



APIXABAN

TARGET AUDIENCE: All Canadian health care professionals.

OBJECTIVE:

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

ABBREVIATIONS:

aPTT	activated partial thromboplastin time
BID	twice daily
CrCl	creatinine clearance
INR	international normalized ratio
PT	prothrombin time

MECHANISM OF ACTION:

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

INDICATION:

Apixaban is currently licensed in Canada for thromboprophylaxis after elective hip or knee replacement surgery, and for stroke prevention in patients with atrial fibrillation who are candidates for oral anticoagulation therapy. Clinical trials for its use in patients with deep vein thrombosis, pulmonary embolism or both are ongoing.

DOSING:

- Thromboprophylaxis: 2.5 mg twice daily (BID) starting 12-24 h after surgery and continuing for 14 or 30 days after knee or hip replacement, respectively (see Thromboprophylaxis: Orthopedic guide).
- Stroke prevention in atrial fibrillation: 5 mg BID. No dose adjustment is necessary in patients with mild renal impairment (CrCl > 50 mL/min). In patients with moderate renal impairment (CrCl 25-50 mL/min) 5 mg BID can be used but 2.5 mg BID should be given in patients with 2 of 3 of the following characteristics: (1) serum creatinine $\geq 133 \mu\text{mol/L}$ (1.5 mg/dL); (2) age ≥ 80 years; (3) body weight ≤ 60 kg. In patients with CrCl 15-24 mL/min, no dosing recommendation can be made as clinical data are very limited.

MONITORING:

Routine laboratory monitoring is unnecessary. The prothrombin time/international normalized ratio (PT/INR) and activated partial thromboplastin time (aPTT) do not provide reliable measures of its anticoagulant activity. Anti-factor Xa assays using apixaban calibrators can be used to determine the plasma apixaban 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. Apixaban should be avoided in patients with indwelling epidural catheters or with a history of repeated or traumatic spinal punctures, in order to reduce the risk of epidural or spinal hematomas.

PERI-PROCEDURAL MANAGEMENT:

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

SPECIAL CONSIDERATIONS:

Apixaban crosses the placenta and should not be used in pregnancy or in nursing mothers. There is limited information on apixaban in patients with CrCl < 25 mL/min and in those with moderate to severe hepatic impairment (Child-Pugh class B or C), particularly those with an associated coagulopathy.

Drugs that inhibit or induce CYP3A4 and P-glycoprotein should be avoided. Examples include azole antifungals (e.g. ketoconazole), erythromycin, ritonavir and rifampin. There is no specific antidote for apixaban.

PEDIATRICS:

There are no studies evaluating the use of apixaban in children, although studies are underway. Apixaban in children is not recommended 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.

REFERENCES:

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Please note that the information contained herein is not to be interpreted as an alternative to medical advice from your doctor or other professional healthcare provider. If you have any specific questions about any medical matter, you should consult your doctor or other professional healthcare providers, and as such you should never delay seeking medical advice, disregard medical advice or discontinue medical treatment because of the information contained herein.