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Emeritus Professor Lloyd Sansom AO
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Dear Professor Sansom

Re: Review of anticoagulation therapies in atrial fibrillation

NPS is pleased to provide a submission for this review in the context of quality use of medicines. In considering anticoagulation therapies in atrial fibrillation, we would like to draw attention to the issues surrounding the recent dabigatran product familiarisation program (PFP), and highlight information from our anticoagulant educational programs and research that may be helpful to consider as part of this review process.

Our position is that all anticoagulants are likely to carry a risk that must be well articulated and understood. The harms and benefits of warfarin are well recognised and documented. A shift to other products should be made with both this understanding and an appreciation of the new harms and benefits likely to be associated with the new product(s).

Dabigatran product familiarisation program (PFP)
We believe the appropriate context for providing PFPs across all health care sectors needs to be better articulated in supporting guidelines and frameworks. The recent PFP for dabigatran was implemented in primary care, and it became apparent that the existing guidelines did not safeguard against some important unintended events. Many of the issues appeared to rise from the capacity of general practices to undertake the required consent and monitoring activities and a lack of engagement with emergency departments and hospitals.

In our view there were substantial systemic and product-related issues that contributed to the problems with the dabigatran PFP. We believe safety and efficacy warnings were seriously understated by the manufacturer, including dabigatran's unsuitability for Webster pack use. It appeared the majority of hospitals were unaware and ill equipped to manage patients presenting who were receiving this treatment. MIMs and most other reference texts carried the old product information (relating to the VTE indication) and did not pick up the new stroke prevention in atrial fibrillation indication. In addition, most prescribing and dispensing systems carried inaccurate information on dose, interactions etc, ie **once** daily not twice a day.

Principles for conducting PFPs in the hospital sector have been clearly articulated. However we believe principles that suit application to a whole of health system approach are necessary in order to address the risks associated with anticoagulants and other high risk products.

A formal risk management plan articulated for introducing new medicines in the context of PFPs needs to include both the risks and benefits of a medicine, which in the case of anticoagulants are significant.

NPS is keen to see both the pharmaceutical sector and health professionals well supported to implement PFPs safely and effectively, and is reviewing this issue to identify gaps in the existing support frameworks and guidelines. We believe we are well placed to work with industry and others in coordinating the appropriate parties to develop a risk management framework that takes a whole of health system approach for introducing new drugs via PFPs.

NPS program: anticoagulant therapy in stroke prevention
We have undertaken significant work examining the use of anticoagulant therapy in stroke prevention.

The use of anticoagulants for stroke prevention has been the focus of two NPS visiting programs, commencing in 2003 and 2009. A visiting program is provisionally planned for 2013 with the scope of this program yet to be determined. NPS is well placed to deliver this work which will aim to improve health outcomes for patients treated with antithrombotic medicines

The key messages in our 2009 program focused on assessment of risk-benefit of warfarin and antiplatelet agents, appropriate choice of antiplatelet agents and use of strategies to ensure concordance and maintenance of the patient's INR in therapeutic range.

We conducted 5461 educational visits to health professionals (mainly GPs), 4446 health professionals attended divisional case scenario discussions, 282 health professionals attended interactive workshops and 959 GPs completed the clinical audit. Print publications were also distributed to GPs, pharmacists and other health professionals. Evaluation of the 2009 program is in progress with a publication date of end 2012.

In 2009, 959 GPs completed a clinical audit of their use of antiplatelet and anticoagulant therapy in stroke prevention. Each GP audited their care of 15 patients with:

- paroxysmal, persistent or permanent atrial fibrillation (AF) or atrial flutter, and/or
- a previous ischaemic stroke or transient ischaemic attack (TIA), and/or
- oral antiplatelet and/or anticoagulant therapy prescribed for primary or secondary prevention of stroke.

