CONSULTATION

PHARMAC
Pharmaceutical Management Agency

**7 August 2014**

# Novartis multiproduct proposal

PHARMAC is seeking feedback on a proposal involving 17 products, resulting from a provisional agreement with Novartis New Zealand Limited. The proposal includes the funding of new products and changes relating to other currently funded products.

A separate consultation is also underway involving fingolimod (which is included in the provisional agreement to which this consultation relates) and other multiple sclerosis treatments. For details on that proposal go to the PHARMAC website:

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

## New listings

The proposal would result in the following new treatments being listed on the Pharmaceutical Schedule from 1 November 2014:

- deferasirox (Exjade) for patients with chronic transfusional iron overload due to congenital inherited anaemias;
- everolimus (Afinitor) for patients with subependymal giant cell astrocytomas (a form of brain tumour);
- fingolimod (Gilenya) for patients with multiple sclerosis;
- glycopyrronium (Seebri Breezhaler) for patients with the respiratory condition chronic obstructive pulmonary disease (COPD);
- indacaterol (Onbrez Breezhaler) for patients with COPD;
- nilotinib (Tasigna) for patients with chronic myeloid leukaemia;
- omalizumab (Xolair) for patients with severe persistent allergic asthma;
- tobramycin solution for inhalation (Tobi) for patients with cystic fibrosis;
- rivastigmine transdermal patches (Exelon) as a second-line treatment for patients with dementia;
- a possible future listing of indacaterol with glycopyrronium (Ultibro Breezhaler) for patients with COPD - subject to Medsafe approval and recommendation to fund from PHARMAC's clinical advisors.

## Amendments to terms of listings for currently listed products:

The proposal would also result in amendments to the terms of listings, including widening of access in some cases, for the following products currently listed on the Pharmaceutical Schedule:

- 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).



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Further details of this proposal, including how to provide feedback and background information can be found on the following pages.



**Feedback sought**

PHARMAC welcomes feedback on this proposal. **Please specify in your response which product(s) your feedback relates to.** To provide feedback, please submit it in writing by **5pm Friday, 29 August 2014** to:


Sue Anne Yee
Senior Therapeutic Group Manager
PHARMAC
PO Box 10 254
Wellington 6143

Email: multiproduct@pharmac.govt.nz

Fax: 04 460 4995


All feedback received before the closing date will be considered by PHARMAC's Board (or its delegate) prior to making a decision on this proposal.

Feedback we receive is subject to the Official Information Act 1982 (OIA) and we will consider any request to have information withheld in accordance with our obligations under the OIA. Anyone providing feedback, whether on their own account or on behalf of an organisation, and whether in a personal or professional capacity, should be aware that the content of their feedback and their identity may need to be disclosed in response to an OIA request.

We are not able to treat any part of your feedback as confidential unless you specifically request that we do, and then only to the extent permissible under the OIA and other relevant laws and requirements. If you would like us to withhold any commercially sensitive,

confidential proprietary, or personal information included in your submission, please clearly state this in your submission and identify the relevant sections of your submission that you would like it withheld. PHARMAC will give due consideration to any such request.

## Part 1: Proposed new listings

### Deferasirox (Exjade)

PHARMAC is proposing to list deferasirox (Exjade) on the Pharmaceutical Schedule for patients with chronic transfusional iron overload due to congenital inherited anaemias.

- Deferasirox (Exjade) would be listed in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 at the following prices and subsidies (ex-manufacturer and excluding GST):

| Chemical | Presentation | Brand | Strength | Pack size | Price and subsidy |
|---|---|---|---|---|---|
| Deferasirox | Tablet | Exjade | 125 mg | 28 | $276.00 |
| Deferasirox | Tablet | Exjade | 250 mg | 28 | $552.00 |
| Deferasirox | Tablet | Exjade | 500 mg | 28 | $1,105.00 |

- A confidential rebate would apply to Exjade which would reduce the net price of the treatment.

- Exjade would have subsidy and delisting protection until 31 October 2017.

- Deferasirox would be listed subject to the following restrictions in Section B and Part II of Section H of the Pharmaceutical Schedule:

**Section B**

**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 transfusional 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.

## Part II of Section H

**Initiation**
Haematologist
Re-assessment required after 2 years
All of the following:

1. The patient has been diagnosed with chronic transfusional 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.

### *About deferasirox*

Deferasirox is an oral iron chelator (binder) used to remove excess iron from the body.

The listing of deferasirox for patients with iron overload due to congenital inherited anaemias would provide another treatment option for patients who have not responded to an alternative funded oral iron chelator, deferiprone, or who cannot take deferiprone due to contraindication or intolerance.

PTAC and the Cancer Treatments Subcommittee of PTAC (CaTSoP) have reviewed deferasirox on a number of occasions. Most recently, at its April 2011 review, CaTSoP recommended that deferasirox be funded with high priority for patients with chronic transfusional iron overload due to congenital inherited anaemia who have not responded to deferiprone therapy and for patients who are intolerant or contraindicated to deferiprone. PTAC recommended a small amendment to the funding criteria proposed by CaTSoP but otherwise accepted CaTSoP's recommendation.

