Formulary Fact Sheet: Dabigatran for prevention of stroke and systemic embolism in atrial fibrillation

NHS Cornwall and Isles of Scilly

This factsheet should be used in conjunction with the full Peninsula Heart and Stroke Network Guideline on the new oral anticoagulants for the prevention of stroke and systemic embolism in atrial fibrillation. Its purpose is to inform prescribers and other healthcare professionals about the appropriate introduction of dabigatran (Pradaxa) as an ***option*** for the prevention of stroke and systemic embolism in people with non-valvular AF. As we all know this is a new indication for this drug and there are clear benefits and risks. The introduction of dabigatran under the NICE TAG was discussed at the Cornwall Area Prescribing Committee with specialist advice provided by RCHT consultants. There are four main groups of patients where the use of dabigatran could be considered:

1. **Patients with AF not taking warfarin for reasons of intolerance, significant adverse effects, interactions, or circumstances where routine monitoring may be impractical**
2. **Patients with AF with poor INR control on warfarin**

These groups represent a significant proportion of patients with AF, most of which may be at a high risk of stroke. Patients need to be reviewed on an individual basis to ascertain whether dabigatran would be an appropriate treatment option.

3. Warfarin-naïve patients

In view of cost and long term outcome and safety data local GP Leads feel that it is appropriate to have a trial of warfarin in the majority of patients. The NICE TAG suggests that this should not be insisted upon if the patient after counselling expresses a strong preference for starting dabigatran.

4. Patients with AF currently well controlled on warfarin

There is evidence that stable patients with good INR control may not gain additional clinical benefit by switching to dabigatran. However the NICE TAG states that even patients with very good control should not be refused dabigatran as a potential treatment option. Local expert opinion however at this stage would be that this group of patients would not be an immediate priority for active switching. The additional cost to the prescribing budget if all patients on warfarin were switched to Dabigatran could be as high as £2.4 million.

The Bottom Line

The decision about whether to start treatment with dabigatran should be made after an informed discussion between the clinician and the person about the risks and benefits of dabigatran compared with warfarin. For people who are taking warfarin, the potential risks and benefits of switching to dabigatran should be considered in light of their level of INR control. (NICE, 2012)

Key Considerations

- Dabigatran requires dose adjustment in renal impairment and is contraindicated in severe impairment. Renal function should be checked prior to initiation and monitored as necessary, especially if any decline is suspected. Monitor at least annually in patients older than 75 years and in those with renal impairment.
- Due to short half life (12-17 hours vs 40 hours for warfarin) dabigatran must be taken twice daily.
- As a new drug for stroke prevention in AF, there are no long term safety data on the use or effectiveness of dabigatran beyond the 2 year average in the RE-LY trial.
- Despite its short half life there remains a significant concern in that there is no specific antidote for dabigatran patients presenting with life threatening haemorrhage requiring emergency treatment. A RCHT in-hospital strategy to manage haemorrhage or suspected overdose is included on this factsheet.
- Dabigatran can be associated with significant drug interactions. See the product SPC for full details.
- Dabigatran is not suitable for inclusion within a monitored dosage system, i.e. a blisterpack as the capsules are moisture sensitive.

Initiating Dabigatran

- The recommended daily dose of Pradaxa is 300 mg taken as one 150 mg capsule twice daily. Therapy should be continued long term. (For 75-80 yr olds, 110mg twice daily may be considered)
- Patients aged 80 years or above should be treated with a daily dose of 220 mg taken as one 110 mg capsule twice daily due to the increased risk of bleeding in this population.

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- When switching from a Vitamin K antagonist such as warfarin, the current drug should be stopped and dabigatran initiated at the appropriate dose when the INR drops below 2.0.

What about Rivaroxaban?

Rivaroxaban is another oral anticoagulant that has recently been granted a license for AF and its use is covered as part of the Peninsula guideline. This drug inhibits factor Xa in the clotting process, unlike dabigatran that inhibits thrombin. It is currently being assessed by NICE but until the NICE TAG is released, this drug is not routinely commissioned in CIOS for this indication.

RCHT Strategy: Bleeding risk, its assessment and the reversal of direct oral anticoagulants:

	Dabigatran etexilate (Pradaxa)
Mechanism	Direct thrombin inhibitor (anti-IIa)
Effect on coagulation tests	May affect the pro-thrombin time (PT) and thrombin time (TT)
Excretion	Renal
Half life	12-17 hours
Indication Dose	In atrial fibrillation 150mg bd "consider" 110mg bd if • Elderly (over 75-80 years of age) • Dyspepsia/GORD • Moderate renal impairment CrCL 30-50 l/min if patient is at high risk of bleeding
Severe renal impairment	CrCL < 30 ml/min **dabigatran is contraindicated**
Incidence of bleeding	serious gastro-intestinal or cerebral = <3% per annum
Reversal agent	None
Over dose	Oral charcoal if within 2 hours of ingestion dabigatran can be dialysed

The avoidance of bleeding: Patient education – <u>prevention</u> and management

- **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 patient card.
- 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
- Patients need to understand the benefits and risks of dabigatran therapy through fully informed decision making.
- Patients and carers must have a copy of the patient information leaflet
- A forgotten dose may still be taken up to 6 hours prior to the next scheduled dose. From 6 hours prior to the next scheduled dose, the missed dose should be omitted. No double doses should be taken.

Assessment and in-hospital management of significant bleeding (cerebral or GI)

- Determine time since last dose of therapy as interruption of treatment may well be sufficient**
- Check FBC, U&E's and <u>a coagulation screen (PT, **Thrombin Time (TT)** and APTT).</u> If within normal reference range there is likely to be only a low level of the drug
- Institute resuscitation with IV fluids and blood transfusion if necessary

*NB** The estimated time for restoration of haemostasis after cessation of therapeutic doses, with adequate renal function is "usually within 12 h".*

Surgery

- <u>Wait 12 hours</u> after last dabigatran dose

Thrombosis

- <u>Wait 12 hours</u> after last dabigatran dose before switching to a parenteral anticoagulant.

Reference: Journal of Thrombosis and Haemostasis, 9: 1705–1712
SPC: http://www.medicines.org.uk/EMC/medicine/24839/SPC/Pradaxa+150+mg+hard+capsules/
PIL: http://www.medicines.org.uk/EMC/medicine/24840/PIL/Pradaxa+150+mg+hard+capsules/
Boehringer-Ingleheim: Management of bleeding in emergency situations for patients treated with Pradaxa®.
Consideration for surgery for patients treated with Pradaxa®