Haematology Subcommittee of PTAC
Meeting held 1 October 2014

(minutes for web publishing)

Haematology 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 Haematology Subcommittee meeting; only the relevant portions of the minutes relating to Haematology Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.

The Haematology 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 7 & 8 February 2015, the record of which are now available.

Chair

Record of the Haematology Subcommittee of PTAC meeting held at PHARMAC on 1 October 2014

1 Summary of recommendations

The Subcommittee recommended that:

1.1 The second sentence in Item 8.7.3 from its previous meeting minute is amended as follows (deletions in strikethrough, additions in bold) to better reflect their discussion:

> The Subcommittee considered that, overall, these agents are not inferior to warfarin in the prevention acute treatment of recurrent VTEs.

1.2 Amendments are made to the PHARMAC guidelines for dabigatran;

1.3 Ferric carboxymaltose is listed in Section B of the Pharmaceutical Schedule subject to Special Authority restriction set out in relevant section below.

2 Minutes of previous meeting

2.1 The Subcommittee recommended that the second sentence in paragraph 8.7.3 is amended as follows (deletions in strikethrough, additions in bold) to better reflect the discussion:

> The Subcommittee considered that, overall, these agents are not inferior to warfarin in the prevention acute treatment of recurrent VTEs.

3 Matters arising and correspondence

Dabigatran guidelines

3.1 The Subcommittee considered that it would be appropriate to review the guidelines developed by PHARMAC on the management of bleeding associated with dabigatran and the issue of testing and perioperative management of the treatment to ensure that the advice is up to date with current available evidence. The Subcommittee noted that other guidelines have since been published in Australia (Tran et al. Internal Medicine Journal 2014;44:525-536), Europe (Heidbuchel et al. European Heart Journal 2013; doi:10.1093/eurheartj/eht134) and the UK (Makris et al. British Journal of Haematology 2012;160:35-46). The Subcommittee considered that the Australasian guidelines offered the most detail and are similar to the existing PHARMAC guidelines.

3.2 Based on the updated information available, the Subcommittee recommended that the following amendments are made to the PHARMAC guidelines:

Guidelines for management of bleeding with dabigatran

Chair

3.3 Addition of a statement at the beginning of the flow chart to mention that if Thrombin Time is normal, bleeding is unlikely to be due to dabigatran therapy.

3.4 Under the 'Mild bleeding' heading, amend the reference to tranexamic acid to state 'Consider tranexamic acid orally, 1 g three times a day'.

3.5 Under the 'Moderate to Severe bleeding' heading, lower the level for platelet transfusion to 50 × 109/L instead of 70 – 80 × 109/L. Amend the recommendation pertaining to tranexamic acid to state 'Consider the administration of tranexamic acid IV (15-30 mg/kg) +/- continuous infusion (1 mg/kg/hr).

3.6 Under the 'Life threatening bleeding' heading, replace the current statement about recombinant factor VIIa with 'Consider the use of a bypassing agent like Factor VIII inhibitor bypassing fraction (FEIBA) with haematology guidance. There is currently limited data supporting the efficacy of these pro-haemostatic agents in patients with bleeding associated with dabigatran'. The current footnote about the potential use of Prothrombinex-VF and recombinant factor VIIa can be removed.

3.7 Addition of a footnote to state that Australian (Tran et al. Internal Medicine Journal 2014; 44: 525-536), European (Heidbuchel et al. European Heart Journal 2013; doi:10.1093/eurheartj/eht134) and UK guidelines (Makris et al. British Journal of Haematology 2012; 160: 35-46) have been published on this topic.

Guidelines for testing and perioperative management of dabigatran

3.8 The level for platelet transfusion to be lowered to 50 X 109 / L from 70 – 80 X 109 / L.

3.9 Under the 'Urgent surgery' heading, replace reference to recombinant factor VIIa with Factor VIII inhibitor bypassing fraction (FEIBA) as a potential measure tocontrol bleeding prior to and during the surgery.

Ferric carboxymaltose

3.10 The Subcommittee noted that PHARMAC had recently listed ferric carboxymaltose in Section H of the Pharmaceutical Schedule. The Subcommittee noted that PHARMAC intends to develop a proposal to list it in Section B pending resolution of service provision issues and development of Special Authority criteria that would target the treatment to the group most likely to benefit.

