Safety Alert

Direct Oral Anticoagulants (DOACs)

Issue

Direct Oral Anticoagulants (DOACs), previously known as NOACs (Novel Oral Anticoagulants) are licensed for various indications including the prevention and treatment of venous thromboembolism (VTE) and for non-valvular atrial fibrillation (Afib). There are four DOACs currently licensed in Ireland – a direct thrombin inhibitor dabigatran (Pradaxa®), and three factor Xa inhibitors: apixaban (Eliquis®), edoxaban (Lixiana®), and rivaroxaban (Xarelto®).

DOACs are high-risk drugs, with risks including **bleeding or haemorrhage,** particularly when prescribed:

- in combination with medicines increasing the bleeding risk
- In patients with renal impairment, chronic or acute (e.g. with sepsis), which prolongs the half-life of these drugs

Dabigatran does have a reversal agent, idarucizumab; however at present, there is no reversal agent available for factor Xa inhibitors and if bleeding occurs, prolonged supportive treatment may be required

- **Stroke or venous thromboembolism can result of omission or under-dosing**. DOACs have a short duration of action so omission of even one dose may rapidly lead to a loss of anticoagulant effect.
- Failure by healthcare professionals to recognise these medicines as belonging to the DOAC therapeutic class

Evidence 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 (GI) bleed. This combination is contra-indicated.

A patient was admitted on apixaban. Enoxaparin was commenced for venous thromboembolism prophylaxis. Patient experienced a GI bleed. DOACs and low molecular weight heparins (LMWH) should never be concurrently prescribed.

How to Reduce the Risks

- **Organisations must have processes and local guidance in place to ensure safe use of DOACs.**
- **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.** Calculate renal function using the Cockcroft & Gault equation. In acute or chronic renal impairment, dose reduction/alternative therapy may be required.
- **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.hpra.ie (PIL) or from the manufacturers of the medicines.
  See also the Anticoagulation in Afib booklet available at http://www.imsn.ie/images/publications/AnticoagAfib.pdf
- **Check concomitant therapy to reduce the risk of interactions,** e.g.
  - Anticoagulants – avoid therapeutic duplication, e.g. unfractionated heparin, LMWH or other DOACs.
  - 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. Be aware of inadvertent co-prescribing e.g. when Afib is first diagnosed in a patient who is already taking 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 can increase bleeding risk.
  - Check product information for specific contraindications and interactions, e.g. with dronedarone, rifampicin and anti-epileptics.
- **Report any medication errors or adverse drug reactions** via local incident reporting, to the Health Products Regulatory Authority (www.hpra.ie) and to the State Claims Agency as appropriate.

References: Summaries of Product Characteristics for Xarelto®, Eliquis® , Lixiana® & Pradaxa®. Accessed at www.hpra.ie , Jan 2018.

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