Formulary Fact Sheet: Off-Licence use of Dabigatran and Rivaroxaban

NHS Cornwall and Isles of Scilly

The purpose of this fact sheet is to advise clinicians on the appropriateness of prescribing the newer anticoagulants dabigatran and rivaroxaban for off-licence indications. Doing so has legal, clinical and financial implications that need to be considered.

In addition to the prophylaxis of venous thromboembolism following hip or knee surgery **Dabigatran** is licensed and approved under a NICE TAG for the prevention of stroke and systemic embolism in adult patients with non-valvular AF with one or more of the following risk factors: previous stroke, transient ischemic attack, or systemic embolism (SEE), left ventricular ejection fraction < 40 %, symptomatic heart failure, New York Heart Association (NYHA) Class 2, age 75 years, age 65 years associated with one of the following: diabetes mellitus, coronary artery disease, or hypertension.

As well as for post-surgery indications, **Rivaroxaban** is licensed and NICE approved for the:

- Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (AF) with one or more risk factors, such as congestive heart failure, hypertension, age 75 years, diabetes mellitus, prior stroke or transient ischaemic attack.
- Treatment of deep vein thrombosis (DVT), and prevention of recurrent DVT and pulmonary embolism (PE) following an acute DVT in adults.

What about Warfarin, Acenocoumarol or Phenindione?

Warfarin and related vitamin K antagonists (VKAs) are licensed for anticoagulation in a wider range of indications including prosthetic heart valves, rheumatic heart disease etc and there is a wealth of experience with their use. Dabigatran and rivaroxaban are not as yet licensed for these indications and there is no evidence of whether or not doses used in AF or DVT/PE prevention are effective.

There are patients with prosthetic heart valves or congenital heart disease etc requiring anticoagulation, where warfarin and other VKAs are not tolerated and/or are unsuitable. In addition the strict INR monitoring requirements and lifestyle issues may mean that certain patients do not engage with effective treatment. Although the clinical effectiveness is unknown, the use of dabigatran or rivaroxaban could be considered to be better than no anticoagulation at all. The dose would be determined based on the individual patient in conjunction with the product's SPC for its licensed indications.

Cornwall Area Prescribing Committee Decision

The CAPC has made a decision on the use of dabigatran and rivaroxaban for off-licence indications.

Until dosing studies are complete, dabigatran or rivaroxaban at current AF doses are likely to be less effective than optimal anti-coagulation with a VKA.

For any patient where the use of dabigatran or rivaroxaban is being considered, there will need to be a risk/benefit analysis and the patient's individual cardiologist would need to be involved.

The decision about whether to start treatment with dabigatran should be made after an informed discussion between the clinician and the patient about the risks and benefits of dabigatran compared with a traditional VKA.

If dabigatran or rivaroxaban are to be used, applications to the PCT Special Cases panel will not be necessary

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Patient/Prescriber FAQ

- ***I can't/won't take warfarin. Can I have dabigatran or rivaroxaban for my prosthetic heart valves?***

Anticoagulation with warfarin/phenindione/acenocoumarol has been shown over many years to be effective. There is a lot of experience with their use. Dabigatran and rivaroxaban have only been recently introduced and although they have been shown to be effective in atrial fibrillation, deep vein thrombosis and pulmonary embolism, there are no studies as yet showing that they are effective for patients with other conditions requiring anticoagulation. Dabigatran and rivaroxaban are therefore unlicensed for the prevention of blood clots in patients with prosthetic heart valves etc. This does not mean that they can not be prescribed, but the patient must understand the potential benefits and risks associated with off-licence use and the prescriber must be willing to accept full clinical responsibility for the outcome.

- ***Will it work?***

As yet there are no studies showing that dabigatran or rivaroxaban are effective at preventing blood clots in patients with prosthetic heart valves. As anticoagulants the use of these newer agents may offer a real alternative for patient's unable or unwilling to take warfarin, although the response may be sub-optimal.

- ***What dose should I take?***

There are no studies to inform a clinician's decision as to the optimal dose to prescribe for anticoagulation in conditions other than AF, DVT, or PE. As patients with prosthetic heart valves and other cardiac conditions are routinely treated to a different target INR to patients with AF, DVT, or PE we don't know if the current licensed doses of dabigatran or rivaroxaban will be effective.

- ***Is it safe?***

At licensed doses, dabigatran and rivaroxaban are generally well tolerated, although some patients may experience gastrointestinal disturbances. The main risk is bleeding and unlike over-anticoagulation with warfarin, the effect can not be reversed. Dabigatran and rivaroxaban do have short half lives and discontinuation of the drug may be all that is needed to reverse the anticoagulation effect. These are new drugs and until there is more experience in their use clinicians are likely to be cautious about prescribing them, especially for unlicensed indications.

- ***What about monitoring?***

Routine INR monitoring is not required nor indicated during dabigatran or rivaroxaban therapy. This may be an issue for some patients and clinicians who rely on knowing an INR level to gauge effectiveness of treatment. Patients should be advised that in the event of haemorrhage or significant acute illness to OMIT medication and seek urgent assessment by, and advice from a doctor

- ***Should I carry an alert card***

Patients should be advised to carry an appropriate anticoagulant alert card. The current yellow NPSA Oral Anticoagulant Therapy card may be useful, or alternatively the Pradaxa/Xarelto patient card.

References

Dabigatran (Pradaxa) and Rivaroxaban (Xarelto) SPCs: http://www.medicines.org.uk/emc/