3.11 The Subcommittee considered that the listing of ferric carboxymaltose in Section B would potentially present a fiscal risk if it is used inappropriately ahead of oral iron preparations. Members noted that gastrointestinal side-effects are common with oral iron preparations. The Subcommittee considered that a serum ferritin level should be specified in the Special Authority criteria and a level of <20 mcg/L would be an appropriate threshold for treatment of iron deficient anaemia in the community setting. The Subcommittee considered that a relevant specialist should be consulted prior to treatment in patients with a ferritin level of >20 mcg/L.

3.12 The Subcommittee recommended that ferric carboxymaltose be listed in Section B of the Pharmaceutical Schedule subject to the following Special Authority restriction:

Initial application – (serum ferritin ≤ 20 mcg/L) from any Specialist. Approval valid for 3 months for applications meeting the following criteria:
Both:
1. Patient has been diagnosed with iron-deficiency anaemia with a serum ferritin level of ≤ 20 mcg/L; and
2. Any of the following:
   1.1. Treatment with oral iron has proven ineffective;
   1.2. Treatment with oral iron has resulted in dose-limiting intolerance; or
   1.3. Rapid correction of anaemia is required.

Initial application – (serum ferritin >20 mcg/L) only from an internal medicine specialist, obstetrician, gynaecologist or anaesthetist or any other Specialist on recommendation of an internal medicine specialist, obstetrician, gynaecologist or anaesthetist. Approval valid for 3 months for applications meeting the following criteria:
Both:
1. Patient is likely to have iron-deficiency anaemia with a serum ferritin level of > 20 mcg/L; and
2. Any of the following:
   2.1. Treatment with oral iron has proven ineffective;
   2.2. Treatment with oral iron has resulted in dose-limiting intolerance; or
   2.3. Rapid correction of anaemia is required.

Renewal – (serum ferritin ≤ 20 mcg/L) from any Specialist. Approval valid for 3 months for applications meeting the following criteria:
1. Patient continues to have iron-deficiency anaemia with a serum ferritin level of ≤ 20 mcg/L; and
2. A re-trial with oral iron is clinically inappropriate.

Renewal – (serum ferritin >20 mcg/L) only from an internal medicine specialist, obstetrician, gynaecologist or anaesthetist or Specialist on recommendation of an internal medicine specialist, obstetrician, gynaecologist or anaesthetist. Approval valid for 3 months for applications meeting the following criteria:
Both:
1. Patient continues to have iron-deficiency anaemia with a serum ferritin level of > 20 mcg/L; and
2. A re-trial with oral iron is clinically inappropriate.

4 Therapeutic Group Review

4.1 The Subcommittee considered that there was no available treatment alternative to tranexamic acid in New Zealand. Aminocaproic acid was a potential treatment alternative but the treatment is not available here.

4.2 The Subcommittee noted that the current eltrombopag Special Authority restriction did not include patients in whom splenectomy is contraindicated, unlike that for rituximab. The Subcommittee noted that this was due to the fiscal risk associated with funding eltrombopag for that patient population. The Subcommittee noted that these patients could be considered for funding through

the Named Patient Pharmaceutical Assessment (NPPA) pathway and it could review its recommendation for this patient group in the future if necessary.

4.3 The Subcommittee noted that PHARMAC is currently carrying out further analysis on the novel oral anticoagulants market. The Subcommittee considered that the availability of either rivaroxaban or apixaban would improve the treatment of venous thromboembolism (VTE) because these treatments do not require bridging with enoxaparin. The Subcommittee considered that enoxaparin bridging treatment adds complexity to the treatment algorithm for VTE, not just because it is an injection, but also because of the additional patient or caregiver education required and potential additional health services required for administration of the treatment. The Subcommittee considered that apixaban was preferred over rivaroxaban because apixaban has a better safety profile in terms of lower bleeding rates. The Subcommittee considered that there was no clinical need for both products to be funded in view of current funded treatment alternatives. The Subcommittee noted the option of running a competitive process for the funding of a Factor Xa inhibitor (i.e apixaban or rivaroxaban) with market exclusivity for the preferred bidder for a specified number of years, after which other Factor Xa inhibitors could potentially be listed. The Subcommittee considered that it would be reasonable to run such a process and for either apixaban or rivaroxaban to be chosen for funding based on their relative cost-effectiveness.

4.4 The Subcommittee noted that there have been a few NPPA applications for eltrombopag in aplastic anaemia. The Subcommittee noted that the supplier intends to submit a funding application for eltrombopag in that indication after it obtains Medsafe registration but it is estimated that this is likely to be several years away.

