

## Rivaroxaban (Xarelto®) Considerations for Use\*

US/FDA Approved Indications: Stroke Prevention in Non-valvular Atrial Fibrillation

<b>Black Box Warning*</b>	<b>Discontinuing rivaroxaban in patients with atrial fibrillation increases the risk of thrombotic events. Epidural and spinal hematomas may occur in patients who are anticoagulated and are receiving neuraxial anesthesia or undergoing spinal punctures.</b>
<b>Mechanism of Action</b>	Direct factor Xa inhibitor
<b>Dosing<sup>†</sup></b>	<p><u>Adult</u>: 20 mg PO daily with evening meal</p> <p><u>Elderly</u>: No dosage adjustment necessary</p> <p><u>Hepatic Impairment</u>: No dosage adjustment necessary</p> <p><u>Renal Impairment</u>:  <u>CrCl 15 to 50 mL/min</u>: 15 mg PO daily with evening meal  <u>CrCl &lt; 15 mL/min or on dialysis</u>: not recommended</p>
<b>Contraindications</b>	Active pathological bleeding
<b>Major Side Effects</b>	Hemorrhagic event
<b>Dosage forms and Strengths</b>	PO: 10, 15, 20 mg tablets
<b>Reversal</b>	<p>There is no rapid reversal agent for rivaroxaban</p> <ul style="list-style-type: none"> <li>Discontinue rivaroxaban</li> <li>Because of the high plasma protein binding, dialysis may not remove rivaroxaban</li> <li>Use of procoagulant reversal agents such as prothrombin complex concentrate , activated prothrombin complex concentrate , or recombinant factor VIIa may be considered, but has not been evaluated in clinical trials</li> </ul> <p><u>Surgery and interventions</u>:  If possible, discontinue at least 24 hours prior to procedure</p>
<b>Conversion to/from other drugs</b>	<p><u>From rivaroxaban to warfarin</u>:</p> <ul style="list-style-type: none"> <li>No clinical trial data available to guide converting from rivaroxaban to warfarin</li> <li>Rivaroxaban affects INR, so INR measurements made during coadministration with warfarin may not be useful for determining the appropriate dose of warfarin</li> <li>Discontinue rivaroxaban and begin both a parenteral anticoagulant and warfarin at the time the next dose of rivaroxaban would have been taken</li> </ul> <p><u>From rivaroxaban to an anticoagulant with rapid onset</u>:</p> <ul style="list-style-type: none"> <li>Discontinue rivaroxaban and give the first dose of the other anticoagulant (oral or parenteral) at the time that the next rivaroxaban dose would have been taken</li> </ul> <p><u>From warfarin to rivaroxaban</u>:</p> <ul style="list-style-type: none"> <li>Discontinue warfarin and start rivaroxaban when INR &lt; 3</li> </ul> <p><u>From low molecular weight heparin or non-warfarin oral anticoagulant to rivaroxaban</u>:</p> <ul style="list-style-type: none"> <li>Give rivaroxaban 0 to 2 hrs before next scheduled evening dose (e.g., low molecular weight heparin or non-warfarin oral anticoagulant) and omit administration of other anticoagulant</li> </ul> <p><u>From unfractionated heparin given by continuous infusion to rivaroxaban</u>:</p> <ul style="list-style-type: none"> <li>Start rivaroxaban at the time the heparin infusion is discontinued</li> </ul>

<p><b>Special Notes</b></p>	<p>Has many potential drug interactions.</p> <ul style="list-style-type: none"> <li>• Rivaroxaban is a substrate of CYP3A4, CYP2J2, and P-gp and ATP-binding cassette (ABCG2) transporters. Inhibitors and inducers of CYP450 enzymes or transporters (ex. P-gp) may change rivaroxaban exposure.</li> <li>• <u>Do not use</u> with drugs that are combined P-gp and strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, posaconazole, voriconazole, lopinavir/ritonavir, ritonavir, indinavir/ritonavir, and conivaptan).</li> <li>• <u>Do not use</u> with drugs that are combined P-gp and strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, St. John’s wort).</li> </ul> <p>Only use if the potential benefit justifies the potential risk with CrCL 15 to 50 mL/min and concomitant combined P-gp and weak or moderate CYP3A4 inhibitors (e.g., amiodarone, dronedarone, diltiazem, verapamil, quinidine, ranolazine, felodipine, erythromycin, azithromycin).</p>
<p><b>Counseling</b></p>	<p>Take daily with evening meal.</p> <p>Do not discontinue this medication without talking to the healthcare provider who prescribed it.</p> <p>Consult healthcare professional prior to using new drug (prescription, OTC, herbal).</p> <p>Report signs and symptoms of bleeding (e.g., unexpected bleeding or bleeding that lasts a long time; red or black, tarry stool; pink or brown urine; unusual bruising; coughing up blood; vomiting blood or vomit that looks like coffee grounds; unexplained pain, swelling, or joint pain; unusual headaches, dizziness, or weakness; recurring nose bleeds).</p> <p>Tell your healthcare professional if you have had or will have surgery to place a prosthetic heart valve.</p> <p>Tell your healthcare professional if you are pregnant or plan to become pregnant or are breastfeeding or plan to breastfeed during treatment.</p>

\*Refer to prescribing information for more complete information.

†Dosages given in the table may differ from those recommended by the manufacturers.

Sources:

1. Xarelto® Prescribing information, 11/2/12.
2. Chest Supplement, Antithrombotic Therapy and Prevention of Thrombosis, 9<sup>th</sup> edition, American College of Chest Physicians.