Prescribing...

DOACs July and August 2020

- Three direct-acting oral anticoagulants or DOACs are available via the Prescribing List.
- The bulletin looks at the risk of bleeding with DOACs, which is not insignificant.
- Renal function monitoring is required to prescribe the correct dose.
- DOACs are not recommended in patients with antiphospholipid syndrome.
- Dabigatran is contraindicated and other DOACs are not recommended in patients with prosthetic heart valves.

Background

Direct-acting oral anticoagulants (DOACs) are licensed for a variety of indications requiring anticoagulation. Available DOACs include the direct factor Xa inhibitors apixaban, edoxaban, and rivaroxaban. All three are still black triangle drugs. The direct thrombin inhibitor dabigatran etexilate is prescribed privately on the islands. Any individual taking any DOAC has increased risk of bleeding, which can be serious and potentially fatal. The MHRA recieves reports of bleeds, often life-threatening or fatal, in association with DOACs in patients in the UK. In many reported cases, patients have underlying factors that suggest they are at increased risk of bleeding events.

All DOACs should therefore be used with caution in patients at increased risk of bleeding such as older people and patients with low body weight or renal impairment. The expected benefit from the drug should out-weigh any risks of harm. Although routine anticoagulant monitoring is not required for DOACs as it is for vitamin K antagonists, patients (particularly those with an increased bleeding risk) should be advised of the risk of bleeding and be routinely examined clinically for signs of bleeding or anaemia. Bleeding can occur at any site during treatment with a DOAC and treatment should be discontinued if severe bleeding occurs.

DOACs interact with a number of drugs, some of which increase bleeding risk. Refer to product information for advice. DOACs should not be taken with other anticoagulants. Strong inhibitors of P- glycoprotein or CYP3A4 (or both) increase circulating levels of DOACs therefore may be not recommended or may require DOAC dose reduction.

Management of bleeding

The product information for DOACs includes guidance on the management of bleeds and bleeding complications. For adults on a DOAC when rapid reversal of its anti-coagulant effect is needed in life-threatening or uncontrolled bleeding, specific reversal agents are available for dabigatran,

namely idarcizumab and apixaban and rivaroxaban, namely andexanet alfa. Both are black triangle drugs. There is currently no specific licensed reversal agent yet available for edoxaban, but trials are ongoing. Because of their very high cost, reversal agants are available in the PEH only when recommended by both the On-call Consultant Physician and the On-call Consultant Heamatologist at Heartlands.

Dose and renal function

Exposure to DOACs is increased in patients with renal impairment and it is therefore important that patients receive an appropriate dose depending on renal function. The MHRA and the SPCs of the products advise the calculation of creatinine clearance (CrCl) in order to determine renal function for dosing of DOACs. This was the method used in the drug trails and is recommended by the Visiting Renal Consultant. There are a number of on-line tools that will quickly calculate the creatinine clearance. Estimated glomerular filtration rate (eGFR) is not recommended as it can overestimate renal function and increase the risk of bleeding events.

Dose adjustment may be necessary if renal function significantly changes during treatment. The product information for dabigatran and edoxaban advises an assessment of renal function if a decline in function is suspected during treatment (for example, due to hypovolaemia, dehydration, and in case of concomitant use of certain medicinal products).

DOACs can be used in patients with moderate renal impairment (creatinine clearance of 30mL/min or higher) but a reduced dose may be required. Renal function should be assessed and the results recorded in all patients commencing a DOAC and during treatment. Renal function should also be assessed when a change in renal function is suspected during treatment (e.g. hypovolaemia, dehydration, and in case of concomitant use of certain medicinal products). If the patient's eGFR is below 60ml/minute/1.73m^2 assessment of renal function by calculating the creatinine clearance using the Cockcroft-Gault formula is advised. It is available on-line at the following link. https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation.

Finally

- Clinicians are reminded that DOACs are not recommended in patients with antiphospholipid syndrome.
- Dabigatran is contraindicated and other DOACs are not recommended in patients with prosthetic heart valves.

Reference:https://www.gov.uk/drug-safety-update/direct-acting-oral-anticoagulants-doacs-reminder-of-bleeding-risk-including-availability-of-reversal-agents

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