

20 February 2014

## Widening of funding restrictions for rituximab and eltrombopag

PHARMAC is pleased to announce the approval of proposals to widen the restriction on rituximab use in DHB hospitals and expand the funding of eltrombopag in both hospitals and the community. This was the subject of consultation letters dated 13 September 2013 and 4 November 2013 respectively. The consultation letters can be found at:

- <http://www.pharmac.health.nz/assets/consultation-2013-11-04-eltrombopag-zanamivir-and-others.pdf>
- <http://www.pharmac.health.nz/assets/consultation-2013-09-13-rituximab-indications.pdf>

In summary, the effects of the decisions are that:

- The restriction on rituximab use in hospitals will be widened to include nine new indications; and
- The funding for eltrombopag will be widened to include patients with 20,000 to 30,000 platelets per microlitre and evidence of significant mucocutaneous bleeding.

### Details of the decisions

#### **Rituximab**

From 1 March 2014, the restriction on the use of rituximab in hospitals will be widened to include nine new indications. These will be in addition to the seven indications in which rituximab is already able to be used. The new indications are:

- Cold haemagglutinin disease (CHAD);
- Warm autoimmune haemolytic anaemia (warm AIHA);
- Immune thrombocytopenic purpura (ITP);
- Thrombotic thrombocytopenic purpura (TTP);
- Pure red cell aplasia (PRCA);
- ANCA associated vasculitis;
- Systemic lupus erythematosus (SLE);
- Antibody-mediated renal transplant rejection; and
- ABO-incompatible renal transplant.

Rituximab use in the indications above will be subject to restriction criteria which are detailed in the attached Appendix (<http://www.pharmac.health.nz/assets/notification-2014-02-20-rituximab-eltrombopag-appendix.pdf>).

Please note that, following consideration of consultation feedback, an additional indication (above those consulted on) was added - pure red cell aplasia. Several amendments were also made to the access criteria initially consulted upon, and these are identified in the 'Feedback received' section below.

## **Eltrombopag**

When PHARMAC consulted on a proposal to list eltrombopag in November 2013, we received feedback that access to the treatment should also include patients with platelet counts between 20,000 and 30,000 platelets per microlitre. Eltrombopag was listed in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 January 2014 but this patient group was excluded because PHARMAC wanted to obtain further clinical advice before making a decision.

PTAC and the Haematology Subcommittee have since advised PHARMAC that they consider this change to be appropriate.

The changes to the eltrombopag access criteria are detailed in the attached Appendix (<http://www.pharmac.health.nz/assets/notification-2014-02-20-rituximab-eltrombopag-appendix.pdf>).

### **Feedback received**

We appreciate all of the feedback that we received and acknowledge the time people took to respond. All consultation responses were considered in their entirety in making a decision on the proposed changes. Most responses were supportive of the proposal, and the following issues were raised in relation to general and specific aspects of the proposal:

<b>Theme</b>	<b>PHARMAC response</b>
Clinicians (haematologists, rheumatologists and nephrologists) and organisations like Arthritis New Zealand as well as the New Zealand Rheumatology Association (NZRA) are supportive of this proposal as it would reflect rituximab usage prior to 1 July 2013 (the inception of the Hospital Medicines List (HML)) and reduce the administrative work required currently for NPPA applications.	Feedback noted.
Bay of Plenty DHB is supportive of the rituximab proposal.	Feedback noted.
Southern DHB responded that this proposal would result in increased cost to them as rituximab use was more restricted in the DHB when compared to the access criteria in this proposal.	We acknowledge the fiscal impact of this proposal on some DHBs. This proposal is in line with PHARMAC's efforts to establish a national HML from 1 July 2013 and it was always anticipated that with a nationally consistent list there would be different levels of impact at different DHBs. In the last few years, the PHARMAC Board has approved a number of transactions which resulted in cost-shifting from DHB hospitals to the Combined Pharmaceuticals Budget which would help mitigate the cost increases as a result of the HML. Examples of these include, the funding of influenza vaccines, filgrastim and pegfilgrastim which were previously funded by DHB hospitals.

