Pharmacist quick reference guide: oral anticoagulants for stroke prevention in atrial fibrillation

Stroke preventers, not blood thinners!

Evaluate clinical, patient, and practical factors to ensure the most appropriate oral anticoagulant (OAC) is prescribed for each person

Confirm the clinical indication

- use CHA_2DS_2-VA tool to determine stroke risk after AF diagnosis

OAC recommended when score ≥ 2

Consider additional bleeding/stroke risk factors to determine benefit when score = 1

No OAC recommended when score = 0.

Individualise OAC selection

- use shared decision-making to confirm choice

Factors influencing OAC selection include:

- patient factors: age, renal function, comorbidities and bleeding risk
- medicine factors
- formulary restrictions
- concurrent medicines.

Enhance medicine safety

- identify and address modifiable bleeding risk factors
- review medicines for cumulative bleeding risk

Empower your patient

- provide individualised counselling and advice

CHA_2DS_2-VA tool

Risk factors	Points
C: congestive heart failure (HFrEF or HFpEF)	+1
H: hypertension (current or any history of)	+1
A: age ≥75 years	+2
D: diabetes mellitus	+1
S: prior stroke, TIA or thromboembolism	+2
V: vascular disease (PAD, complex aortic plaque or prior MI)	+1
A: age 65-74 years	+1

All DOACs (apixaban, dabigatran, rivaroxaban) are preferred over warfarin* to reduce stroke risk in AF.

*except for those with antiphospholipid syndrome, mechanical heart valves or rheumatic mitral stenosis

Patient factors influencing OAC selection

Age - older adults may have an increased bleeding risk, if >80 years may require apixaban dose reduction.

Weight - apixaban may require dosage reduction for those weighing <60 kg.

Renal and hepatic function - impaired kidney or liver function can affect the metabolism and clearance of OACs. Dose adjustments or alternative medicines may be required.

Patient preference - discuss the benefits, risks, and lifestyle implications of different OACs to align with preferences.

Medicine factors influencing OAC selection

	apixaban	dabigatran	rivaroxaban	warfarin
once daily dosing	X	X	✓	✓
can be crushed	✓	X	✓	✓
dosage administration aid suitability	✓	X	✓	✓
can be taken without regard to food	✓	✓	X	✓

Oral anticoagulants and atrial fibrillation

Atrial fibrillation (AF) is the most common recurrent cardiac arrhythmia.

Over 500,000 Australians live with AF.

AF is associated with a 5-fold increase in the risk of stroke.

Anticoagulant therapy can **reduce stroke risk by up to 70%.**

Table 1. Identify and address modifiable bleeding risk factors

Risk Factor	Rationale	Potential actions
Alcohol consumption	Alcohol interferes with the bone marrow's ability to produce platelets and affects platelet function. Chronic alcohol use can damage the liver, which produces many of the proteins necessary for blood clotting. Abstinence from alcohol has been shown to reduce symptoms of AF.	Reduce alcohol consumption to <3 standard drinks per week to reduce bleeding risk.
Obesity	Obesity is associated with chronic inflammation, which can disrupt normal blood clotting mechanisms, it affects how the body processes OACs and often comes with other health issues like hypertension and diabetes, which can further complicate bleeding risks.	Discuss healthy eating strategies and the benefits of exercise.
Comorbidities: including diabetes, heart failure and reduced kidney function, if not optimally managed.	High blood sugar levels can damage blood vessels and impair platelet function, making it harder for blood to clot. Heart failure can lead to congestion and increased pressure in blood vessels, which can cause them to rupture more easily. Reduced kidney function can disrupt the balance of clotting factors and reduce platelet production, both of which are crucial for proper blood clotting.	Advise the patient on what appropriate targets are for their conditions. Refer appropriately if titration of management is required.
Uncontrolled hypertension	High blood pressure can damage the inner lining of arteries, making them more prone to rupture and bleeding.	Empower the patient to have a blood pressure monitoring plan. Ensure they know their target blood pressure and when to seek medical attention.
Falls and the participation in hazardous activities.	Falls can cause direct injury to blood vessels, leading to external or internal bleeding. Activities that increase risk of head knock and/or bruising may not be recommended.	Discuss modifiable risk factors for falls. This includes wearing suitable footwear, reviewing prescription of glasses and attending balance classes. Review medicines that may contribute to falls.
An increased falls risk is rarely a reason to withhold the OAC.		