The minutes for the relevant reviews can be found on the PHARMAC website through the following links:

- www.pharmac.govt.nz/2011/11/04/April%20CaTSoP%20Subcommittee%20web%20minutes.pdf
- www.pharmac.health.nz/assets/ptac-minutes-2011-08.pdf

**Everolimus (Afinitor)**

PHARMAC is proposing to list everolimus (Afinitor) on the Pharmaceutical Schedule for patients with subependymal giant cell astrocytomas.

- Everolimus (Afinitor) would be listed in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 at the following prices and subsidies (ex-manufacturer, excluding GST):

| Chemical | Presentation | Brand | Strength | Pack size | Price and subsidy |
|---|---|---|---|---|---|
| Everolimus | Tablet | Afinitor | 5 mg | 30 | $4,555.76 |
| Everolimus | Tablet | Afinitor | 10 mg | 30 | $6,512.29 |

- A confidential rebate would apply to Afinitor which would reduce the net price of the treatment.

- Afinitor would have subsidy and delisting protection until 31 October 2017.

- Everolimus would be listed subject to the following restrictions in Section B and Part II of Section H of the Pharmaceutical Schedule:

### Section B

**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 3 months for applications meeting the following criteria:
Both:
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.

### Part II of Section H

**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 after 3 months
Both:
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.

***About everolimus***

Everolimus is approved by Medsafe for the treatment of patients aged 3 years and older with sub-ependymal giant cell astrocytomas (SEGAs), a form of brain tumour, associated with tuberous sclerosis complex (TSC) who require therapeutic intervention but are not amenable to surgery.

The listing of everolimus would provide a non-invasive treatment option for patients with progressively enlarging SEGAs.

PTAC and its Cancer Treatments Subcommittee (CaTSoP) and the Neurological Subcommittee of PTAC have each reviewed everolimus for treatment of SEGAs. In May 2014 PTAC accepted the Neurological Subcommittee's November 2013 recommendation to fund everolimus for tuberous sclerosis patients with progressively enlarging SEGAs requiring treatment, with high priority.

The minutes for the relevant reviews can be found on the PHARMAC website through the following link:

- http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=753

**Fingolimod (Gilenya)**

PHARMAC is proposing to list fingolimod (Gilenya) on the Pharmaceutical Schedule for patients with relapsing-remitting multiple sclerosis.

- Fingolimod (Gilenya) would be listed in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 at the following price and subsidy (ex-manufacturer, excluding GST):

| Chemical | Presentation | Brand | Strength | Pack size | Price and subsidy |
|---|---|---|---|---|---|
| Fingolimod | Capsule | Gilenya | 0.5 mg | 28 | $2,650.00 |

- A confidential rebate would apply to Gilenya which would reduce the net price of the treatment.

- Gilenya would have subsidy and delisting protection until 31 October 2017.

- Fingolimod would be listed subject to access criteria in Section B and Part II of Section H of the Pharmaceutical Schedule:

**Further background information**

PHARMAC is also consulting on a separate proposal to:

- list another new MS treatment, natalizumab (Tysabri) on the Pharmaceutical Schedule; and

- amend funding restrictions for the currently listed MS treatments:
    - interferon-1-alpha (Avonex);
    - interferon beta-1-beta (Betaferon); and
    - glatiramer acetate (Copaxone).

For further detail on the overall proposal involving MS treatments, including the proposed access criteria that would apply to all five MS treatments including fingolimod, please refer to the MS treatments proposal consultation which can be found on our website at:

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

**Glycopyrronium (Seebri Breezhaler), indacaterol (Onbrez Breezhaler) and indacaterol with glycopyrronium (Ultibro Breezhaler)**

PHARMAC is proposing to list the following chronic obstructive pulmonary disease (COPD) treatments on the Pharmaceutical Schedule:

- Glycopyrronium (Seebri Breezhaler);
- Indacaterol (Onbrez Breezhaler); and
- a possible future listing of indacaterol with glycopyrronium (Ultibro Breezhaler) for patients with COPD - subject to Medsafe approval, recommendation to fund from PHARMAC's clinical advisors, consultation and PHARMAC approval.

We are also proposing to make a new sub-heading in the Respiratory and Allergies therapeutic group which would include tiotropium (Spiriva) and glycopyrronium.

**Details of the proposal**

- Glycopyrronium (Seebri Breezhaler) and indacaterol (Onbrez Breezhaler) would be listed in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 at the following prices and subsidies (ex- manufacturer; ex GST):

| Chemical | Presentation | Brand | Strength | Pack size | Price and subsidy |
|---|---|---|---|---|---|
| Glycopyrronium | Powder for inhalation | Seebri Breezhaler | 50 mcg | 30 dose OP | $61.00 |
| Indacaterol | Powder for inhalation | Onbrez Breezhaler | 150 mcg | 30 dose OP | $61.00 |
| Indacaterol | Powder for inhalation | Onbrez Breezhaler | 300 mcg | 30 dose OP | $61.00 |

- Confidential rebates would apply to Seebri Breezhaler and Onbrez Breezhaler which would reduce the net prices of the treatments.
- Seebri Breezhaler and Onbrez Breezhaler would have subsidy and delisting protection until 31 October 2017.
- A new heading 'Long-Acting Muscarinic Antagonists' would be added under the current subgroup 'Inhaled Anticholinergic Agents' in the Respiratory System and Allergies therapeutic group in Section B, and Part II of Section H, of the Pharmaceutical Schedule.
- Seebri Breezhaler and Spiriva would be listed under the Long-Acting Muscarinic Antagonists heading and would be listed subject to the following restrictions (which are the current restriction applying to Spiriva) which would sit at the Long-Acting Muscarinic Antagonists heading level in Section B and Part II of Section H of the Pharmaceutical Schedule (i.e. the restrictions would apply to both Seebri Breezhaler and Spiriva):

  **Section B**

  **Special Authority for Subsidy**

**Initial application** from a general practitioner or relevant specialist. Approvals valid for 2 years for applications meeting the following criteria:
All of the following:

1 To be used for the long-term maintenance treatment of bronchospasm and dyspnoea associated with COPD; and
2 In addition to standard treatment, the patient has trialled a short acting bronchodilator dose of at least 40 µg ipratropium q.i.d for one month; and
3 Either:
The patient's breathlessness according to the Medical Research Council (UK) dyspnoea scale is:
3.1 Grade 4 (stops for breath after walking about 100 meters or after a few minutes on the level); or
3.2 Grade 5 (too breathless to leave the house, or breathless when dressing or undressing); and

Applicant must state recent measurement of:

4 All of the following:
4.1 Actual $FEV_1$ (litres); and
4.2 Predicted $FEV_1$ (litres); and
4.3 Actual $FEV_1$ as a % of predicted (must be below 60%); and
5 Either:
5.1 Patient is not a smoker (for reporting purposes only); or
5.2 Patient is a smoker and has been offered smoking cessation counselling; and
6 The patient has been offered annual influenza immunization;

**Renewal only** from a general practitioner or relevant specialist. Approvals valid for 2 years for applications meeting the following criteria:
All of the following:

1 Patient is compliant with the medication; and
2 Patient has experienced improved COPD symptom control (prescriber determined); and

Applicant must state recent measurement of:

3 All of the following:
3.1 Actual $FEV_1$ (litres); and
3.2 Predicted $FEV_1$ (litres); and
3.3 Actual $FEV_1$ as a % of predicted.

## Part II of Section H

**Initiation**
All of the following:

1 To be used for the long-term maintenance treatment of bronchospasm and dyspnoea associated with COPD; and
2 In addition to standard treatment, the patient has trialled a short acting bronchodilator dose of at least 40 µg ipratropium q.i.d for one month; and
3 Either:
The patient's breathlessness according to the Medical Research Council (UK) dyspnoea scale is:
3.1 Grade 4 (stops for breath after walking about 100 meters or after a few minutes on the level); or
3.2 Grade 5 (too breathless to leave the house, or breathless when dressing or undressing); and

4 Actual $FEV_1$ as a % of predicted, must be below 60%
5 Either:
5.1 Patient is not a smoker (for reporting purposes only); or
5.2 Patient is a smoker and has been offered smoking cessation counselling; and
6 The patient has been offered annual influenza immunization; and

- The following note would be added to the listing of Spiriva (tiotropium bromide, powder for inhalation, 18 mcg per dose) in Section B of the Pharmaceutical Schedule.

Note: tiotropium treatment will not be subsidised if patient is also receiving treatment with subsidised glycopyrronium

- The following note would be added to the listing of Spiriva (tiotropium bromide, powder for inhalation, 18 mcg per dose) in Part II of Section H of the Pharmaceutical Schedule.

  > Note: tiotropium treatment must not be used if the patient is also receiving treatment with subsidised glycopyrronium

- The following note would be added to the listing of Seebri Breezhaler in Section B of the Pharmaceutical Schedule:

  > Note: glycopyrronium treatment will not be subsidised if patient is also receiving treatment with subsidised tiotropium

- The following note would be added to the listing of Seebri Breezhaler in Part II of Section H of the Pharmaceutical Schedule:

  > Note: glycopyrronium treatment must not be used if the patient is also receiving treatment with subsidised tiotropium

- Indacaterol with glycopyrronium (Ultibro Breezhaler) would be listed in Section B and Part II of Section H of the Pharmaceutical Schedule provided it becomes Medsafe registered and it receives a positive funding recommendation from PTAC. We would likely consult again prior to listing Ultibro Breezhaler on the Pharmaceutical Schedule, particularly with respect to any Special Authority criteria that may apply or be amended. If listed, Ultibro Breezhaler would be listed at a price (ex GST) and subsidy of $110.00 per 30 capsules containing indacaterol 100 mcg with glycopyrronium 50 mcg powder for inhalation. A confidential rebate would apply to Ultibro Breezhaler which would reduce its net price.

