

Safety Alert

Novel Oral Anticoagulants (NOACs)

Issue

Apixaban (Eliquis®), dabigatran (Pradaxa®) and rivaroxaban (Xarelto®) are **anticoagulants** licensed in varying doses in adults for prevention and treatment of venous thromboembolism and for non-valvular atrial fibrillation. Other NOACs may become available, e.g. **edoxaban (Savaysa® or Lixiana®)**. Anticoagulants are high-risk drugs, with risks including:

- **Bleeding or haemorrhage**, particularly with:
 - Use in combination with medicines increasing the bleeding risk.
 - Renal impairment, chronic or acute (e.g. with sepsis), which prolongs the half-life of these drugs. If bleeding occurs, there are no reversal agents and prolonged supportive treatment may be required.
- **Stroke or venous thromboembolism as a result of omission or under-dosing**. The NOACs have a short duration of action so omission of a dose(s) may rapidly lead to a loss of anticoagulant effect.
- **Lack of familiarity** of healthcare professionals and patients with these medicines.

Examples of Harm

- A patient who had been taking dabigatran for 2 years developed acute kidney injury associated with an infection. This resulted in accumulation of dabigatran, contributing to a major haemorrhage.
- A patient was discharged from hospital on rivaroxaban, which was subsequently omitted from his prescription in the community. The patient suffered a stroke.
- A patient on rivaroxaban was commenced on dronedarone in an out-patient clinic. The patient was admitted 2 weeks later with a gastrointestinal bleed. This combination is contra-indicated.
- A patient was admitted with anaemia and a raised INR. Was taking warfarin and dabigatran, instead of dabigatran alone. Patient had not switched from warfarin to dabigatran as intended.

How to reduce the risk

- **Organisations must have processes and local guidance in place to ensure safe use of NOACs.**
- **All healthcare professionals must recognise and understand anticoagulants;** names, indications, contra-indications, cautions, dosing and drug interactions, peri-procedural use, switching and how to counsel patients on safe use. Ensure product information is accessible and used.
- **Ensure doses are appropriate** for the patient's indication, age, renal function and other factors. Calculate renal function using the Cockcroft & Gault equation. In acute or chronic renal impairment, dose reduction or alternative therapy may be required (consult product information).
- **Patients must understand these medicines;** including the indication, dose and duration of therapy, how to recognise signs of bleeding or anaemia and to seek medical help if bleeding occurs. Patients require counselling and written patient information. Leaflets, booklets and alert cards may be accessed on www.medicines.ie (PIL) or from the manufacturers of the medicines.
- **Check concomitant therapy to reduce the risk of interactions, e.g.**
 - Anticoagulants – avoid therapeutic duplication, e.g. heparin, warfarin, enoxaparin or other NOACs
 - Antiplatelets (e.g. aspirin, clopidogrel, ticagrelor, prasugrel) - combination is only indicated in specific circumstances e.g. after coronary artery stenting, with careful consideration of the risks of bleeding and thrombosis. Avoid inadvertent co-prescribing e.g. when atrial fibrillation is first diagnosed in a patient on aspirin for primary prevention of coronary heart disease.
 - NSAIDs & COX 2 inhibitors (e.g. ibuprofen, diclofenac, etoricoxib) – increase bleeding risk
 - Antidepressants, e.g. SSRIs, SNRIs and tricyclics – increase bleeding risk
 - Check product information for specific contraindications and interactions, e.g. with dronedarone, rifampicin and antiepileptics.
- **Report any medication errors or adverse drug reactions** via local incident reporting, to the Health Products Regulatory Agency (www.hpra.ie) and/or to the State Claims Agency as appropriate.

References: Summaries of Product Characteristics for Xarelto®, Eliquis® & Pradaxa®. Accessed at www.medicines.ie Feb 2015
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The Irish Medication Safety Network (IMSN) is an independent group of pharmacists and other specialists working in the acute sector, whose principal aim is to improve patient safety with regard to the use of medicines through collaboration, shared learning and action.