**Is Rivaroxaban (Xarelto®) an Option for Your Patient?**

Prior to prescribing, please review the following information

### Indications

- Non-Valvular Atrial Fibrillation (NVAF)* to prevent stroke & systemic embolism
- Acute VTE treatment & prevention of recurrent VTE [for deep vein thrombosis (DVT) and pulmonary embolism (PE)]
- Prevention of venous thromboembolic events (VTE) in elective total hip or knee replacement surgery (THR, TKR)

*CSC definition: AF without mechanical heart valves, rheumatic mitral stenosis, or moderate/severe non-rheumatic mitral stenosis

### Requirements

- **NOTE:** Rivaroxaban accumulates in hepatic and/or renal dysfunction
  - Stable creatinine clearance (CrCl) 30 mL/min or more
  - Stable liver function or Child-Pugh A (i.e. score less than 7) [refer to Contraindications section below]

### Contraindications

- Prosthetic heart valves requiring anticoagulation due to the valvular status itself (with/without atrial fibrillation)
- Rivaroxaban, like other anticoagulants, is contraindicated in patients at high risk for bleeding
- Pregnant/Breastfeeding: Safety & dosing has not been studied.
- Moderate to severe hepatic impairment (including Child-Pugh Class B and C: Score 7 or greater) associated with coagulopathy and clinically relevant bleeding risk. Patients with severe hepatic impairment have not been studied.
- Drug Interactions: Concomitant use of strong inducers or inhibitors of both CYP 3A4 and P-glycoprotein - See below

### Potential Limitations

- Drug Interactions: AVOID rifampin, select azole antifungals (e.g. ketoconazole, itraconazole but excluding fluconazole), select anticonvulsants (e.g. phenytoin, carbamazepine, phenobarbital), HIV protease inhibitors, St. John’s Wort & other strong CYP 3A4/P-gp inducers and inhibitors as there is minimal knowledge of clinical outcomes
- Little data when therapeutic doses are used in combination with ticagrelor, prasugrel or ASA + clopidogrel
- Rapid decline in anticoagulant effect after a missed dose; adherence is critical
- No dosing adjustment required for patients with extremes of weight (under 50 kg; over 120 kg), but limited outcome data
- Less than 18 years of age: Safety & dosing has not been established.
- Must be able to afford medication; cost varies by drug plan coverage and/or provincial criteria
- Limited information on reversal of effect, clinical studies with specific antidotes are underway
- AF Indication Only: Higher GI bleed rate than warfarin, although less critical bleeding events

### May offer an advantage over warfarin if:

- Difficulty stabilizing on warfarin for reasons other than poor medication adherence
- INR monitoring is problematic (e.g. poor venous access, frequent travel, remote location). **NOTE:** Use of warfarin with point-of-care (POC) INR testing (e.g. Coaguchek XS™) may be an alternative solution
- AF: lower rate of critical site bleeding including intracranial hemorrhage

### Dosing Recommendations

<table>
<thead>
<tr>
<th>Indication</th>
<th>CrCl 50 mL/min or greater</th>
<th>CrCl 30–49 mL/min</th>
<th>CrCl less than 30mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke Prevention in Non-Valvular Atrial Fibrillation</td>
<td>20 mg Once Daily</td>
<td>15 mg Once Daily</td>
<td>Not Recommended</td>
</tr>
<tr>
<td>Acute DVT/PE Treatment</td>
<td>15 mg bid for 3 weeks**, followed by 20 mg Once Daily</td>
<td></td>
<td></td>
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<tr>
<td>Hip &amp; Knee Replacement</td>
<td>10 mg Once Daily x 14 days (TKR); x 35 days (THR)</td>
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*Limited data suggests may crush & suspend in water to give orally or via NG; or mix with applesauce

**During initial 3 weeks: Very important to take 30 mg/day; may mean taking 2 tablets at once (i.e. double dose) if 1 dose is missed

### Inform Your Patient:

- Atrial Fibrillation: Should decrease risk of stroke by 2/3 compared to no anticoagulation
- Carry information indicating they are on an anticoagulant and inform their healthcare providers, including dentists
- Venous Thromboembolism: Ensure clarity of dose change after initial 3 weeks
- 15 and 20 mg dose: Take with food
- Adherence is essential to avoid treatment failure
- Report symptoms/signs of bleeding, stroke, or DVT/PE

