RIVAROXABAN

TARGET AUDIENCE: All Canadian health care professionals.

OBJECTIVE:

To provide an overview of the mechanism of action, licensed indications, dosing regimens and side-effects for rivaroxaban.

ABBREVIATIONS:

aPTT	activated partial thromboplastin time
BID	twice daily
CrCl	creatinine clearance
DVT	deep vein thrombosis
INR	international normalized ratio
OD	once daily
PT	prothrombin time

MECHANISM OF ACTION:

Rivaroxaban (Xarelto™) is an oral factor Xa inhibitor. By binding reversibly to the active site of factor Xa, rivaroxaban attenuates thrombin generation and reduces fibrin formation.

INDICATION:

Rivaroxaban is currently licensed in Canada for thromboprophylaxis after elective hip or knee replacement surgery (see Thromboprophylaxis: Orthopedic guide); for treatment of patients with deep vein thrombosis (DVT) (see DVT Treatment guide); for treatment of patients with pulmonary embolism (PE); and for stroke prevention in patients with atrial fibrillation who are candidates for oral anticoagulation therapy.

DOSING:

a) Thromboprophylaxis: 10 mg daily (OD) starting 6-8 h after surgery and continuing for 14 or 30 days after knee or hip replacement, respectively.

b) DVT treatment: 15 mg twice daily (BID) for 3 weeks and 20 mg OD thereafter, or 15 mg OD for those with CrCl 30-49 mL/min.

c) PE treatment: 15 mg twice daily (BID) for 3 weeks and 20 mg OD thereafter, or 15 mg OD for those with CrCl 30-49 mL/min.

d) Stroke prevention in atrial fibrillation: 20 mg OD in patients with CrCl $\geq$ 50 mL/min or 15 mg OD for those with CrCl 30-49 mL/min.

MONITORING:

Routine laboratory monitoring is unnecessary. Prothrombin time/international normalized ratio (PT/INR) and activated partial thromboplastin time (aPTT) do not provide a reliable measure of its activity. Anti-factor Xa assays using rivaroxaban calibrators can be used to determine the plasma rivaroxaban concentration. These assays are not available in all laboratories. For specific testing, see Monitoring of New Oral Anticoagulant Drugs guide.

ADVERSE EFFECTS:

A major adverse effect is bleeding; concomitant use of antiplatelet drugs or other anticoagulants increases the bleeding risk. Rivaroxaban should be avoided in patients with indwelling epidural catheters or with a history of repeated or traumatic spinal punctures prior to spinal/epidural anesthesia, in order to reduce the risk of post-operative epidural hematomas.

PERI-PROCEDURAL MANAGEMENT:

See Peri-Operative Management of New Oral Anticoagulant Drugs guide.

SPECIAL CONSIDERATIONS:

Rivaroxaban crosses the placenta and should not be used in pregnancy or in nursing mothers. There is limited information on rivaroxaban in patients with CrCl < 30 mL/min and in those with moderate or severe hepatic impairment (Child-Pugh class B or C), particularly those with an associated coagulopathy.

Drugs that inhibit or induce both CYP3A4 and P-glycoprotein should be avoided. Examples include azole antifungals (e.g. ketoconazole), erythromycin, ritanovir and rifampin. There is no specific antidote that will counter rivaroxaban-related bleeding.

PEDIATRICS:

There are ongoing studies in children to establish the pharmacokinetics, pharmacodynamics, safety and efficacy of rivaroxaban in neonates and children. Rivaroxaban is not recommended for use in children until dosing, safety and efficacy are confirmed. See Pediatrics guide.

Pediatricians with expertise in thromboembolism should manage, where possible, pediatric patients with thromboembolism. When this is not possible, a combination of a neonatologist/pediatrician and an adult hematologist, supported by consultation with an experienced pediatric hematologist, is recommended.

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