- Access to Spiriva remains the same under this proposal and the proposal would have no effect on the Special Authority numbers currently applying to Spiriva patients.

***About indacaterol and glycopyrronium***

Indacaterol is a long acting inhaled beta-adrenoceptor agonist registered for long term, once-daily, maintenance bronchodilator treatment of airflow limitation in patients with chronic obstructive pulmonary disease ($FEV_1$ ≥30% to ≤80% of predicted values).

PTAC discussed indacaterol at its February 2012 meeting and recommended that indacaterol be listed on the Pharmaceutical Schedule only at a price that is cost neutral to a long acting beta-adrenoceptor agonist (LABA).

Glycopyrronium is a once a day inhalation Long-Acting Muscarinic Antagonist (LAMA) registered as a once-daily maintenance bronchodilator treatment to relieve symptoms of patients with chronic obstructive pulmonary disease.

PTAC discussed glycopyrronium at its February 2014 meeting and recommended glycopyrronium be listed on the Pharmaceutical Schedule under the same Special Authority criteria as tiotropium and only if it is cost-neutral to tiotropium.

Under this proposal, the Special Authority criteria for glycopyrronium is the same as that applying to tiotropium and would allow for patients to switch between the two products

without re-applying under the initial criteria but does not allow for patients to be co-prescribed the two products.

The indacaterol/glycopyrronium combination product (Ultibro Breezhaler) would only be listed on the Pharmaceutical Schedule following Medsafe registration and a positive recommendation from PTAC (low, medium or high) and under any Special Authority criteria recommended by PTAC.

The minutes for the relevant reviews can be found on the PHARMAC website through the following links:

- http://www.pharmac.health.nz/assets/ptac-minutes-2012-02.pdf
- http://www.pharmac.health.nz/assets/ptac-minutes-2014-02.pdf

**Nilotinib (Tasigna)**

PHARMAC is proposing to list nilotinib (Tasigna) on the Pharmaceutical Schedule for patients with chronic myeloid leukaemia.

- Nilotinib (Tasigna) would be listed in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 at the following prices and subsidies (ex-manufacturer, excluding GST):

| Chemical | Presentation | Brand | Strength | Pack size | Price and subsidy |
|---|---|---|---|---|---|
| Nilotinib | Capsule | Tasigna | 150 mg | 120 | $4,680.00 |
| Nilotinib | Capsule | Tasigna | 200 mg | 120 | $6,532.00 |

- A confidential rebate would apply to Tasigna which would reduce the net price of the treatment.

- Tasigna would have subsidy and delisting protection until 31 October 2017.

- Nilotinib would be listed subject to the following restrictions in Section B and Part II of Section H of the Pharmaceutical Schedule:

### Section B

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

1. Patient has a diagnosis of chronic myeloid leukaemia (CML) in blast crisis, accelerated phase, or in chronic phase; and
2. Either:
   2.1. Patient has documented CML treatment failure* with imatinib; or
   2.2. Patient has experienced treatment limiting toxicity with imatinib precluding further treatment with imatinib; and
3. Maximum nilotinib dose of 800 mg/day; and
4. Subsidised for use as monotherapy only.

Notes: *treatment failure as defined by Leukaemia Net Guidelines.

**Renewal** only from a haematologist. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:

1. Lack of treatment failure while on nilotinib as defined by Leukaemia Net Guidelines; and
2. Nilotinib treatment remains appropriate and the patient is benefiting from treatment; and
3. Maximum nilotinib dose of 800 mg/day; and
4. Subsidised for use as monotherapy only.

### Part II of Section H

**Initiation**
Haematologist
Re-assessment required after 6 months
All of the following:

1. Patient has a diagnosis of chronic myeloid leukaemia (CML) in blast crisis, accelerated phase, or in chronic phase; and

2. Either:
   2.1. Patient has documented CML treatment failure* with imatinib; or
   2.2. Patient has experienced treatment limiting toxicity with imatinib precluding further treatment with imatinib; and
3. Maximum nilotinib dose of 800 mg/day; and
4. Subsidised for use as monotherapy only.

Notes: *treatment failure as defined by Leukaemia Net Guidelines.

**Continuation**
Haematologist
Re-assessment required after 6 months
All of the following:

1. Lack of treatment failure while on nilotinib as defined by Leukaemia Net Guidelines; and
2. Nilotinib treatment remains appropriate and the patient is benefiting from treatment; and
3. Maximum nilotinib dose of 800 mg/day; and
4. Subsidised for use as monotherapy only.

- Tasigna when used in the community would be distributed under a direct-to-patient mechanism, which would be managed by PHARMAC and funded by Novartis.