4.5 The Subcommittee noted that there continues to be a number of NPPA applications for enoxaparin in various indications. The Subcommittee noted that enoxaparin will be included in the upcoming tender and reduced pricing would potentially enable PHARMAC to widen access to the treatment.

5 Competitive process for haemophilia treatments

5.1 The Subcommittee noted a memorandum from PHARMAC staff seeking the Subcommittee's views on different supply models for recombinant factor VIII (rFVIII). The Subcommittee noted that this will also be discussed with the National Haemophilia Management Group (NHMG) and the Treaters group in November 2014.

5.2 The Subcommittee noted that PHARMAC is considering issuing a Request for Proposals (RFP) for haemophilia treatments. Currently, three brands of rFVIII (Advate, Kogenate FS and Xyntha) are funded in New Zealand. Although Xyntha is the NHMG preferred brand given its favourable pricing structure, there are no actual limitations on what brand of rFVIII can be used in New Zealand. The Subcommittee noted that PHARMAC would like to explore the possibility of a different supply model of rFVIII in New Zealand to facilitate better pricing.

5.3 The Subcommittee noted that at this stage, the new longer-acting rFVIII and recombinant factor IX (rFIX) products would be excluded from the scope of any RFP at this stage; it is PHARMAC's intention that these new products would be evaluated by PHARMAC under its usual processes following Medsafe registration and receipt of funding applications for the products.

5.4 The Subcommittee noted a number of publications outlining the experience with different rVIII supply models in Ireland (Bacon CL et al. Haemophilia 2011; 17: 407-11), Canada (Rubinger M et al. Haemophilia 2008; 14: 281-6), UK (Hay CRM et al. Haemophilia 2012; 18: 828-32 and Hay CRM. Haemophilia 2013; 19: 660-667) and Australia (Stone M. Poster presented at World Federation of Haemophilia Congress; 2014 May 11-15). The Subcommittee also noted the outcomes of the recent 2014 Australian tender for rFVIII where Advate (Baxter) will be the national preferred rFVIII product whilst Xyntha (Pfizer) can only be used by patients where a change to Advate will likely compromise appropriate treatment and care.

5.5 The Subcommittee considered that, from a clinical perspective, it would be possible to implement a supply model in New Zealand similar to that in Australia. The Subcommittee noted that there would potentially be resistance to change in New Zealand due to concerns around development of inhibitors, supply security and loss of patient choice. However, the Subcommittee noted that there is now a growing body of evidence from international experience that inhibitor rates are not increased by brand switches.

5.6 The Subcommittee noted that PHARMAC would need to enforce a switch to the preferred brand and considered that this would be a significant change to prescribing practice but it would be in line with the practice for funded pharmaceuticals in all other therapeutic areas.

5.7 The Subcommittee considered that there may be a need to ensure temporary or longer-term continued supply of any 'delisted' brand for defined patient groups, potentially including those undergoing tolerisation and patients who have had less than 50 exposure days to treatment. The Subcommittee suggested that PHARMAC seek advice from Australian funders around this issue.

5.8 The Subcommittee considered that it would be preferable if the RFP defined a supply period of 5 years instead of the usual 3 years. The Subcommittee considered that this longer timeframe would be appropriate given the relative complexity of a brand switch for rfVIII when compared to other medicines. The Subcommittee considered that a 6-month transition would likely be sufficient to enable all patients to be switched safely.

5.9 The Subcommittee noted that these patients are currently closely monitored and a brand switch would not require additional clinic visits. Specialist haemophilia nurses would be key clinicians involved in a brand switch in this patient group and training sessions would be required to help patients to transition to a new brand. The Subcommittee considered that there would likely be an increase in inhibitor testing as a result of a brand switch and it would be appropriate to assume that, on average, 4 additional tests would be performed per patient.

5.10 The Subcommittee considered that there is limited scope to widen access to the currently available haemophilia treatments (e.g. in exchange for price reductions) in a cost-effective manner. There is the possibility of increasing the use of bypassing agents in patients with inhibitors but the Subcommittee considered that this would not be a cost-effective treatment option. The Subcommittee also noted that the use of prophylactic treatment could be increased in older patients but this is already occurring to a certain extent.

5.11 The Subcommittee considered that it would be beneficial to organise a meeting involving expert members of the Haematology Subcommittee, PHARMAC staff, Haemophilia Treaters from Australia and the Australian National Blood Authority to discuss the experience in Australia in further detail.