

30 September 2010

Proposal for rivaroxaban, moxifloxacin, interferon beta-1-beta and other funded treatments for multiple sclerosis

PHARMAC is seeking feedback on a provisional agreement with Bayer New Zealand Limited to:

- fund rivaroxaban (Xarelto), a new agent for the prophylaxis of venous thromboembolism following orthopaedic surgery, including listing in Section H of the Pharmaceutical Schedule;
- fund moxifloxacin (Avelox), an alternative treatment for treatment resistant mycobacterium tuberculosis, including listing in Section H of the Pharmaceutical Schedule; and
- change the terms of listing for interferon beta-1-beta (Betaferon).

In addition, it is proposed that restrictions for funded multiple sclerosis treatments (interferon beta-1-alpha, interferon beta-1-beta, and glatiramer acetate) would be amended to:

- ease the exit criteria; and
- permit switching between the funded treatments in patients with a stable or increasing relapse rate over 12 months of treatment providing that no other exit criteria are met.

Further details of this proposal can be found on the following pages. All changes are proposed for implementation from 1 December 2010.

Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **Thursday, 14 October 2010** to:

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All feedback received before the closing date will be considered by PHARMAC's Board (or Chief Executive acting under delegated authority) prior to making a decision on this proposal.

Details of the proposal

Rivaroxaban (Xarelto)

- Rivaroxaban would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule at the following prices and subsidies (ex-manufacturer, excluding GST):

Chemical	Brand	Presentation	Strength	Pack size	Proposed price and subsidy
Rivaroxaban	Xarelto	Tablet	10 mg	15	\$153.00
Rivaroxaban	Xarelto	Tablet	10 mg	30	\$306.00

- Rivaroxaban would be listed in Section B of the Pharmaceutical Schedule subject to Special Authority criteria as follows:

Initial application from any relevant practitioner. Approvals valid for 5 weeks for applications meeting the following criteria:

Either:

- For the prophylaxis of venous thromboembolism following a total hip replacement; or
- For the prophylaxis of venous thromboembolism following a total knee replacement.

Renewal from any relevant practitioner. Approvals valid for 5 weeks where prophylaxis for venous thromboembolism is required for patients following a subsequent total hip or knee replacement.

Note: Rivaroxaban is only currently indicated and subsidised for up to 5 weeks therapy for prophylaxis of venous thromboembolism following a total hip replacement and up to 2 weeks therapy for prophylaxis of venous thromboembolism following a total knee replacement.

- A confidential rebate would apply to all community subsidies and hospital sales of Xarelto, which would reduce its net price.
- Rivaroxaban would have protection from subsidy reduction until 30 June 2012 and from delisting until 30 June 2014.

Moxifloxacin (Avelox)

- Moxifloxacin 400 mg tablets would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule at a price and subsidy of \$52.00 per pack of 5 (ex-manufacturer, excluding GST).
- Moxifloxacin 1.6 mg per ml, 250 ml infusion would be listed in Part II of Section H of the Pharmaceutical Schedule at a price of \$70.00 per injection (ex-manufacturer, excluding GST).
- Moxifloxacin tablets would be listed in Section B of the Pharmaceutical Schedule subject to Special Authority criteria as follows:

Initial application only from a respiratory specialist or infectious disease specialist. Approvals valid for 1 year for applications meeting the following criteria:

Either:

- 1 Both:
 - 1.1 Treatment-resistant active tuberculosis*; and
 - 1.2 Any of the following:
 - 1.2.1 Documented resistance to one or more first-line medications; or
 - 1.2.2 Suspected resistance to one or more first-line medications (tuberculosis assumed to be contracted in an area with known resistance), as part of regimen containing other second-line agents; or
 - 1.2.3 Impaired visual acuity (considered to preclude ethambutol use); or
 - 1.2.4 Significant pre-existing liver disease or hepatotoxicity from tuberculosis medications; or
 - 1.2.5 Significant documented intolerance and/or side effects following a reasonable trial of first-line medications; or
- 2 Mycobacterium avium-intracellulare complex not responding to other therapy or where such therapy is contraindicated.*

Renewal only from a respiratory specialist or infectious disease specialist. Approvals valid for 1 year where the treatment remains appropriate and the patient is benefiting from treatment.

Note: Indications marked with * are Unapproved Indications (refer to Section A: General Rules, Part I (Interpretations and Definitions) and Part IV (Miscellaneous Provisions) rule 4.6).

Interferon beta-1-beta (Betaferon)

- The price and subsidy for interferon beta-1-beta injection 8 million iu per ml would be reduced in Section B of the Pharmaceutical Schedule from \$1,407.33 to \$1,322.89 for a pack of 15 (ex-manufacturer, excluding GST).
- A confidential rebate would apply to all community subsidies of Betaferon, which would reduce its net price.

Multiple sclerosis treatment restrictions

- The Stopping Criteria for funded access to the multiple sclerosis treatments glatiramer acetate (Copaxone), interferon beta-1-alpha (Avonex) and interferon beta-1-beta (Betaferon) would be amended as follows (additions in bold, deletions in strikethrough):

Stopping Criteria

- 1) Confirmed progression of disability that is sustained for ~~three~~ **six** months after a minimum of one year of treatment. Progression of disability is defined as ~~either~~ **any of:**
 - (a) an increase of 2 EDSS points where starting EDSS was 2.0; or**
 - (b) an increase of 1.5 EDSS points where starting EDSS was 2.5 or 3.0; or**
 - (c) an increase of 1 EDSS point from the where starting EDSS was 3.5 or greater; or**
 - (d) an increase in EDSS score to 6.0 or more; or**
- 2) stable or increasing relapse rate over 12 months of treatment (compared with the relapse rate on starting treatment); or
- 3) pregnancy and/or lactation; or
- 4) within the 12 month approval year, intolerance to interferon beta-1-alpha, and/or interferon beta-1-beta and/or glatiramer acetate; or
- 5) non-compliance with treatment, including refusal to undergo annual assessment or refusal to allow the results of the assessment to be submitted to MSTAC; or
- 6) patients may, subject to conclusions drawn from published evidence available at the time, be excluded if they develop a high titre of neutralising anti-bodies to beta-interferon or glatiramer acetate.

- The access criteria would be further amended to permit switching between funded treatments in patients with a stable or increasing relapse rate over 12 months of treatment (compared with relapse rate prior to starting treatment), providing that no other exit (stopping) criteria are met.

Background

Rivaroxaban

Rivaroxaban is an oral antithrombotic agent indicated for use in the prevention of venous thromboembolism following major orthopaedic surgery.

The Pharmacology and Therapeutics Advisory Committee (PTAC) has reviewed an application from Bayer New Zealand Limited for the funding of rivaroxaban. In summary, PTAC recommended that rivaroxaban be funded for the prophylaxis of venous thromboprophylaxis following major orthopaedic surgery with medium priority.

The full published PTAC minute relating to rivaroxaban can be found on PHARMAC's website at: www.pharmac.govt.nz/2010/01/29

Moxifloxacin

Moxifloxacin is an oral antibiotic indicated for the treatment of various bacterial infections namely bronchitis, pneumonia, sinusitis, complicated skin and intra-abdominal infections.

When reviewing anti-tuberculotics at its April 2010 meeting, the Anti-Infective Subcommittee of PTAC considered that moxifloxacin was the next agent to be considered following resistance or intolerance to first-line agents for mycobacterial infections including tuberculosis. The relevant minutes are as follows:

Antituberculotics and Antileprotics

The Subcommittee noted the tabled data on HEC applications for moxifloxacin for use in treating mycobacterium infection. The Subcommittee noted the World Health Organisation (WHO) guidelines which suggest that moxifloxacin is the next agent to be considered following resistance or intolerance to first line agents for mycobacterial infection. Members noted that there was some evidence that moxifloxacin was more effective than ethambutol for treating mycobacterial infection.

The Subcommittee noted the tabled correspondence from the Tuberculosis Advisory Group (TbAG) requesting a simpler HEC form for a product which is standard of care. Members considered that the proposed criteria were appropriate and would provide the basis of any restriction for moxifloxacin.

Members noted that it would be inappropriate to list moxifloxacin without restriction as this could potentially lead to resistance. Members noted that if moxifloxacin was listed there was the potential for leakage into other indications such as chronic obstructive pulmonary disease and pneumonia management.

Moxifloxacin is not registered by Medsafe for the proposed indication.

Multiple Sclerosis treatments

PHARMAC has received applications and submissions from various parties proposing three key changes to the access criteria for funded multiple sclerosis treatments, broadly summarised as follows:

- to allow funded treatment with a second type of MS medication after failure of treatment (as defined by current criteria) with the first type of treatment (referred to as “treatment switching”);
- to amend the entry criteria to allow earlier treatment; and
- to amend or remove the exit criteria to allow longer treatment.

PTAC has reviewed these proposals on several occasions. Full published minutes can be found on PHARMAC’s website at:

www.pharmac.govt.nz/2009/01/21;

www.pharmac.govt.nz/2009/10/15;

www.pharmac.govt.nz/2010/04/20; and

www.pharmac.govt.nz/2010/09/23

The most recent recommendations from PTAC are to amend the exit criteria as proposed in this consultation letter (PTAC gave a medium priority to this recommendation) and to permit treatment switching as proposed in this letter (also with a medium priority).

The Committee deferred re-consideration of a previous recommendation to decline all applications to amend the entry criteria for funded access to MS treatments pending an updated cost-utility analysis (CUA) to be performed by PHARMAC staff for review by the Committee. This work is ongoing.