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Collaborative Learning on Thrombosis (CLOT) – Canadian Prairie pharmacists with an interest in thromboembolic disorders

This is intended only as a general reference to supplement existing knowledge of healthcare professionals & is not a substitute for sound clinical judgement

CLOT members cannot be held responsible for any harm as a result of application of this information (November 2017)
Monitoring Patients on Rivaroxaban

- CrCl should be determined at baseline and at least annually. Monitor more frequently if older than 75y, with moderate renal dysfunction (CrCl 30-59ml/min), or when a decline in renal function suspected
- Monitor for symptoms and signs of bleeding
- No routine coagulation testing required. NOTE: INR is not useful for monitoring. Do not target INR 2 to 3. More specialized testing should only be considered in consultation with an expert in anticoagulation.

Switching Between Agents

From warfarin to rivaroxaban:
- Discontinue warfarin and start rivaroxaban when INR is 2.5 or less.

From non-warfarin anticoagulant (oral or parenteral - e.g. LMWH, apixaban, dabigatran, edoxaban) to rivaroxaban:
- Start rivaroxaban 0 - 2 hours before the next scheduled dose of the non-warfarin anticoagulant was to be administered. NOTE: For prophylactic dosing of parenteral anticoagulants, rivaroxaban can be started 6 or more hours after the last dose.
- For agents administered by continuous infusion, stop the infusion and start rivaroxaban at the same time

From rivaroxaban to warfarin:
- Start warfarin and only discontinue rivaroxaban once INR is 2 or greater. NOTE: Rivaroxaban can affect INR; therefore when starting warfarin, INR may initially be unreliable. If possible, checking INR just prior to next rivaroxaban dose may reflect the anticoagulant effect of warfarin.

From rivaroxaban to non-warfarin anticoagulants (oral or parenteral): (e.g. LMWH, apixaban, dabigatran, edoxaban)
- Discontinue rivaroxaban and give 1st dose of non-warfarin anticoagulant at the time next dose of rivaroxaban is due

Management of Bleeding Episodes with Rivaroxaban

- Vitamin K, protamine, plasma and/or idarucizumab will not reverse drug effects
- In the event of major hemorrhagic complications, discontinue rivaroxaban and refer patient for urgent assessment and locally developed management strategies
- Limited evidence demonstrates prothrombin complex concentrates (e.g. Octaplex®/Beriplex®) are able to reverse the anticoagulant effect, but the effect of these agents on bleeding has not been studied.
- Clinical study with an antidote (e.g. andexanet alfa) is underway

Anticoagulation around Invasive Procedures (e.g. surgery, elective day procedures, major dental procedures)

- As with warfarin, very low risk bleed procedures (such as dental extraction) do not require withholding rivaroxaban
- Management plans should be made in consultation with the provider performing the procedure
- Renal and hepatic function significantly impacts clearance of rivaroxaban. If the recommendations below cannot be met, consultation with an expert in anticoagulation management is encouraged.
- Due to the onset/offset time of rivaroxaban, peri-procedural use of LMWH is not required

Pre-Procedural – If required, stop rivaroxaban before procedure as follows:

<table>
<thead>
<tr>
<th>Renal function(^a) (CrCl mL/min)</th>
<th>Last intake of drug prior to procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Standard Bleeding Risk</td>
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<tr>
<td>30 or more</td>
<td>at least 24 hours</td>
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</table>

\(^a\) If CrCl less than 30ml/min (rivaroxaban not recommended), last dose at least 36h if standard risk; at least 48h if high risk

* Make a careful decision (i.e. hold longer) for patients undergoing major surgery, spinal puncture, or other regional anaesthesia in whom complete hemostasis is required. Consult specialist in these high risk patients/procedures.

Post Procedure: Resumption should not be initiated until adequate hemostasis has been achieved and clinical situation allows (usually 1 - 2 days). NOTE: Full therapeutic effect occurs approximately 2 hours after ingestion.

References: