CONSULTATION

PHARMAC
Pharmaceutical Management Agency

**11 October 2016**

# Multi-product proposal involving nine pharmaceuticals

PHARMAC is seeking feedback on a proposal to fund three new treatments, widen access to three currently funded treatments, and change the contractual terms for five currently funded treatments through a provisional agreement with Roche Products (NZ) Limited (Roche).

In addition to the provisional agreement with Roche, PHARMAC is also seeking feedback on both a proposal to widen access to two currently funded treatments supplied by Roche and a proposal to apply reference pricing to a funded treatment supplied by AstraZeneca.

In summary, this proposal would result in the following changes from 1 January 2017:

- Funding of three new treatments supplied by Roche:
  - obinutuzumab (Gazyva) for chronic lymphocytic leukaemia
  - pertuzumab (Perjeta) for metastatic breast cancer
  - pirfenidone (Esbriet) for idiopathic pulmonary fibrosis

- Widening of access to seven new indications for currently funded treatments supplied by Roche:
  - dornase alfa (Pulmozyme) for children under the age of 5 years with cystic fibrosis
  - rituximab (Mabthera) for hairy cell leukaemia; re-treatment of chronic lymphocytic leukaemia; and MPO-ANCA positive vasculitis
  - tocilizumab (Actemra) for polyarticular juvenile idiopathic arthritis; rheumatoid arthritis; and Castleman's disease

- Amended contractual terms (including pricing, rebates and protection periods) for:
  - dornase alfa
  - rituximab
  - tocilizumab
  - trastuzumab (Herceptin)
  - erlotinib (Tarceva)

and from 1 April 2017:

- Reduction of the subsidy for gefitinib (Iressa, supplied by AstraZeneca) from 1 April 2017 via the application of reference pricing to the new proposed price for erlotinib.

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






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

### Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **4pm** on **Tuesday 8 November 2016** to:


| | |
|---|---|
| Geraldine MacGibbon | Email: consult@pharmac.govt.nz |
| Senior Therapeutic Group Manager | Fax: 04 460 4995 |
| PHARMAC | Post: PO Box 10 254, Wellington 6143 |


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.

## Details of the proposal

### New listings

***Obinutuzumab (Gazyva) –*** *for chronic lymphocytic leukaemia*

- Obinutuzumab (Gazyva) would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 January 2017 at the following prices and subsidies (ex-manufacturer, excluding GST):

| Presentation | Pack size | Proposed price and subsidy |
|---|---|---|
| Inj 25 mg per ml, 40 ml vial | 1 | $5,910.00 |
| Inj 1 mg for ECP | 1 mg | $6.21 |

*The proposed price and subsidy for the 1 mg for ECP presentation assumes 5% wastage based on the expected average dose, dosing schedule and number of patients treated.

- A confidential rebate would apply to Gazyva that would reduce its net price to the Funder.

- Obinutuzumab would be listed in the Pharmaceutical Schedule as a Pharmaceutical Cancer Treatment only (PCT only – Specialist), meaning that only DHB hospitals would be able to claim for its use.

- Obinutuzumab would be listed in Section B of the Pharmaceutical Schedule, for claiming purposes only, subject to the following Special Authority criteria:

Special Authority for Subsidy
**I**nitial application – (chronic lymphocytic leukaemia) only from a haematologist. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:

1. The patient has progressive Binet stage A, B or C CD20+ chronic lymphocytic leukaemia requiring treatment; and
2. The patient is obinutuzumab treatment naive; and
3. The patient is not eligible for full dose FCR due to comorbidities with a score > 6 on the Cumulative Illness Rating Scale (CIRS) or reduced renal function (creatinine clearance <70mL/min); and
4. Patient has absolute neutrophil count ≥1.5 x $10^9$/L and platelets ≥75 x $10^9$/L and no evidence of additional bone marrow dysfunction; and
5. Patient has good performance status; and
6. Obinutuzumab to be administered at a maximum cumulative dose of 8000 mg and in combination with chlorambucil for a maximum of 6 cycles.