***About nilotinib***

Nilotinib is an oral tyrosine kinase inhibitor, selective for the oncogene BCR-ABL. Nilotinib is indicated for:

- treatment of adult patients with newly diagnosed chronic phase Philadelphia chromosome positive (Ph +) chronic myeloid leukaemia (CML), and
- treatment of chronic and accelerated phase Ph + CML in adult patients resistant to or intolerant to at least one prior therapy including imatinib.

Currently, two other tyrosine kinase inhibitors are funded for patients with CML, imatinib mesylate (Imatinib-AFT) and dasatinib (Sprycel). Imatinib-AFT is funded without restriction, whereas dasatinib is funded under Special Authority for patients with CML up to a maximum dose of 100 mg/day for patients with chronic phase CML or up to 140 mg/day for accelerated or blast phase CML. The funding of nilotinib as proposed would provide another treatment option for patients who are unable to tolerate imatinib or whose CML disease develops imatinib-resistant mutations.

PTAC and its Cancer Treatments Subcommittee (CaTSoP) have reviewed the funding of nilotinib on a number of occasions. Most recently, at its October 2012 meeting, CaTSoP recommended that nilotinib be funded with high priority for patients intolerant to, or with CML disease resistant to, imatinib or dasatinib. In May 2013 PTAC considered that there would be a significant fiscal risk with funding nilotinib as recommended by CaTSoP given the subjective nature of 'intolerance' criterion. PTAC recommended decline of the application for funding nilotinib on the Pharmaceutical Schedule and considered that it would be more appropriate to assess these patients on a case-by-case basis through the NPPA scheme.

Since March 2013 a total of 12 patients have accessed funded nilotinib through application under the Named Patient Pharmaceutical Assessment (NPPA) Policyat full price. This proposal would be cost saving for these patients and we consider that the proposed net pricing manages the financial risk identified by PTAC as the barrier to Schedule listing.

The minutes for the relevant reviews can be found on the PHARMAC website through the following links:

- http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=478
- http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=189

**Omalizumab (Xolair)**

PHARMAC is proposing to list omalizumab (Xolair) on the Pharmaceutical Schedule for patients with severe persistent allergic asthma.

- Omalizumab (Xolair) would be listed in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 at the following prices (ex GST) and subsidies (ex-manufacturer, excluding GST):

| Chemical | Presentation | Brand | Strength | Pack size | Price and subsidy |
|---|---|---|---|---|---|
| Omalizumab | Injection | Xolair | 150mg | 1 | $500.00 |

- A confidential rebate would apply to Xolair which would reduce the net price of the treatment.

- Xolair would have subsidy and delisting protection until 31 October 2017.

- Omalizumab would be listed subject to the following restrictions in Section B and Part II of Section H of the Pharmaceutical Schedule:

## Section B

**Special Authority for Subsidy**
**Initial application** only from a respiratory physician. 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 physician. Approvals valid for 2 years for applications meeting the following criteria:
Both

1. A reduction in the Asthma Control Questionnaire (ACQ-5) score of at least 1.0 from baseline; and
2. A reduction in the maintenance oral corticosteroid dose of at least 50% from baseline.

## Part II of Section H

**Initiation**
Respiratory physician
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 physician
Re-assessment required after 6 months
Both:
1. A reduction in the Asthma Control Questionnaire (ACQ-5) score of at least 1.0 from baseline; and
2. A reduction in the maintenance oral corticosteroid dose of at least 50% from baseline.

***About omalizumab***

Omalizumab is a humanised monoclonal antibody indicated for the reduction of asthma exacerbations and control of asthma symptoms when given as add on therapy for patients with severe persistent allergic asthma who have an IgE level ≥ 30 IU/mL and a positive test to a perennial aeroallergen that is uncontrolled by current treatments.

Omalizumab is administered by a subcutaneous injection.

PTAC and its Respiratory Subcommittee have reviewed omalizumab on a number of occasions most recently at their meetings on the 8th November 2013 and 24th May 2013 respectively. The recommendation has been that omalizumab be listed on the Pharmaceutical Schedule with a medium priority. PTAC recommended that PHARMAC develop Special Authority criteria with strict entry and exit criteria and the facility for a trial of treatment.

The criteria proposed for omalizumab in this consultation are those recommend by the Respiratory Subcommittee in April 2014 at its meeting in April 2014. The minutes of this meeting have not yet been reviewed by PTAC; they will be reviewed at its August meeting, The Application Tracker for omalizumab will be updated as soon as possible after PTAC's meeting.

The minutes for the relevant reviews can be found on the PHARMAC website through the following links:

- http://www.pharmac.health.nz/assets/ptac-respiratory-subcommittee-minutes-2013-05-24.pdf

- http://www.pharmac.health.nz/assets/ptac-minutes-2013-11.pdf

**Tobramycin solution for inhalation (Tobi)**

PHARMAC is proposing to list tobramycin solution for inhalation (Tobi) on the Pharmaceutical Schedule for patients with cystic fibrosis.