<b>Rituximab for ITP</b>	
Restricting rituximab in ITP to patients who have already had splenectomy or in whom splenectomy is "an absolute" contraindication is open to subjective interpretation, unjustifiably restrictive and contrary to international practice.	PHARMAC's clinical advisors, PTAC and the Haematology Subcommittee, recommended that splenectomy is used ahead of rituximab in ITP treatment algorithms because splenectomy is more effective and results in more durable responses. The Subcommittee also noted that there are significant side effects associated with rituximab therapy and its long term safety with repeated use in ITP is unknown.  The Subcommittee noted that although the criteria 'splenectomy is an absolute contraindication' could be subjective it was difficult to further define the criterion and it should be left unchanged.
Patients with good responses of less than 12 months, possibly as short as four months, should be considered for retreatment, especially if no maintenance was used following the first treatment and/or steroids were withdrawn completely.	PTAC and the Haematology Subcommittee considered that it would be appropriate to maintain the requirement that patients would only be considered for funded rituximab retreatment if they have had a response lasting at least 12 months to prior rituximab treatment, which reflects current New Zealand practice.
The platelet threshold for rituximab treatment should be 30,000 platelets per microlitre rather than 20,000, which is in line with international guidelines.	PTAC and the Haematology Subcommittee have advised that this would be appropriate and the criteria have been amended accordingly.
<b>Rituximab for TTP</b>	
The criterion 'clinical response to plasma exchange was sub-optimal or plasma exchange is contra-indicated' is too vague.	The access criterion has been amended for clarity after consultation with the Haematology Subcommittee of PTAC.
<b>Rituximab for ANCA associated vasculitis</b>	
Rituximab should only be used if pulse intravenous cyclophosphamide has failed to achieve complete absence of disease after six months rather than three months, because cyclophosphamide often only starts to work after four months and may take up to six or nine months to achieve a complete absence of disease.	PTAC recommended that the criterion be amended to provide flexibility to clinicians to use their judgement regarding the appropriate length of cyclophosphamide treatment, and to enable those who truly have progressive, unresponsive disease to have the option of changing to rituximab. The criterion has been amended accordingly.

<p>Mycophenolate should not be used ahead of rituximab in MPO positive vasculitis as there is very weak evidence supporting mycophenolate as an induction agent in this condition. Mycophenolate is not even funded for this based on its Special Authority restriction because azathioprine is not a treatment option for induction therapy in this patient group.</p>	<p>PTAC considered it reasonable to keep this requirement noting moderate evidence of effect of mycophenolate in MPO-ANCA vasculitis compared with cyclophosphamide. The Committee recommended that this funding application for rituximab in MPO-ANCA associated vasculitis is referred to the Nephrology Subcommittee for advice and PHARMAC intends to do so.</p> <p>PHARMAC staff are currently reviewing the mycophenolate Special Authority restriction. In the meantime, clinicians can apply for mycophenolate funding for patients with MPO-ANCA vasculitis by annotating the Special Authority form with the relevant clinical information.</p>
<p>Male fertility can be affected by exposure to cyclophosphamide, and rituximab should be allowed as an alternative treatment for a man who wishes to preserve his fertility and sperm banking is unavailable, unsuccessful or unacceptable.</p>	<p>PTAC noted that cyclophosphamide is known to affect male fertility; however, in some centres sperm banking prior to cytotoxic treatment is funded. PTAC had sympathy for patients for whom sperm banking was not an option, however considered that if the criteria were amended as proposed it would be associated with significant financial risk as effectively it could result in all male patients bypassing the requirement to have tried cyclophosphamide prior to rituximab.</p>
<p>The Special Authority restriction should allow the alternative dosing regimen where rituximab 1 g is given on Day 0, again on Day 15, then a 1 g single infusion every six months for total of two years (i.e. six doses in total).</p>	<p>When consulted about this alternative dosing regimen, the New Zealand Rheumatology Association confirmed that there is emerging evidence for maintenance treatment in ANCA vasculitis, but considered that the first priority is for rituximab to be funded as an induction agent as proposed.</p>
<p><b>Rituximab for PRCA</b></p>	
<p>Rituximab is also currently used to treat PRCA and it would be restricted to PRCA considered to be autoimmune and associated with a demonstrable B-cell lymphoproliferative disorder.</p>	<p>PTAC and the Haematology Subcommittee of PTAC considered that it was reasonable that rituximab be funded for this small group. Access to rituximab has been widened to include this patient group.</p>
<p><b>Rituximab for idiopathic nephrotic syndrome</b></p>	
<p>Rituximab is also used to treat idiopathic nephrotic syndrome, including children, and the Section H listing should be widened to include this group.</p>	<p>PHARMAC is intending to seek clinical advice on the use of rituximab in this patient group from the Nephrology Subcommittee, which is in the process of being established.</p>
<p><b>Eltrombopag in ITP</b></p>	
<p>The qualifying platelet count of <math>\leq 20,000</math> platelets per microlitre cut-off is dangerously low and not in line with international consensus that ITP patients with a platelet count of <math>\leq 30,000</math> platelets per microlitre require treatment.</p>	<p>PTAC and the Haematology Subcommittee considered that this was reasonable and the criteria have been amended accordingly.</p>

## More information

If you have any questions about this decision, you can email us at [enquiry@pharmac.govt.nz](mailto:enquiry@pharmac.govt.nz) or call our toll free number (9 am to 5 pm, Monday to Friday) on 0800 66 00 50.