
    - Reduction of risk of stroke and systemic embolism in nonvalvular atrial fibrillation
    - Treatment of deep vein thrombosis (DVT)
    - Treatment of pulmonary embolism (PE)
    - Reduction in the risk of recurrence of DVT and/or PE
    - Prophylaxis of DVT following hip or knee replacement surgery
    - Prophylaxis of venous thromboembolism in acutely ill medical patients at risk for thromboembolic complications not at high risk of bleeding
    - Reduction of risk of major cardiovascular events in patients with coronary artery disease
    - Reduction of risk of major thrombotic vascular events in patients with peripheral artery disease (PAD), including patients after lower extremity revascularization due to symptomatic PAD.

- In addition to the new indications, the FDA approved a new 1 mg/mL oral suspension formulation of Xarelto.
    - Xarelto was previously approved as a 2.5 mg, 10 mg, 15 mg, and 20 mg tablet.

- The approval of Xarelto for treatment of VTE and reduction in risk of recurrent VTE in pediatric patients was based on EINSTEIN Junior, an open-label, active-controlled, randomized study in 500 pediatric patients from birth to less than 18 years with confirmed VTE. Patients received initial treatment with therapeutic dosages of unfractionated heparin (UFH), low molecular weight heparin (LMWH), or fondaparinux for at least 5 days, and were randomized to receive either Xarelto or comparator group (UFH, LMWH, fondaparinux or vitamin K antagonist) for a main study treatment period of 3 months (or 1 month for children < 2 years with central venous catheter-related VTE). The primary endpoint was symptomatic recurrent VTE.
    - Symptomatic VTE occurred in 1.2% of patients in the Xarelto group vs. 3.0% in the comparator group (hazard ratio 0.40, 95% CI: 0.11, 1.41).

- The approval of Xarelto for thromboprophylaxis in pediatric patients with congenital heart disease after the Fontan procedure was based on UNIVERSE, an open-label, active controlled, 2-part study. The study was designed to evaluate the single- and multiple-dose pharmacokinetic properties of Xarelto (Part A), and to evaluate the safety and efficacy of Xarelto when used for thromboprophylaxis for 12 months compared with aspirin (Part B) in children 2 to 8 years of age with single ventricle physiology who had the Fontan procedure. The primary endpoint was any thrombotic event.
    - In part B, thrombotic events occurred in 1.6% of patients in the Xarelto group vs. 8.8% of patients in the aspirin group (risk difference of -7.3%, 95% CI: -21.7, 1.1).

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- Xarelto carries a boxed warning for premature discontinuation of Xarelto increases the risk of thrombotic events and spinal/epidural hematoma.

- The most common adverse reactions (> 10%) with Xarelto use in pediatric patients were bleeding, cough, vomiting, and gastroenteritis.

- Dosing for Xarelto's new indications for pediatric patients is weight-based. Refer to the Xarelto drug label for complete pediatric dosing and administration recommendations as well as adult dosing for Xarelto's other indications.
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