Table 2. Signs and symptoms of bleeding

	Signs and symptoms	Potential actions
Minor bleed	• mild blood noses • mild bruising • cuts when shaving	If the bleeding concerns the patient, is heavier than usual or takes an unusually long time to stop, they should speak to their GP right away.
Critical bleed	• red or dark brown urine • red or black bowel motions • coughing up blood or blood in your spit • dark or blood-stained vomit • unexplained pain, swelling or discomfort. • unexpected bleeding or bleeding that lasts a long time (this includes nose bleeds, bleeding from your gums, bleeding from cuts and scrapes, and/or menstrual periods) • severe unexplained bruising or bruising that gets bigger	Patients should see their GP or go to the emergency department of their local hospital.
Life-threatening bleed	• severe headache or dizziness • trouble breathing or swallowing • any of the signs or symptoms of a stroke may indicate haemorrhagic or intracranial bleeding. See Think… F.A.S.T. resources	Patients should call an ambulance or go straight to the emergency department of their local hospital (if safe to do so) if they experience these symptoms.
Even if there are no visible signs of injury, patients should tell their clinician or go to the emergency department if they have any falls, knocks to the head or body or other major injuries. Consider calling '000'.		

The net benefit of stroke prevention with OACs almost always outweighs the risks of bleeding.

Conduct a medication review to evaluate *cumulative* bleeding risk.

Taking multiple medicines can increase bleeding risk due to the potential for interactions and combined side effects. Careful management and monitoring are essential to minimise these risks.

Compile a Best Possible Medication History

Identify medicines, supplements and foods that contribute to bleeding risk

Identify medicines that contribute to stroke risk

Create a plan with the patient and GP to reduce bleeding and stroke risk from medicines

Recommended patient resource:

Care plan - using anticoagulants for atrial fibrillation.

Refer to

Clinical guide: anticoagulation management for atrial fibrillation for more information.

Tools such as **GARFIELD-AF** can be used to provide a useful visual representation of mortality, ischaemic stroke and major bleeding risk for patients.

Table 3. Pharmacokinetic interactions with DOACs

The type of interaction will either increase the risk of bleeding or stroke.

Mechanism	Examples
P-glycoprotein (P-gp) inhibitors increase the levels of DOACs, such as dabigatran, by inhibiting P-gp, which is involved in medicine transport.	verapamil clarithromycin ritonavir itraconazole
P-glycoprotein (P-gp) inducers can decrease the levels of DOACs by inducing P-gp, leading to increased medicine clearance.	rifampicin St. John's wort
CYP3A4 inhibitors can increase the levels of DOACs, like apixaban and rivaroxaban, by inhibiting their metabolism.	ketoconazole ritonavir grapefruit
CYP3A4 inducers can decrease the levels of DOACs by inducing CYP3A4, leading to increased metabolism.	phenytoin carbamazepine

Common medicines that directly increase bleeding risk		
aspirin P2Y12 inhibitors selective serotonin reuptake inhibitors (SSRIs)	NSAIDs fish oil corticosteroids	heparin warfarin enoxaparin DOAC
Medication classes that may contribute to falls		
antihypertensive anticonvulsant antidepressant	antipsychotic antiarrhythmic antidiabetic	diuretics opioid sedatives/ hypnotics
Any medicine causing postural hypotension/ dizziness/ syncope, drowsiness/ sedation, confusion, hypoglycaemia, or visual disturbances/ blurred vision can increase the risk of falls.		

When completing your medicine review:

- ☐ assess the implications of current medication management on both bleeding and stroke risk
- ☐ the cumulative effects on bleeding need to be considered when multiple agents combine to increase bleeding risk
- ☐ confirm if aspirin is being taken by your patient and ensure the prescriber of the DOAC is informed of duration and indication
- ☐ determine if regular monitoring for bleeding and renal function is in place
- ☐ confirm there is planned, regular review of the ongoing need for the DOAC
- ☐ if warfarin is selected, educate the patient about the importance of maintaining a therapeutic INR range for more than 70% of the time. If this is not achievable, consider an alternative OAC.

When the risk assessment no longer favours the continuation of a medicine or supplement, liaise with the patient and prescriber to create a deprescribing plan.

Procedures and OACs

When NOT to withhold an OAC

If a procedure has a minimal risk of bleeding, **interruption of DOAC therapy is usually not required**.

Procedures with minimal risk include:

- minor dental procedures (e.g. extractions, fillings)
- cataract surgery
- endoscopy without biopsy or resection
- minor dermatological procedures
- coronary angiography using radial artery access.

When to restart an OAC

If an OAC is **withheld prior to a procedure**, **ASK** the patient if they know when to restart their medicine.

If the patient is unsure about the restart timing, they should **CHECK** with the clinician who advised them to withhold the medicine.

CONFIRM the **restart dates** of OACs with patients when dispensing post-procedure pain relief.

For **guidance** on local hospital protocols, **ENGAGE** with your colleagues in the hospital pharmacy department.

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