Notes: Chronic lymphocytic leukaemia includes small lymphocytic lymphoma. Comorbidity refers only to illness/impairment other than CLL induced illness/impairment in the patient.

- The same restrictions would apply in Part II of Section H of the Pharmaceutical Schedule (the Hospital Medicines List; HML).

- Gazyva would have protection from delisting and subsidy reduction until 31 December 2019.

*Obinutuzumab background*

Obinutuzumab is a glycoengineered type II anti-CD20 monoclonal antibody. The CD20 antigen is expressed on the surface of pre B- and mature B-lymphocytes; upon binding to CD20, obinutuzumab activates complement-dependent cytotoxicity, antibody-dependent cellular cytotoxicity and antibody-dependent cellular phagocytosis, resulting in cell death.

Obinutuzumab is registered for use in combination with chlorambucil for patients with previously untreated chronic lymphocytic leukaemia (CLL). Information regarding obinutuzumab dosing and administration can be found in the Medsafe datasheet.

A funding application for obinutuzumab as first-line treatment in patients with CLL who have comorbidities preventing treatment with fludarabine, cyclophosphamide and rituximab (FCR) was reviewed by our Pharmacology and Therapeutics Advisory Committee (PTAC) at its meeting in February 2015 and by the Cancer Treatments Subcommittee of PTAC (CaTSoP) in March 2015. Both committees recommended that obinutuzumab be funded in this indication with medium priority.

More information, including links to PTAC and Subcommittee minutes, can be found in the Application Tracker records for obinutuzumab at: http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=1308

***Pertuzumab (Perjeta) –*** *for metastatic breast cancer*

- Pertuzumab (Perjeta) would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 January 2017 at the following prices and subsidies (ex-manufacturer, excluding GST):

| Presentation | Pack size | Proposed price and subsidy |
|---|---|---|
| Inj 30 mg per ml, 14 ml vial | 1 | $3,927.00 |
| Inj 1 mg for ECP | 1 mg | $9.82 |

*The proposed price and subsidy for the 1 mg for ECP presentation assumes 5% wastage based on the expected average dose, dosing schedule and number of patients treated.

- A confidential rebate would apply to Perjeta that would reduce its net price to the Funder.

- Pertuzumab would be listed in the Pharmaceutical Schedule as a Pharmaceutical Cancer Treatment only (PCT only – Specialist), meaning that only DHB hospitals would be able to claim for its use.

- Pertuzumab would be listed in Section B of the Pharmaceutical Schedule, for claiming purposes only, subject to the following Special Authority criteria:

> PCT only – Specialist – Special Authority
> Special Authority for Subsidy
> **I**nitial application – (metastatic breast cancer) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months for applications meeting the following criteria:
> All of the following:
> 1. The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
> 2. Either:
>    2.1. Patient is chemotherapy treatment naïve; or
>    2.2. Patient has not received prior treatment for their metastatic disease and has had a treatment free interval of at least 12 months between prior (neo)adjuvant chemotherapy treatment and diagnosis of metastatic breast cancer; and
> 3. The patient has good performance status (ECOG grade 0-1);
> 4. Pertuzumab to be administered in combination with trastuzumab;
> 5. Pertuzumab maximum first dose of 840 mg, followed by maximum of 420 mg every 3 weeks; and
> 6. Pertuzumab to be discontinued at disease progression.
>
> Renewal application - (metastatic breast cancer) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months for applications meeting the following criteria:
> Both:
> 1. The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including ISH or other current technology); and
> 2. The cancer has not progressed at any time point during the previous 12 months whilst on pertuzumab and trastuzumab.

- The same restrictions would apply in Part II of Section H of the Pharmaceutical Schedule (the Hospital Medicines List; HML).

- Note that pertuzumab would not be funded for patients with metastatic breast cancer who have already started trastuzumab treatment prior to 1 January 2017.

- Perjeta would have protection from delisting and subsidy reduction until 31 December 2019.

*Pertuzumab background*

Pertuzumab is a recombinant humanized monoclonal antibody that binds to the extracellular dimerization domain of the human epidermal growth factor receptor-2 protein (HER-2) to inhibit signaling pathways and can result in cell growth arrest and apoptosis.

Pertuzumab is indicated for use in combination with trastuzumab and docetaxel for patients with HER-2 positive metastatic breast cancer who have not received prior anti-HER-2 therapy or chemotherapy for their metastatic disease until disease progression of unmanageable toxicity. Information regarding pertuzumab dosing and administration can be found on the Medsafe datasheet.

PTAC and CaTSoP have reviewed the funding for pertuzumab for the first line treatment of patients with HER-2 positive metastatic breast cancer in combination with trastuzumab and docetaxel on a number of occasions, most recently by PTAC at its meeting in May 2015. Both committees recommended that pertuzumab should be funded, when used in combination with trastuzumab for the first line treatment of patients with HER-2 positive metastatic breast cancer with low priority.

More information, including links to PTAC and Subcommittee minutes, can be found in the Application Tracker records for pertuzumab at: http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=1173

***Pirfenidone (Esbriet)*** *– for idiopathic pulmonary fibrosis*

- Pirfenidone (Esbriet) would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 January 2017 at the following prices and subsidies (ex-manufacturer, excluding GST):

| Presentation | Pack size | Proposed price and subsidy |
|---|---|---|
| Cap 267 mg | 270 | $3,645.00 |

- A confidential rebate would apply to Esbriet which would reduce its net price to the Funder.

- Pirfenidone would be listed in Section B of the Pharmaceutical Schedule subject to the following Special Authority criteria:

> Retail Pharmacy - Specialist
> Special Authority for Subsidy
> Initial application – (idiopathic pulmonary fibrosis) only from a respiratory specialist. Approvals valid for 12 months for applications meeting the following criteria:
> All of the following:
> 1. Patient has been diagnosed with idiopathic pulmonary fibrosis as confirmed by histology, CT or biopsy; and
> 2. Forced vital capacity is between 50% and 80% predicted; and
> 3. Pirfenidone is to be discontinued at disease progression (See Notes).
>
> Renewal application – (idiopathic pulmonary fibrosis) only from a respiratory specialist. Approvals valid for 12 months for applications meeting the following criteria:

Both:
1. Treatment remains clinically appropriate and patient is benefitting from and tolerating treatment.
2. Pirfenidone is to be discontinued at disease progression (See Notes).

Notes: disease progression is defined as a decline in percent predicted FVC of 10% or more within any 12 month period.

- The same restrictions would apply in Part II of Section H of the Pharmaceutical Schedule (the Hospital Medicines List; HML).

- Esbriet would have protection from delisting and subsidy reduction until 30 June 2018.

*Pirfenidone background*

Pirfenidone is an antifibrotic indicated for the treatment of idiopathic pulmonary fibrosis. Information regarding pirfenidone dosing and administration can be found on the Medsafe datasheet.

The Respiratory Subcommittee of PTAC reviewed a clinician funding application for pirfenadone for the treatment of idiopathic pulmonary fibrosis at its meeting in March 2015. The Subcommittee recommended the product to be listed with a high priority. The proposed Special Authority criteria are based upon criteria developed by the National Institute for Health and Care Excellence (NICE, Final appraisal determination, September 2016).

More information, including a link to the Subcommittee minutes, can be found in the Application Tracker records for pirfenidone at:
http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=1316

**Existing listings – access widening and amendment of contractual terms**

***Dornase alfa (Pulmozme)***

- Access to dornase alfa (Pulmozyme) would be widened in Section B of the Pharmaceutical Schedule from 1 January 2017 to include treatment of children with cystic fibrosis under the age of 5 years as follows (new criteria below):

