NOTIFICATION

PHARMAC
Pharmaceutical Management Agency

10 October 2014

Approval of Novartis multiproduct proposal

PHARMAC is pleased to announce the approval of an agreement with Novartis New Zealand Ltd involving the listing of nine new products and amendments to the listing of seven other products, details of which can be found below. This proposal was the subject of a consultation letter dated 7 August 2014 which can be found on the PHARMAC website at:

www.pharmac.health.nz/news/consultation-2014-08-07-multiproduct/

A separate notification about the related proposal for multiple sclerosis treatments, which includes the funding of fingolimod (a pharmaceutical included in this agreement with Novartis) has also been issued and this can be found at the following link:

www.pharmac.health.nz/news/notification-2014-10-10-mstreatments/

In summary, the effect of the decision is that:

From 1 November 2014 the following products will be listed on the Pharmaceutical Schedule:

- Deferasirox dispersible tablets (Exjade) for patients with chronic iron overload due to congenital inherited anaemias;
- Everolimus tablets (Afinitor) for patients with subependymal giant cell astrocytomas (SEGAs - a form of brain tumour);
- Fingolimod capsules (Gilenya) for patients with multiple sclerosis;
- Glycopyrronium powder for inhalation (Seebri Breezhaler) for patients with the respiratory condition chronic obstructive pulmonary disease (COPD);
- Indacaterol powder for inhalation (Onbrez Breezhaler) for patients with COPD;
- Nilotinib capsules (Tasigna) for patients with chronic myeloid leukaemia;
- Omalizumab injections (Xolair) for patients with severe persistent allergic asthma;
- Rivastigmine transdermal patches (Exelon) as a second-line treatment for patients with dementia;
- Tobramycin solution for inhalation (Tobi) for patients with cystic fibrosis.

There will be changes to the terms of listings for the following currently funded products:

- Zoledronic acid (Zometa)
- Zoledronic acid (Aclasta)
- Carbamazepine (Tegretol and Tegretol CR)
- Clozapine (Clozaril)
- Imatinib (Glivec)
- Methylphenidate hydrochloride (Ritalin LA) and
- Diclofenac sodium dispersible tablets (Voltaren D).

The approved agreement includes the possible future listing of indacaterol with glycopyrronium (Ultibro Breezhaler) for patients with COPD – subject to Medsafe approval, a

Level 9, 40 Mercer Street, PO Box 10-254, Wellington 6143, New Zealand
Phone: 64 4 460 4990 - Fax: 64 4 460 4995 - www.pharmac.govt.nz

recommendation to fund from PHARMAC's clinical advisors, consultation feedback and a further PHARMAC Board decision.

Amendments made as a result of consultation feedback

The price/subsidy and timings for changes for all products will be as outlined in the consultation letter, so please refer to the consultation letter for this information. For the following products:

- Deferasirox dispersible tablets (Exjade);
- Everolimus tablets (Afinitor);
- Fingolimod capsules (Gilenya);
- Omalizumab injections (Xolair); and
- Zoledronic acid (Zometa)

the restrictions will be different to those outlined in the consultation letter. The restrictions that will apply are outlined below. For the avoidance of doubt, for all other products please refer to the consultation letter for information on the restrictions that will apply.

Deferasirox (Exjade)

Following consideration of consultation feedback, the Special Authority and hospital restriction criteria for deferasirox in Section B and Part II of Section H have been amended so that patients with congenital inherited anaemias who are iron overloaded independent of blood transfusions can also access funded deferasirox.

Deferasirox will be listed in Section B of the Pharmaceutical Schedule from 1 November 2014 with the following Special Authority criteria:

> **Special Authority for Subsidy**
> **Initial application** only from a haematologist. Approvals valid for 2 years for applications meeting the following criteria:
> All of the following:
> 1. The patient has been diagnosed with chronic iron overload due to congenital inherited anaemia; and
> 2. Deferasirox is to be given at a daily dose not exceeding 40 mg/kg/day; and
> 3. Any of the following:
>   - 3.1. Treatment with maximum tolerated doses of deferiprone monotherapy or deferiprone and desferrioxamine combination therapy have proven ineffective as measured by serum ferritin levels, liver or cardiac MRI T2*; or
>   - 3.2. Treatment with deferiprone has resulted in severe persistent vomiting or diarrhoea; or
>   - 3.3. Treatment with deferiprone has resulted in arthritis; or
>   - 3.4. Treatment with deferiprone is contraindicated due to a history of agranulocytosis (defined as an absolute neutrophil count (ANC) of < 0.5 cells per µL) or recurrent episodes (greater than 2 episodes) of moderate neutropenia (ANC 0.5 - 1.0 cells per µL).
>
> **Renewal** only from a haematologist. Approvals valid for 2 years for applications meeting the following criteria:
> Either:
> 1. For the first renewal following 2 years of therapy, the treatment has been tolerated and has resulted in clinical improvement in all three parameters namely serum ferritin, cardiac MRI T2* and liver MRI T2* levels; or
> 2. For subsequent renewals, the treatment has been tolerated and has resulted in clinical stability or continued improvement in all three parameters namely serum ferritin, cardiac MRI T2* and liver MRI T2* levels.

Deferasirox will be listed in Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 with the following restriction:

Initiation
Haematologist
Re-assessment required after 2 years
All of the following:
1. The patient has been diagnosed with chronic iron overload due to congenital inherited anaemia; and
2. Deferasirox is to be given at a daily dose not exceeding 40 mg/kg/day; and
3. Any of the following:
   - 3.1. Treatment with maximum tolerated doses of deferiprone monotherapy or deferiprone and desferrioxamine combination therapy have proven ineffective as measured by serum ferritin levels, liver or cardiac MRI T2*; or
   - 3.2. Treatment with deferiprone has resulted in severe persistent vomiting or diarrhoea; or
   - 3.3. Treatment with deferiprone has resulted in arthritis; or
   - 3.4. Treatment with deferiprone is contraindicated due to a history of agranulocytosis (defined as an absolute neutrophil count (ANC) of < 0.5 cells per µL) or recurrent episodes (greater than 2 episodes) of moderate neutropenia (ANC 0.5 - 1.0 cells per µL)

Continuation
Haematologist
Re-assessment required after 2 years
Either:
1. For the first renewal following 2 years of therapy, the treatment has been tolerated and has resulted in clinical improvement in all three parameters namely serum ferritin, cardiac MRI T2* and liver MRI T2* levels; or
2. For subsequent renewals, the treatment has been tolerated and has resulted in clinical stability or continued improvement in all three parameters namely serum ferritin, cardiac MRI T2* and liver MRI T2* levels.

Amendments will also be made to the restriction criteria for the other funded oral iron chelator, deferiprone, in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 as follows (deletions in strikethrough):

Section B

Initial application only from a haematologist. Approvals valid without further renewal unless notified for applications meeting the following criteria:
Either:
1 The patient has been diagnosed with chronic ~~transfusional~~ iron overload due to congenital inherited anaemia; or
2 The patient has been diagnosed with chronic ~~transfusional~~ iron overload due to acquired red cell aplasia.

Part II of Section H

Patient has been diagnosed with chronic ~~transfusional~~ iron overload due to congenital inherited anaemia or acquired red cell aplasia.

Everolimus (Afinitor)

Following consideration of consultation feedback, the Special Authority and hospital restriction criteria for everolimus in Section B and Part II of Section H will be amended to reduce the required frequency of MRI scanning to once every 12 months, rather than once every three months.

Everolimus (Afinitor) will be listed in Section B of the Pharmaceutical Schedule from 1 November 2014 with the following Special Authority criteria:

Special Authority for Subsidy
Initial application only from a neurologist or oncologist. Approvals valid for 3 months for applications meeting the following criteria:
Both:
1. Patient has tuberous sclerosis; and
2. Patient has progressively enlarging sub-ependymal giant cell astrocytomas (SEGAs) that require treatment.

Renewal only from a neurologist or oncologist. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:
1. Documented evidence of SEGA reduction or stabilisation by MRI within the last 3 months; and
2. The treatment remains appropriate and the patient is benefiting from treatment; and
3. Everolimus to be discontinued at progression of SEGAs.

Note: MRI should be performed at minimum once every 12 months, more frequent scanning should be performed with new onset of symptoms such as headaches, visual complaints, nausea or vomiting, or increase in seizure activity.

Everolimus (Afinitor) will be listed in Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 with the following restriction:

Initiation
Neurologist or oncologist
Re-assessment required after 3 months
Both:
1. Patient has tuberous sclerosis; and
2. Patient has progressively enlarging sub-ependymal giant cell astrocytomas (SEGAs) that require treatment.

Continuation
Neurologist or oncologist
Re-assessment required after12 months
All of the following:
1. Documented evidence of SEGA reduction or stabilisation by MRI within the last 3 months; and
2. The treatment remains appropriate and the patient is benefiting from treatment; and
3. Everolimus to be discontinued at progression of SEGAs.

Note: MRI should be performed at minimum once every 12 months, more frequent scanning should be performed with new onset of symptoms such as headaches, visual complaints, nausea or vomiting, or increase in seizure activity.

Fingolimod (Gilenya)

Details of changes made to the listing of fingolimod following consultation can be found in the multiple sclerosis products notification document:

www.pharmac.health.nz/assets/notification-2014-10-10-mstreatments.pdf

Omalizumab (Xolair)

Following consideration of advice from the Respiratory Subcommittee of PTAC and review by PTAC, the renewal criteria for omalizumab have been amended to add the following criterion – 'Hospital admissions have been reduced as a result of treatment'.