- Tobramycin (Tobi) would be listed in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 at the following prices and subsidies (ex-manufacturer, excluding GST):

| Chemical | Presentation | Brand | Strength | Pack size | Price and subsidy |
|---|---|---|---|---|---|
| Tobramycin | Solution for inhalation | Tobi | 60 mg per ml, 5ml | 56 | $2,200.00 |

- A confidential rebate would apply to Tobi which would reduce the net price of the treatment.
- Tobi would have subsidy and delisting protection until 31 October 2017.
- Tobramycin solution for inhalation would be listed subject to the following restrictions in Section B and Part II of Section H of the Pharmaceutical Schedule:

**Section B**

> **Subsidy by endorsement**
> Subsidised only if prescribed for a cystic fibrosis patient and the prescription is endorsed accordingly.

**Part II of Section H**

> **Restricted**
> Patient has cystic fibrosis.

***About tobramycin***

Tobramycin is an aminoglycoside antibiotic produced by *Streptomyces tenebrarius*. It acts primarily by disrupting protein synthesis, leading to altered cell membrane permeability, progressive disruption of the cell envelope, and eventual cell death.

Tobi is a tobramycin solution for inhalation indicated for the management of cystic fibrosis patients with *P. aeruginosa* infection. Each single-use 5 mL ampule contains 300 mg tobramycin and 11.25 mg sodium chloride in sterile water for injection.

Currently IV tobramycin is listed on the Pharmaceutical Schedule for patients meeting the following criteria:

> Subsidised only if prescribed for dialysis or cystic fibrosis patient and the prescription is endorsed accordingly

IV tobramycin is not indicated for nebulisation so clinicians are currently prescribing this product for nebulization under Section 25 of the Medicines Act 1984.

The Respiratory Subcommittee reviewed Tobi at its 30 April 2014 meeting. The minutes from this meeting have not been reviewed by PTAC and are not published yet, but the

Application Tracker for tobramycin will be updated as soon as the minutes are available. PHARMAC have also sought advice from Cystic Fibrosis specialists who gave advice about the appropriate therapeutic levels of tobramycin to treat this indication. This proposal aligns with their advice.

## Rivastigmine transdermal patches (Exelon)

PHARMAC is proposing to list rivastigmine transdermal patches (Exelon) on the Pharmaceutical Schedule as a second-line treatment for patients with dementia.

- Rivastigmine transdermal patches (Exelon) would be listed in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 November 2014 at the following prices and subsidies (ex-manufacturer, excluding GST):

| Chemical | Presentation | Brand | Strength | Pack size | Price and subsidy |
|---|---|---|---|---|---|
| Rivastigmine | Transdermal patch | Exelon | 4.6 mg per 24 hour | 30 | $90.00 |
| Rivastigmine | Transdermal patch | Exelon | 9.5 mg per 24 hour | 30 | $90.00 |

- A confidential rebate would apply to Exelon which would reduce the net price of the treatment.

- Exelon would have subsidy and delisting protection until 31 October 2017.

- Rivastigmine transdermal patches would be listed subject to the following restrictions in Section B and Part II of Section H of the Pharmaceutical Schedule:

### Section B

**Special Authority for Subsidy**
**Initial application** from any relevant practitioner. Applications valid for 6 months for applications meeting the following criteria:
Both:
1 The patient has been diagnosed with dementia; and
2 The patient has experienced intolerable nausea and/or vomiting from donepezil tablets.

**Renewal** from any relevant practitioner. Applications valid for 12 months for applications meeting the following criteria:
Both:
1 The treatment remains appropriate; and
2 The patient has demonstrated a significant and sustained benefit from treatment.

### Part II of Section H

**Initiation**
Re-assessment required after 6 months
Both:
1 The patient has been diagnosed with dementia; and
2 The patient has experienced intolerable nausea and/or vomiting from donepezil tablets.

**Continuation**
Re-assessment required after 12 months
Both:
1 The treatment remains appropriate; and
2 The patient has demonstrated a significant and sustained benefit from treatment.

***About rivastigmine***

Rivastigmine is an acetylcholinesterase inhibitor used to treat dementia. It is available in capsule and patch form. Rivastigmine patches are registered in New Zealand for the treatment of mild, moderate and severe dementia of the Alzheimer's type (also termed Alzheimer's disease).

Other medicines in the same therapeutic class as rivastigmine include donepezil, which is funded without restrictions, and galantamine, which is not currently funded. Our clinical advice has been that the three treatments provide broadly similar efficacy.

PTAC has advised that approximately 20% of patients are unable to tolerate the gastrointestinal side effects of donepezil tablets and that this can lead to treatment discontinuation. The Committee noted that patients who are unable to tolerate therapeutic doses of donepezil tablets are unlikely to be able to tolerate any acetylcholinesterase inhibitor taken orally. The Committee considered that there was an unmet clinical need for a different presentation of an acetylcholinesterase inhibitor in these patients and, therefore, recommended that rivastigmine patches be funded subject to the funding criteria outlined in this proposal, with a low priority.