The data represented the care of 14,168 patients: 9,604 with a diagnosis of atrial fibrillation, 5,880 with a previous ischaemic stroke or transient ischaemic attack and 1,368 with another reason for stroke prevention therapy. The use of antithrombotic therapy for at-risk patients was generally broadly in line with guidelines. Several areas were identified where improvements could be made:

- Only 34% of patients with non-valvular atrial fibrillation (NVAF) or atrial flutter with a CHADS2 score = 0 were using aspirin unless contraindicated. Australian Guidelines recommend aspirin for this group of patients.
- An oral anticoagulant was used in 52% (295/567) of patients with NVAF or atrial flutter at low risk of stroke (CHADS2 = 0), which was not in line with Australian guidelines at the time (although we recognise that emerging evidence in this area may change future guidance).
- Only 66% (680/1036) of patients with paroxysmal NVAF and a CHADS2 score ≥ 2 were using an oral anticoagulant compared with 86% (2766/3236) of patients with persistent/permanent NVAF and a CHADS2 score ≥ 2. This is despite paroxysmal, persistent and permanent AF all posing the same stroke risk.
- Of patients
  using an oral

anticoagulant, 79% had their most recent INR in the recommended range for stroke prevention (2.0–3.0). Thus 21% had their most recent INR outside the recommended range.

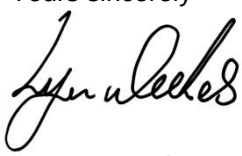
From the audit findings we were able to make the following recommendations:

- Consider warfarin in all patients with valvular atrial fibrillation (AF), or with non-valvular AF / atrial flutter at moderate to high risk of stroke ($CHADS_2 \geq 2$). Most patients with valvular AF (93%), or with non-valvular AF (or atrial flutter) and a $CHADS_2 \geq 2$ (90%) were using an oral anticoagulant (warfarin or phenindione) unless contraindicated.
- Use warfarin in patients with previous cardioembolic stroke unless contraindicated; these patients are at high risk of a subsequent stroke. Most patients with previous cardioembolic stroke (83%) were using an oral anticoagulant.
- Use warfarin or aspirin in patients with non-valvular AF or atrial flutter at moderate risk of stroke ($CHADS_2 = 1$). Of patients with non-valvular AF or atrial flutter with a $CHADS_2 = 1$, 96% were using aspirin or an oral anticoagulant unless both were contraindicated.
- Consider aspirin in patients with non-valvular AF or atrial flutter at low risk of stroke ($CHADS_2 = 0$). Only 34% of patients with non-valvular AF. For atrial flutter with a $CHADS_2 = 0$ were using aspirin unless contraindicated. An oral anticoagulant was used in 52% of patients with non-valvular AF (or atrial flutter) at low risk of stroke ($CHADS_2 = 0$).
- Consider long-term antiplatelet agents for all patients with a previous stroke due to arterial disease. These patients are at high risk of a subsequent stroke. Of patients with a previous ischaemic stroke or TIA due to arterial disease, 74% were using aspirin, clopidogrel or aspirin plus dipyridamole (79% were using an antiplatelet agent) unless contraindicated.
- Paroxysmal, persistent and permanent AF all pose the same stroke risk. Only 66% 680/1036) of patients with paroxysmal non-valvular AF and a $CHADS_2 \geq 2$ were using an oral anticoagulant compared with 86% (2766/3236) of patients with persistent/ permanent non-valvular AF and a $CHADS_2 \geq 2$.
- Aim for a target INR of 2.0 to 3.0 for all indications except prosthetic heart valves. Of patients using an oral anticoagulant, 79% had their most recent INR in the recommended range for stroke prevention (2.0–3.0).

We have also published a number of articles and reviews in NPS publications *NPS News, Prescribing Practice Review*, *Australian Prescriber* and *NPS RADAR* that may be relevant to this review. In addition, we are currently in the early stages of our formative research phase for our 2013 program and this involves the preparation of a comprehensive report. We would be pleased to provide more details about our published resources and the formative research currently underway if this would be of assistance.

Please contact Keinwen Shephard, External Relations & Policy Advisor, on 02 8217 8784 or email kshephard@nps.org.au if you would like additional information or have any questions in relation to this submission.

Yours sincerely



Dr Lynn Weekes
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