Omalizumab will be listed in Section B of the Pharmaceutical Schedule from 1 November 2014 with the following Special Authority criteria:

Special Authority for Subsidy
Initial application only from a respiratory specialist. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:

1. Patient is over the age of 6; and
2. Patient has a diagnosis of severe, life threatening asthma; and
3. Past or current evidence of atopy, documented by skin prick testing or RAST; and
4. Total serum human immunoglobulin E (IgE) between 76 IU/mL and 1300 IU/ml at baseline; and
5. Proven compliance with optimal inhaled therapy including high dose inhaled corticosteroid (budesonide 1600 micrograms per day or fluticasone propionate 1000 micrograms per day or equivalent), plus long-acting beta-2 agonist therapy (at least salmeterol 50 micrograms bd or eformoterol 12 micrograms bd) for at least 12 months, unless contraindicated or not tolerated; and
6. Patient has received courses of systemic corticosteroids equivalent to at least 28 days treatment in the past 12 months, unless contraindicated or not tolerated; and
7. At least four admissions to hospital for a severe asthma exacerbation over the previous 24 months with at least one of those being in the previous 12 months; and
8. An Asthma Control Questionnaire (ACQ-5) score of at least 3.0 as assessed in the previous month

Renewal only from a respiratory specialist. Approvals valid for 2 years for applications meeting the following criteria:
All of the following:

1. Hospital admissions have been reduced as a result of treatment; and
2. A reduction in the Asthma Control Questionnaire (ACQ-5) score of at least 1.0 from baseline; and
3. A reduction in the maintenance oral corticosteroid dose of at least 50% from baseline

Omalizumab will be listed in Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 with the following restriction:

Initiation
Respiratory specialist
Re-assessment required after 6 months
All of the following:

1. Patient is over the age of 6; and
2. Patient has a diagnosis of severe, life threatening asthma; and
3. Past or current evidence of atopy, documented by skin prick testing or RAST; and
4. Total serum human immunoglobulin E (IgE) between 76 IU/mL and 1300 IU/ml at baseline; and
5. Proven compliance with optimal inhaled therapy including high dose inhaled corticosteroid (budesonide 1600 micrograms per day or fluticasone propionate 1000 micrograms per day or equivalent), plus long-acting beta-2 agonist therapy (at least salmeterol 50 micrograms bd or eformoterol 12 micrograms bd) for at least 12 months, unless contraindicated or not tolerated; and
6. Patient has received courses of systemic corticosteroids equivalent to at least 28 days treatment in the past 12 months, unless contraindicated or not tolerated; and
7. At least four admissions to hospital for a severe asthma exacerbation over the previous 24 months with at least one of those being in the previous 12 months; and
8. An Asthma Control Questionnaire (ACQ-5) score of at least 3.0 as assessed in the previous month

Continuation
Respiratory specialist
Re-assessment required after 6 months
All of the following:

1. Hospital admissions have been reduced as a result of treatment; and
2. A reduction in the Asthma Control Questionnaire (ACQ-5) score of at least 1.0 from baseline; and
3. A reduction in the maintenance oral corticosteroid dose of at least 50% from baseline.

Zoledronic acid (Zometa)

Following consideration of consultation feedback, the Special Authority and hospital restriction criteria for zoledronic acid (Zometa) in Section B and Part II of Section H have been amended to allow applications from haematologists in addition to oncologists and palliative care specialists. The criteria have also been amended to clarify the intent in relation to the inclusion of patients with bone involvement in haematological malignancies, not just patients with bone metastases. Zoledronic acid (Zometa) will be listed in Section B of the Pharmaceutical Schedule from 1 February 2015 as follows:

Special Authority for Subsidy
Initial application only from an oncologist, haematologist or palliative care specialist. Approvals valid without further renewal for applications meeting the following criteria:
Any of the following:
1. Patient has hypercalcaemia of malignancy; or
2. Both:
   2.1. Patient has bone metastases or involvement; and
   2.2. Patient has severe bone pain resistant to standard first-line treatments; or
3 Both:
   3.1. Patient has bone metastases or involvement; and
   3.2. Patient is at risk of skeletal-related events (pathological fracture, spinal cord compression, radiation to bone or surgery to bone)

The restriction currently applying to the listing of zoledronic acid (Zometa) in Part II of Section H of the Pharmaceutical Schedule will be amended from 1 February 2015 as follows (additions in bold, deletions in strikethrough):

