Remedy's Rx Specialty Pharmacy

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Novel Oral Anticoagulants (NOAs) in Atrial Fibrillation

Alternatives to warfarin

A newer class of anticoagulants approved in Canada and indicated for atrial fibrillation (AF) are referred to as **Novel Oral Anticoagulants (NOAs)**. The three NOAs in Canada approved for atrial fibrillation are:

Eliquis® (apixaban) **Xarelto® (rivaroxaban)** **Pradaxa® (dabigatran)**

These NOAs are also approved in Canada for other indications. The risk of stroke is increased five-fold in residents with AF. Balancing the risk of stroke with the risk of bleeds is a challenge. NOAs are consistently associated with a lower risk for stroke or systemic embolism compared to warfarin. The 2014 update of the Canadian Cardiovascular Society Atrial Fibrillation Guidelines states, "When oral anticoagulation therapy is indicated, most individuals should receive an NOA in preference to warfarin."

NOA agents demonstrate equivalency (rivaroxaban, low dose dabigatran) or superiority (apixaban) to warfarin in terms of efficacy. Overall safety for NOAs is based on randomized controlled trials, as NOAs do not have enough real-world data. In general, NOAs demonstrate a lower risk of intracranial bleeds, but can increase the risk of GI bleeds. Dabigatran can cause bleeds that are five times more fatal than warfarin.

	Novel Oral Anticoagulants (NOA)	warfarin
Benefits	• Reduced rates of intracranial hemorrhage • Fixed dosing with no routine blood monitoring • Limited drug and food interactions • Quicker onset/offset of action • Fewer drug interactions (but no way to adjust dose)	• Long-standing efficacy established (approximately 60 years of real world experience) • Well understood side effects/challenges • Not dependent on renal function • Indicated with mechanical valve and severe mitral stenosis • Efficacy can be measured • Antidote available
Concerns/ Limitations	• Lack of long-term safety and efficacy data (approximately three years of real-world experience) • Costly • Not suitable for residents with poor renal function • Contraindicated with mechanical heart valves and severe mitral valve stenosis • No established antidote or procedure for reversal • Quicker onset/offset of action (missed dose can affect the anticoagulation status) • Use is limited in hepatic impairment	• Increased risk of intracranial hemorrhage • Variable dosing and need for adjustments • Narrow therapeutic range and difficulty maintaining time in therapeutic range (TTR) • Need for routine blood monitoring • Many drug and food interactions • Slow onset/offset of action

When is warfarin better?

Even though NOA agents are generally preferred over warfarin, warfarin is a better option in some specific conditions. Residents who are best suited to warfarin therapy include those with mechanical heart valves, renal dialysis or CrCl <30 ml/min, advanced liver or kidney disease, risk of dyspepsia and/or GI bleeds, and any residents currently stable on warfarin or who have a need for dual antiplatelet therapy.

Warfarin is also preferred if a resident is taking any of the following medications: phenytoin, carbamazepine, phenobarbital, rifampicin, ketoconazole, itraconazole, posaconazole, ritonavir and NSAIDS. (This list is not a complete list of medications with the potential to interact with NOAs.)

DID YOU KNOW?

The Institute for Safe Medication Practices does not endorse the acronym NOAC as it has been misinterpreted as meaning "No Anticoagulants."

	Eliquis® (apixaban)	Xarelto® (rivaroxaban)	Pradaxa® (dabigatran)	warfarin
Antidote	**No antidote:** options are prothrombin complex concentrate, recombinant factor VIIa, activated charcoal dialysis			Vitamin K
Monitoring	No test for anticoagulation status. Creatinine every 6-12 months for dose adjustment depending on renal function			International normalized ratio (INR)
Half Life	8-15 hours	5-13 hours	12-14 hours	2.5 days
Food Interactions	None	Avoid grapefruit	None	Consistent diet with regard to resident's intake of foods rich in Vitamin K
Dosing	2.5-5 mg twice daily with or without food	15-20 mg once daily with food	110-150 mg twice daily	Daily (dose depends on resident's unique INR value)
Renal Impairment	Use should be avoided in severe renal impairment. (Dose adjustments can be made in minor renal impairment.)			Ok to use

Switching from warfarin therapy to a NOA agent

Warfarin therapy must be stopped for approximately 2-3 days before anticipated switch date. INR is to be monitored daily once warfarin is stopped in order to know which day to initiate NOA. When INR is equal to or falls below 2.5, rivaroxaban can be started, and when INR is equal to or falls below 2, apixaban or dabigatran can be started.

How can you help lower bleeding risk?

Risk of bleeding can be reduced by providing residents with mobility aids to help prevent falling, treating blood pressure to target, encouraging alcohol abstinence, replacing NSAIDS with other analgesics and avoiding ASA unless clearly indicated for secondary prevention. It is recommended to provide GI protection if GI bleeding risk is high.

Conclusion

Overall, NOAs are an innovative new class of medications. Clinical evidence demonstrates distinct advantages over warfarin, and NOAs are considered drugs of choice for most residents compared to warfarin. Most residents on warfarin do not have the perfect time in therapeutic range and often benefit from using a NOA agent. These agents offer a reduced risk for intracranial bleeding with the same or lower risk for bleeding in surgery, meaning they may be as safe, or possibly safer, than warfarin with regards to bleeding. Currently there is not enough data to safely recommend the use of NOAs in severe renal insufficiency.

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