Switching from warfarin to a direct acting oral anticoagulant (DOAC): A practical guide for B.C. primary care clinicians (April 2020)

	Apixaban (Eliquis®)	Rivaroxaban (Xarelto®)	Edoxaban (Lixiana®)	Dabigatran (Pradaxa®)
Is the indication appropriate for a DOAC? **Health Canada indications where switching from warfarin to a DOAC might occur**	Prevention of stroke and systemic embolism in non-valvular atrial fibrillation (AF)[1-4] Treatment of venous thromboembolism and prevention of recurrent venous thromboembolism (VTE)[1-4]			
	DOACs are **not** indicated in several circumstances, including: people with mechanical valves or moderate-to-severe mitral stenosis;[5-6] antiphospholipid syndrome;[1-4] pregnancy or lactation[1-4]			
Is it affordable? **BC PharmaCare Coverage**	Stroke prevention in AF or VTE treatment and prevention: *Special Authority needed*		Non-benefit	Stroke prevention in AF: *Special Authority needed*
Drug Cost *Without markup or fee*	~$105/month	~$90/month	~$95/month	~$105/month
Review renal function **Health Canada recommendations** *Note: CrCl and eGFR use different calculations; CrCl is estimated by using the Cockcroft-Gault equation*	CrCl < 15 mL/min: use not recommended[1] CrCl 15 to 24 mL/min (AF): limited data[1] CrCl 15 to 29 mL/min (VTE treatment, prevention): use with caution[1]	CrCl < 15 mL/min: use not recommended[2] CrCl 15 to 29 mL/min: use with caution[2]	CrCl < 30 mL/min: use not recommended[3]	CrCl < 30 mL/min: use contraindicated[4]
Check for relevant drug interactions	▪ DOACs are susceptible to drug interactions, eg, with some medications that inhibit or induce cytochrome P450 3A4 and P-glycoprotein. ▪ Perform a drug interaction check using an electronic database (eg, Lexicomp®) or consult a pharmacist to identify whether there are interactions that would preclude the use of a specific DOAC or influence the appropriate dose.			
Determine appropriate dose **Atrial Fibrillation**	**5 mg BID** or **2.5 mg BID** if two of: age ≥ 80 years, body weight ≤ 60 kg, SCr ≥ 133 µmol/L[1]	**20 mg once daily** with food or **15 mg once daily** with food if: CrCl 15 to 49 mL/min[2]	**60 mg once daily** or **30 mg once daily** if ≥ one of: CrCl 30 to 50 mL/min, body weight ≤ 60 kg, concomitant P-gp inhibitors (except amiodarone, verapamil)[3]	**150 mg BID** or **110 mg BID** if: ≥ 80 years or at higher risk of bleeding (including age ≥ 75 years plus one bleeding risk factor)[4]
VTE Treatment and Secondary Prevention	**5 mg BID**[1] After 6 months, if continuing for secondary prevention: 2.5 mg BID[1]	**20 mg once daily** with food[2] After 6 months, if continuing for secondary prevention: 10 or 20 mg once daily[2]	**60 mg once daily** or **30 mg once daily** if ≥ one of: CrCl 30 to 50 mL/min, body weight ≤ 60 kg, concomitant P-gp inhibitors (except amiodarone, verapamil)[3]	**150 mg BID** or **110 mg BID** if: ≥ 80 years or at high risk of bleeding (including age ≥ 75 years plus one bleeding risk factor)[4]
	Note: During the acute phase of VTE treatment (eg, first 5 to 21 days) DOAC dosing may differ; the doses above are relevant if switching from warfarin			
When to start DOAC after stopping warfarin **With INR** *Per Health Canada Prescribing Info*	Start apixaban when INR < 2.0[1]	Start rivaroxaban when INR ≤ 2.5[2]	Start edoxaban when INR ≤ 2.5[3]	Start dabigatran when INR < 2.0[4]
	Anticipate a therapeutic INR (range 2.0 to 3.0) to decrease to < 2.0, 2 to 3 days after stopping warfarin.[9]			
Without INR	▪ The safety and efficacy of switching from warfarin to a DOAC without an INR has not been tested in a randomized controlled trial however Thrombosis Canada practically recommends that if INR testing is not available: wait 2 to 3 days after the last dose of warfarin, then start the DOAC.[7] ▪ In older adults or if the INR is supratherapeutic, it may take longer to achieve an INR < 2.0.[8,9] ▪ Switching without the guidance of an INR measurement may not be appropriate in the setting of a recent thromboembolic event (where the avoidance of subtherapeutic anticoagulation is important) or in people with a higher risk of bleeding (where the avoidance of supratherapeutic anticoagulation may be more important). ▪ For additional guidance in complex clinical circumstances, consult anticoagulation specialist or access **R**apid **A**ccess to **C**onsultative **E**xpertise (RACE).			
Important Reminders	▪ Adherence: The anticoagulant effect of DOACs is estimated to diminish within 12 to 24 hours after the last dose. Patient and caregiver education on the importance of strict medication adherence is essential.[10] ▪ DOACs require renal function and clinical monitoring → see Thrombosis Canada's DOAC Follow-Up Checklist			

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Thank you to: Dr. Agnes Lee (MD, MSc, FRCPC), Arden Barry (PharmD), Cait O'Sullivan (PharmD) for their assistance in preparing this infographic

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