Cardiovascular Subcommittee of PTAC meeting held 23 September 2011

(minutes for web publishing)

Cardiovascular Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2008*.

Note:

- that this document is not necessarily a complete record of the Cardiovascular Subcommittee meeting; only the relevant portions of the minutes relating to Cardiovascular Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.
- that any part of the minutes relating to hospital pharmaceuticals and the establishment of a national Preferred Medicines List (PML) will be released, in a complete publication with the original Hospital Pharmaceuticals Subcommittee minutes and final recommendations made by PTAC, once PTAC have reviewed each therapeutic group.

The Cardiovascular Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;
(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or
(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

These Subcommittee minutes were reviewed by PTAC at its meeting on 16 & 17 February 2012, the record of which will be available on the PHARMAC website April 2012.

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1 Minutes of Previous Meeting

1.1 The Subcommittee noted the previous minutes from its October 2010 meeting.

1.2 The Subcommittee noted that prasugrel was reviewed by PTAC at its August 2011 and although the minutes have not been finalised, PTAC had recommended that prasugrel be funded with low priorities for patients undergoing percutaneous coronary intervention (PCI) who are clopidogrel-allergic and patients who experience stent thrombosis whilst on clopidogrel.

1.3 The Subcommitttee noted that PTAC had also considered that in clopidogrel-allergic patients, both prasugrel and ticlopidine would be appropriate. The Subcommittee considered that there was currently a lack of clinical evidence for the use of ticlopidine in drug-eluting stents and ticlopidine was difficult to access to New Zealand as it is not registered here. The Subcommittee re-iterated its previous recommendation that prasugrel should be funded with high priorities for patients undergoing PCI who are clopidogrel-allergic and patients who experience stent thrombosis whilst on clopidogrel. The Subcommittee also noted that PTAC had requested that PTAC re-review its recommendation for prasugrel in the ST-elevation myocardial infarction (STEMI) undergoing immediate PCI group at its meeting in November 2011. The Subcommittee re-iterated its previous recommendation that prasugrel should be funded with medium priority for this patient group.

1.4 The Subcommittee noted that dabigatran had been funded without Special Authority from 1 July 2011 and since then, there have been reports of patients experiencing adverse effects namely bleeding after being prescribed the treatment. The Subcommittee noted that some reports of bleeding due to dabigatran were due to inappropriate prescribing in relation to dosing in the elderly and transitioning a patient prior to the INR dropping below 2. The Subcommittee noted that PHARMAC had prepared a number of documents related to dabigatran prescribing, namely guidelines for reversal of its effects and its management perioperatively as well as prescribing guidelines aimed at primary care prior to its listing. The Subcommittee also noted that there will be further articles on dabigatran which will be published through the Best Practice Journal. The Subcommittee considered that although access was provided to a clinically beneficial treatment, the experience after dabigatran became subsidised highlighted the potential problems with the introduction of new technologies. The Subcommittee noted that clinicians should always familiarise themselves with the relevant prescribing information and clinical evidence before they prescribe a new treatment and this remains the primary responsibility of the prescriber, and that in some circumstances it will be necessary for this to be widely disseminated before the product becomes subsidised. Members noted that there was no clear responsibility for disseminating such information, but that colleges and professional societies had the potential to offer value in this space, in addition to PHARMAC and pharmaceutical suppliers. The Subcommittee considered that the Primary Healthcare Organisations (PHOs) could also be used as a network for dissemination of information to primary care.

2 Dronedarone for atrial fibrillation

Application

1.5 The Subcommittee reviewed a memorandum from PHARMAC staff regarding dronedarone (Multaq) for the treatment of non-permanent and permanent atrial fibrillation (AF).

Recommendation

1.6 The Committee **recommended** that consideration of dronedarone for both non-permanent and permanent AF for inclusion on a national PML or the Pharmaceutical Schedule be deferred until its safety and risk/benefit profile is clarified.

Discussion

1.7 The Subcommittee noted that at its October 2010 meeting, it had requested that dronedarone be formally reviewed on the basis that it was an amiodarone alternative with less efficacy but with a better safety profile given the significant adverse effects that can occur with long-term amiodarone use.

1.8 The Subcommittee noted that dronedarone is not registered in New Zealand but is approved in the United States, Europe and Australia for patients who currently have or had non-permanent AF. The Subcommittee noted that the FDA approval included a Risk Evaluation and Mitigation Strategy with the goal of preventing its use in patients with heart failure due to a greater than two-fold increase in the risk of death.

1.9 The Subcommittee noted the results of the ATHENA (Singh et al. N Engl J Med 2007; 357: 987-99) and ANDROMEDA (Køber et al. N Engl J Med 2008; 358: 2678-87) studies which suggested that dronedarone was of benefit for patients with non permanent AF, due to a significant reduction in cardiovascular hospitalisation or death from any cause, but not congestive heart failure due to a significant increase in mortality.

1.10 The Subcommittee noted that in January 2011, the US Food and Drug Administration (FDA) issued a safety communication following several case reports of hepatocellular liver injury and hepatic failure in patients treated with dronedarone, including two post-marketing reports of acute hepatic failure requiring transplantation.

1.11 The Subcommittee noted that in July 2011, the PALLAS Phase IIIb trial, which was investigating the use of dronedarone in patients with permanent AF (in an effort to expand its indication from non-permanent AF), had been discontinued following an observed significant increase in cardiovascular events in the dronedarone arm.

1.12 The Subcommittee noted that as a result of the severe liver injury reports and the results of the PALLAS study, the European Medicines Agency (EMA) is reviewing dronedarone's risk/benefit profile.

1.13 The Subcommitee noted that while Sanofi considers that the benefit-risk of dronedarone remains unchanged in non-permanent AF, it is examining the trial databases in an effort to clarify the adverse effects profile and is not intending to seek registration in New Zealand, provide compassionate supply for patients, or seek a listing on the Pharmaceutical Schedule until the risk-benefit profile has been examined.

1.14 The Subcommittee considered that the PALLAS trial results suggested that dronedarone should not be used in permanent AF and while the ATHENA trial results suggested that it is appropriate for non-permanent AF the toxicity issues were an outstanding concern