PHARMAC has also received a funding application for rivastigmine capsules, which PTAC has recommended funding only if they were no more expensive than donepezil. Although we are not proposing to fund rivastigmine capsules at this time, this is something we could consider if we were to receive an acceptable commercial proposal or the clinical advice changed.

The minutes for the relevant reviews, and details of the funding applications for rivastigmine, can be found on the PHARMAC website at the following links:

- www.pharmac.govt.nz/ApplicationTracker?ProposalId=180
- www.pharmac.govt.nz/ApplicationTracker?ProposalId=374

## Part 2: Proposed amendments to existing listings

### Zoledronic Acid (Zometa)

PHARMAC is proposing to amend the listing of zoledronic acid 0.8 mg per ml, 5 ml (Zometa) on the Pharmaceutical Schedule to include Hospital and Community funding for treatment of hypercalcaemia of malignancy, treatment of pain in patients with bone metastases and prevention of skeletal related events (SRE) in patients with bone metastases

### Details of the proposal

*Zoledronic acid (Zometa)*

- Zoledronic acid (Zometa) would be listed in Section B of the Pharmaceutical Schedule from 1 February 2015 at the following subsidy (ex-manufacturer, excluding GST):

| Chemical | Presentation | Brand | Strength | Pack size | Price and Subsidy |
|---|---|---|---|---|---|
| Zoledronic acid | Inj | Zometa | 0.8 mg per ml, 5 ml | 1 | $550.00 |

  We note that zoledronic acid (Zometa) is already currently listed in Part II of Section H at the price above.

- A confidential rebate would apply to Zometa which would reduce its net price.

- Zometa would have subsidy and delisting protection until 31 January 2018.

- Zoledronic acid (Zometa) would be listed subject to the following restrictions in Section B and Part II of Section H of the Pharmaceutical Schedule:

  **Section B**

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

  **Part II of Section H**

  **Restricted**
  Oncologist or palliative care specialist
  Either:
  1. Patient has hypercalcaemia of malignancy; or
  2. Both
     2.1. Patient has bone metastases; and
     2.2. Either
        2.2.1. Patient has severe bone pain resistant to standard first-line treatments; or

2.2.2. Patient is at risk of skeletal-related events (pathological fracture, spinal cord compression, radiation to bone or surgery to bone)

***About zoledronic acid***

Zoledronic acid 4 mg in 5 ml (Zometa) is a bisphosphonate indicated for the prevention of skeletal-related events (in patients with advanced malignancies involving bone, and for the treatment of tumour-induced hypercalcaemia. Zoledronic acid 4 mg in 5 ml is currently listed on the Hospital Medicines List (HML) restricted to treatment of hypercalcaemia of malignancy, but is not listed in Section B of the Pharmaceutical Schedule.

PHARMAC has received requests for widening of funded funded access to zoledronic acid (4 mg in 5 ml) for the treatment of hypercalcaemia of malignancy and for the prevention of pain and skeletal-related events (SREs) in patients with bone metastases (including in the absence of hypercalcaemia) both in the hospital and in the primary care setting (hospices and general community). Pamidronate is an alternative bisphosphonate funded without restriction in hospitals and the community; however, it requires a 90 minute infusion which may not be practical in some settings. Bisphosphonate treatment is mainly used in palliative care, however, many hospices cannot access DHB-funded zoledronic acid, even where dispensing into the community is permitted by the HML rules, because this requires a DHB hospital doctor to write the prescription which is not an option or not practical in many instances. For this reason, a Section B listing is being proposed to ensure consistency of access by hospices.

PTAC and its Analgesic Subcommittee have reviewed the funding of zoledronic acid. At its November 2013 meeting PTAC recommended that zoledronic acid (4 mg in 5 ml) should be funded in hospital and in the Community subject to Special Authority criteria for the treatment of hypercalcaemia of malignancy, treatment of pain in patients with bone metastases and prevention of skeletal-related events (SRE) in patients with bone metastases if cost neutral to pamidronate taking into account the costs of infusion services and compounding. The Committee considered that the shorter infusion time of zoledronic acid (15 minutes) compared with pamidronate (90 minutes) may be beneficial and more convenient for patients

The minutes for the relevant reviews can be found on the PHARMAC website through the following links:

- http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=869

**Zoledronic acid (Aclasta)**

- Zoledronic acid solution for infusion 5 mg in 100 ml, 100 ml (Aclasta) is a bisphosphonate indicated for the treatment and prevention of osteoporosis and glucocorticosteroid-induced osteoporosis, the treatment of Paget's disease, and the prevention of fractures in patients after hip fractures. It is funded for the treatment of osteoporosis, glucocorticosteroid-induced osteoporosis and Paget's disease.

- The price and subsidy for zoledronic acid (Aclasta) in Section B and Part II of Section H of the Pharmaceutical Schedule would be unchanged, but the net price would be reduced via confidential rebates from 1 February 2015.

- The access criteria for zoledronic acid (Aclasta) in Section B and Part II of Section H of the Pharmaceutical Schedule would be unchanged.

