APIXABAN (ELIQUIS®)

GUIDELINES FOR ANTICOAGULATION UPDATED JULY 2017

This guideline provides a summary of the inpatient management of **adult** (over the age of 18) patients receiving APIXABAN.

This guideline should be used in conjunction with Therapeutic Goods Administration (TGA) approved Product Information, Clinical Excellence Commission (CEC) Non-Vitamin K Antagonist Oral Anticoagulant (NOAC) Guidelines and specialist advice.

Commencing treatment:

Conduct the following prior to commencing treatment:

- Full blood count (FBC)
- Prothrombin time (PT)
- Activated Partial Thromboplastin Time (aPTT)
- Liver Function Test (LFT)
- Renal function - estimated creatinine clearance (CrCl) should be calculated using the Cockcroft-Gault equation (do not use eGFR reported in pathology results). Ideal body weight should be used for calculating estimated creatinine clearance in patients who are overweight or obese. For all other patients use actual body weight.

Further investigate if results are found to be abnormal.

Review the following:

Contraindications to therapy, drug and antithrombotic interactions, and administration considerations.

Contraindications to therapy[1]:

- Known hypersensitivity
- Creatinine clearance <25mL/min
- Clinically significant active bleeding
- Significant inherited or acquired bleeding disorder
- Hepatic disease with coagulopathy (Child-Pugh C)
- Organ lesions at risk of bleeding including intracranial haemorrhage in previous 6 months
- Indwelling spinal or epidural catheter and during the first six hours after removal
- Mechanical heart valve
- Pregnancy or breastfeeding mother.

Caution:

In any history of gastrointestinal bleeding use APIXABAN with caution and seek patients with advice.

APIXABAN (Eliquis®) **2.5 mg** tablet

APIXABAN (Eliquis®) **5 mg** tablet

Images courtesy of MIMS Australia. Images not to scale.

Drug Interactions*[1]

Class or medicine (Not an exhaustive list)	Advice
Anticonvulsants *phenytoin, carbamazepine, phenobarbitone*	Caution
Azole antifungals *e.g. itraconazole voriconazole, posaconazole*	Contraindicated
HIV protease inhibitors *e.g. ritonavir*	Contraindicated
Macrolides *e.g. clarithromycin, erythromycin*	Caution
Rifampicin	Caution
St John's Wort	Caution
Verapamil	Uncertain

**SSRI and SNRI are not listed in the Product Information; however concurrent use may theoretically increase risk of bleeding*

Antithrombotic interactions[1]

Action	Example (Not an exhaustive list)	Advice
Antiplatelet	NSAIDS Aspirin Clopidogrel Prasugrel Dipyridamole Ticagrelor	Caution
	Dual-antiplatelets	Relative contraindication
Anticoagulant	Warfarin Enoxaparin Heparin	Contraindicated *(unless transitioning between anticoagulants)*

Administration considerations/ instructions:

- Tablets must be swallowed whole with or without food
- Can be crushed (See Don't Rush to Crush Handbook)
- Tablets can be used in dose administration aids e.g. Webster-pak®.

APIXABAN (Eliquis®) dosing[1]

Indication	Risk factors*	Dose	Duration
Prevention of stroke and systemic embolism in non-valvular AF in patients with at least ***one*** of the following risk factors: • prior stroke, TIA or non-central nervous system systemic embolism; • age ≥75 years, • hypertension, • diabetes mellitus or • heart failure and/ or left ventricular ejection fraction ≤35%	Patient with: CrCl ≥25 mL/min and at least ***two*** of the following risk factors: • Age ≥80 years • Weight ≤60 kg • Creatinine ≥133 micromol/L	APIXABAN 2.5 mg twice daily	Indefinite duration
	For all other patients with: CrCl ≥25 mL/min	APIXABAN 5 mg twice daily	Indefinite duration
Prevention of VTE following: • Total hip replacement (THR) ***or*** • Total knee replacement (TKR)	Patient with: CrCl ≥25 mL/min	APIXABAN 2.5 mg twice daily	THR = 32 – 38 days TKR = 10 – 14 days
Treatment of VTE	Patient with: CrCl ≥25 mL/min	APIXABAN 10 mg twice daily	7 days
		then	
		APIXABAN 5 mg twice daily	According to patient requirement
Prevention of recurrent VTE	Patient with: CrCl ≥25 mL/min	APIXABAN 2.5 mg twice daily	Patient dependent (following six months of a therapeutic dose anticoagulant)
*APIXABAN is contraindicated in patients with CrCl <25mL/min			

Perioperative management

- A recent CrCl result should be available.
- For urgent or high bleeding risk elective surgery check: estimated CrCl, and FBC. Consider anti-Xa level (where available).
- Refer to CEC NOAC Guidelines for advice spinal and epidural anaesthesia, or patients undergoing a lumbar puncture.

Timing of ceasing APIXABAN[1]

APIXABAN (Eliquis®)	Minimal bleeding risk procedures*	Low bleeding risk procedures*	High bleeding risk procedures*
Normal/ mildly impaired renal function (CrCl >50 mL/min)	Withholding APIXABAN may not be required	Last dose 24 hours before surgery	Last dose 48 – 72 hours before surgery
Moderately impaired renal function (CrCl 30 - 50 mL/min)	Withholding APIXABAN may not be required	Last dose 48 hours before surgery	Last dose 72 hours before surgery
CrCl <30 mL/min	SEEK SPECIALIST ADVICE		

Refer to CEC NOAC Guidelines for information on minimal, low and high bleeding risk procedures.

Recommencing NOAC post-operatively[2]

Low bleeding risk surgery

- Start or resume 24 hours after surgery

High bleeding risk surgery

- Do not start or resume therapeutic dosing until 48 – 72 hours after surgery
- Consider alternative VTE prophylaxis in the interim

THR and TKR prophylaxis with NOAC may be recommenced 24 hours after surgery.

Managing Bleeding

Mild bleeding

- Establish dose and last time taken
- Initiate standard resuscitation procedures
- Consider: FBC, group and hold, CrCl, anti-Xa level (where available)
- Establish if taking any other medicines with antithrombotic action
- Seek advice from a senior medical officer whether to delay dose or discontinue
- Refer to CEC NOAC Guidelines.

Clinically significant or life-threatening bleeding

- As above
- Consult haematologist
- Refer to CEC NOAC Guidelines.

(NB: No reversal agent available in Australia)

References: 1.Bristol-Myers Squibb Australia Pty Ltd. Product Information Eliquis® (apixaban) Therapeutic Goods Administration Website [updated 3 November 2016], 2.Tran H, Joseph J, Young L, McRae S, Curnow J, Nandurker H, et al. New oral anticoagulants: a practical guide on prescription, laboratory testing and peri-procedural/bleeding management Internal Medicine Journal 2014; 44: 525-36

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