Restricted
~~For hypercalcaemia of malignancy~~

Oncologist, haematologist or palliative care specialist
Any of the following:
1. **Patient has hypercalcaemia of malignancy; or**
2. **Both:**
   2.1. Patient has bone metastases or involvement; and
   2.2. Patient has severe bone pain resistant to standard first-line treatments; or
3. **Both:**
   3.1. Patient has bone metastases or involvement; and
   3.2. Patient is at risk of skeletal-related events (pathological fracture, spinal cord compression, radiation to bone or surgery to bone)

Feedback received

We appreciate all of the feedback that we received and acknowledge the time people took to respond. The responses received in relation to fingolimod are detailed in a separate notification document which can be found at:

www.pharmac.health.nz/assets/notification-2014-10-10-mstreatments.pdf

All consultation responses received by 29 August 2014 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 specific aspects of the proposal:

Pharmaceutical/theme	Comment
Deferasirox	

Pharmaceutical/theme	Comment
Funding of deferiprone and deferasirox sought for patients with congenital anaemia and iron overload independent of blood transfusions. These are mainly patients with thalassaemia intermedia.	We have amended the funding restrictions as suggested following feedback from our clinical advisors that it would be appropriate.
Everolimus	
The Special Authority for funding criteria be amended so that renewal is for 12 months rather than three, with MRI scanning extended to 12 monthly.	The proposed Special Authority criteria have been amended as suggested. Although PTAC recommended more frequent MRI and renewals (three-monthly) to mitigate the risk of ongoing expensive treatment despite disease progression, on balance we consider that frequent MRIs in this patient population would be difficult and costly for DHBs and such frequency is not in line with standard practice. We consider that the addition of the criteria "Everolimus to be discontinued at progression of SEGAs." and a note "MRI should be performed at minimum once every 12 months, more frequent scanning should be performed with new onset of symptoms such as headaches, visual complaints, nausea or vomiting, or increase in seizure activity." would mitigate the risk of patients continuing treatment for the whole approved 12 month renewal period where it is clear they have disease progression with their SEGAs.
Glycopyrronium	
The Special Authority criteria allow patients to switch between tiotropium and glycopyrronium without re-applying under the Special Authority. A concern was raised that there were differences between the two products and that there is no benefit in switching a patient stable on tiotropium to glycopyrronium.	The intent of the same Special Authority criteria applying to both medicines is to enable those patients not responding well to one or other of the medicines to be able to be prescribed the other without needing another Special Authority approval. Patients would have to be reviewed by their clinician and a new prescription would have to be written for the new treatment. We don't expect that patients stabilised on a particular treatment would be switched to another.
We received commentary suggesting that the Respiratory Subcommittee should review new inhaler listings and comments that Breezhaler is a difficult device to use.	New products are reviewed by PTAC and PHARMAC or PTAC can refer the application to Subcommittees if it is considered that more specialised advice is required. Patients and prescribers have a choice of products to use in the treatment of COPD. The suitability of different inhaler devices would be one of the aspects of treatment taken into consideration when making that choice.
A request was received asking that PHARMAC consider that nurse practitioners be allowed to prescribe.	Application for subsidy via the Special Authority must be applied for by a general practitioner or relevant specialist. Once a Special Authority application has been approved it is valid for two years and it would apply to any prescription written for the relevant patient by any authorised prescriber. Therefore nurse practitioners could prescribe funded glycopyrronium (providing it is in the nurse's scope of practice) where a valid Special Authority is in place.

Pharmaceutical/theme	Comment
A request was received asking that the Modified Medical Research Council (MMRC) grade 4 or 5 be removed from the SA criteria relating to LAMAs and replaced with either an MMRC grade of ≥ 2 or with a CAT score of > 10.	PHARMAC intends to review the Special Authority criteria in the near future.
Omalizumab	
A comment was received that the renewal Special Authority criteria did not allow for discontinuation of treatment in someone who comes under control. It was suggested that a mandatory discontinuation after one year of treatment be required, with retreatment criteria developed to enable the patient to resume treatment if control was lost after discontinuation.	We note that if clinicians want to try stopping and restarting treatment later, this can be managed through the Special Authority waiver mechanism. The Special Authority criteria will be reviewed within the next two years with consideration given to whether such a criterion might be required.
Zoledronic acid (Zometa)	
A request was received asking that PHARMAC consider haematologists be added to the list of applicants for Special Authority and hospital restriction as they are significant prescribers of bisphosphonates. The responder suggested changing criteria 'patient has bone metastases' to, 'patient has bone metastases or involvement' as they consider that the term 'metastases' is not used in relation to myeloma, lymphoma or leukaemias.	We agree, and have made these changes to the Special Authority criteria.
MULTIPLE PRODUCTS	
The Pharmacy Guild requested that the Wastage Rule be applied to the listing of deferasirox, everolimus, nilotinib, fingolimod and tobramycin solution for inhalation because they are high cost treatments and there is a risk that community pharmacy could be left with part packs.	The Wastage Rule has been applied to the listing of these products.

More information

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