- Aclasta would have subsidy and delisting protection until 31 January 2018.

**Carbamazepine (Tegretol and Tegretol CR)**

- Tegretol and Tegretol CR would be listed in Part II of Section H of the Pharmaceutical Schedule from 1 February 2015 at the following prices (ex-manufacturer, excluding GST):

| Chemical | Presentation | Strength | Brand | Pack size | Price |
|---|---|---|---|---|---|
| Carbamazepine | Tablet | 200 mg | Tegretol | 100 | $14.53 |
| Carbamazepine | Tablet | 400 mg | Tegretol | 100 | $34.58 |
| Carbamazepine | Oral liquid | 100 mg per 5 ml | Tegretol | 250 ml | $26.37 |
| Carbamazepine | Long-acting tablet | 200 mg | Tegretol CR | 100 | $16.98 |
| Carbamazepine | Long-acting tablet | 400 mg | Tegretol CR | 100 | $39.17 |

- Tegretol and Tegretol CR are currently listed in Section B of the Pharmaceutical Schedule and their prices and subsidies in Section B would be unchanged as a result of this proposal.

- The net price of Tegretol and Tegretol CR would be reduced via confidential rebates.

- Tegretol and Tegretol CR would have subsidy and delisting protection until 31 January 2018.

**Clozapine (Clozaril)**

- The prices and subsidies for Clozaril would be reduced in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 February 2015 as follows (ex-manufacturer and excluding GST):

| Chemical | Presentation | Strength | Brand | Pack size | Current Subsidy and Price | Proposed Subsidy and Price |
|---|---|---|---|---|---|---|
| Clozapine | Tablet | 25 mg | Clozaril | 50 | $13.37 | $5.69 |
| Clozapine | Tablet | 25 mg | Clozaril | 100 | $26.74 | $11.36 |
| Clozapine | Tablet | 100 mg | Clozaril | 50 | $34.65 | $14.73 |
| Clozapine | Tablet | 100 mg | Clozaril | 100 | $69.30 | $29.45 |

- The rebate that currently applies to Clozaril would no longer apply from 1 February 2015 (i.e. there would be no rebate from 1 February 2015).

- Clozaril would have subsidy and delisting protection until 31 January 2018.

**Imatinib (Glivec)**

- The prices and subsidies for Glivec in Section B and Part II of Section H of the Pharmaceutical Schedule would be unchanged as a result of this proposal. The net cost of Glivec would be reduced via confidential rebates.

- The access criteria for Glivec on the Pharmaceutical Schedule and the current distribution arrangement for the treatment would be unchanged.

- Glivec would have subsidy and delisting protection until 31 January 2018.

**Methylphenidate hydrochloride (Ritalin LA)**

- The prices and subsidies for Ritalin LA would be reduced in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 February 2015 as follows (ex-manufacturer and excluding GST):

| Chemical | Presentation | Strength | Brand | Pack size | Current Subsidy and Price | Proposed Subsidy and Price |
|---|---|---|---|---|---|---|
| Methlyphenidate hydrochloride extended-release | Capsule modified-release | 10 mg | Ritalin LA | 30 | $19.50 | $15.60 |
| Methlyphenidate hydrochloride extended-release | Capsule modified-release | 20 mg | Ritalin LA | 30 | $25.50 | $20.40 |
| Methlyphenidate hydrochloride extended-release | Capsule modified-release | 30 mg | Ritalin LA | 30 | $31.90 | $25.52 |
| Methlyphenidate hydrochloride extended-release | Capsule modified-release | 40 mg | Ritalin LA | 30 | $38.25 | $30.60 |

- The rebate that currently applies to Ritalin LA would no longer apply from 1 February 2015 (i.e. there would be no rebate from 1 February 2015).

- The access criteria for Ritalin LA on the Pharmaceutical Schedule would be unchanged.

- Ritalin LA would have subsidy and delisting protection until 31 January 2018.

**Diclofenac sodium dispersible tablets (Voltaren D)**

- From 1 February 2015 the price of diclofenac sodium 50 mg dispersible tablets (Voltaren D) would reduce in Section B and in Part II of Section H of the Pharmaceutical Schedule to match the current subsidy as follows (ex-manufacturer and excluding GST):

| Chemical | Presentation | Strength | Brand | Pack size | Current Subsidy (and Price) | Proposed Subsidy and Price |
|---|---|---|---|---|---|---|
| Diclofenac sodium | Dispersible tablet | 50 mg | Voltaren D | 20 | $1.50 ($8.00) | $1.50 |

- This would mean that Voltaren D would become fully funded for all patients and the current endorsement for higher subsidy would be removed (as it would no longer be required) as follows:

  ~~Higher subsidy of $8.00 per 20 tab with Endorsement~~
  ~~Additional subsidy by endorsement for a patient who cannot swallow whole tablets and in whom ibuprofen oral liquid is ineffective or not tolerated, and the prescription is endorsed accordingly.~~

- Voltaren D would have subsidy and delisting protection until 31 January 2018.