FIVE THINGS TO KNOW ABOUT ...

New oral anticoagulants

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1

Dabigatran etexilate and rivaroxaban are approved in Canada for several indications

These medications are approved for the prevention of venous thromboembolism after hip or knee replacement and the prevention of stroke in patients with nonvalvular atrial fibrillation. Rivaroxaban is also approved for the treatment of deep vein thrombosis in patients without symptomatic pulmonary embolism. All other indications are off label. Although the effectiveness of these drugs is the same as or greater than that of warfarin, the risk of bleeding associated with their use may be higher.

2

Both drugs require dose adjustment in people with renal impairment and are contraindicated in those with liver disease

Because renal impairment prolongs the half-life of these drugs, dose reductions are required in patients with a creatinine clearance of 30–50 mL/min. Their use is contraindicated in patients whose creatinine clearance is less than 30 mL/min.[1,2] Dabigatran can be partially removed through hemodialysis, but studies of this procedure for removing rivaroxaban are lacking. The drugs should not be used in patients with moderate to severe liver dysfunction because of the lack of data in such patients.

3

Normal results of common coagulation tests do not exclude clinically relevant anticoagulation

Although both drugs affect many common coagulation test results (Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.120078/-/DC1), no routine laboratory monitoring is needed because of the drugs' predictable pharmacokinetics.[1,2] However, this does not preclude the need for monitoring for bleeding or changes in risk factors for bleeding. Even if the results of coagulation tests are normal, elective procedures should not be performed until at least 36–48 hours after discontinuation (or longer in patients with renal dysfunction).

4

Other adverse effects and drug interactions may limit their effectiveness

Concomitant use of P-glycoprotein and cytochrome P450 3A4 inhibitors (e.g., azole antifungals) or inducers (e.g., rifampicin, antiepileptics) may increase or decrease the anticoagulant effect of these drugs. Dabigatran has been associated with dyspepsia[3] which may limit compliance.

5

There is no clinically proven agent that can reverse anticoagulation with either drug

Over-anticoagulation should be managed by drug cessation and supportive therapy. Prothrombin complex concentrate can normalize coagulation test results in patients receiving rivaroxaban but not in those receiving dabigatran. Its clinical effectiveness on bleeding is unknown, however.[4] Data supporting the use of factor VIIa are lacking. Use of factor VIIa or prothrombin complex concentrate should be balanced against their risks.

References

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Editor's note: Another oral anticoagulant, abixaban, has recently been approved in Canada for the prevention of venous thromboembolic events in adults who have undergone elective knee or hip replacement. Like rivaroxaban, it selectively and reversibly inhibits coagulation factor Xa. The prescribing considerations for abixaban are similar to those of rivaroxaban.

Competing interests: Alejandro Lazo-Langner has received an unrestricted research grant from Alexion Pharmaceuticals and speaker fees from Pfizer and Leo Pharma. No competing interests declared by Dongmei Sun.

This article has been peer reviewed.

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CMAJ 2013. DOI:10.1503/cmaj.120078