**Initial approval criteria for children under the age of 5**
Approvals valid for twelve months for applications meeting the following criteria:
All of the following:
1. Patients must be assessed at regional cystic fibrosis clinics or centres which are under the control of specialist respiratory physicians/paediatricians with experience and expertise in the management of cystic fibrosis and the prescribing of dornase alfa under the Pharmaceutical Schedule is limited to such physicians; and
2. Any of the following:
   - 2.1. Requiring more than two hospital respiratory admissions in a 12 month period; or
   - 2.2. Requiring a hospital admission to have a PICC line inserted to manage exacerbations; or
   - 2.3. A chest x-ray showing clear mucus plugging, focal consolidation or a Brasfield score <22/25 done at a time of stability despite currently approved treatment, including repeated physiotherapy assessment and education, and having had at least one admission to hospital; or
   - 2.4. A bronchoscopy done as far as possible at a time of stability which shows significant mucus plugging despite currently approved treatment, including repeated physiotherapy assessment and education, and having had at least one admission to hospital; or

2.5. Diagnosis of allergic bronchopulmonary aspergillosis (ABPA); or
2.6. Undertaking eradication treatment is proposed; and

3. Patient has previously undergone a trial with, or are currently being treated with, hypertonic saline; and
4. All patients having treatment with dornase alfa should be included in the national cystic fibrosis database. Prescribing physicians/paediatricians are required to supply updated patient information on a six monthly basis.

**Renewal for children under the age of 5**

Approvals valid for twelve months for applications meeting the following criteria:
All of the following:

1. Patient is compliant with therapy; and
2. In the opinion of the patients treating clinician they believe dornase alfa to be of worthwhile benefit to the patient; and
3. Any of the following:
   3.1. Reduction in hospital admissions in the previous 12 months; or
   3.2. Reduction in the number of treatment courses of oral antibiotics in the previous 12 months; or
   3.3. Significant improvement in radiological or bronchoscopy findings; or
   3.4. An eradication of a pathological organism.

- We anticipate a subsequent change to the existing renewal criteria may be required to provide an opportunity for those children under the age of 5 who have demonstrated benefit from dornase alfa (as per the new renewal criteria above) to be eligible for long term therapy.

- There would be no change to the wording of the restrictions applying to dornase alfa in Part II of Section H of the Pharmaceutical Schedule (the Hospital Medicines List; HML).

- An amended confidential rebate would apply to Pulmozyme that would reduce its net price to the Funder.

- Pulmozyme would have protection from delisting and subsidy reduction until 31 December 2019.

*Dornase alfa background*

Dornase alfa is a mucolytic indicated for the management of cystic fibrosis patients with a forced vital capacity of greater than 40% of predicted to improve pulmonary function. It is delivered by inhalation using a jet nebuliser. Information regarding pirfenidone dosing and administration can be found on the Medsafe datasheet.

PTAC and the Respiratory Subcommittee have reviewed the widening of access to dornase alfa for the treatment cystic fibrosis in children on a number of occasions. Most recently, PTAC at its meeting in February 2016, recommended that access to dornase alfa be widened to include patients under the age of 5 with a medium priority, subject to the access criteria proposed within this consultation.

More information, including a link to the PTAC and Subcommittee minutes, can be found in the Application Tracker records for dornase alfa at:
http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=1333

***Rituximab (Mabthera)***

- Access to rituximab (Mabthera) would be widened from 1 January 2017 as follows:
    - New indications of hairy cell leukaemia and re-treatment of chronic lymphocytic leukemia would apply to the listing of rituximab in Section B and in Part II of Section H of the Pharmaceutical Schedule, subject to the Special Authority criteria outlined below (new criteria below).

PCT Only – Specialist – Special Authority for Subsidy

Initial application - (Hairy cell leukaemia) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 9 months for applications meeting the following criteria:
Both:
1. Patient has CD20+ hairy cell leukaemia* requiring treatment; and
2. Any of the following:
    2.1. Patient has residual disease following purine analogue treatment; or
    2.2. Patient has relapsed or refractory disease following purine analogue treatment; or
    2.3. Patient is ineligible for purine analogue therapy.

Renewal - (Hairy cell leukaemia) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 9 months for applications meeting the following criteria:
All of the following:
1. The patient has had a rituximab treatment-free interval of 12 months or more; and
2. The patient has hairy cell leukaemia* with relapsed disease following prior chemotherapy; and
3. To be used for no more than 6 treatment cycles.

Note: *****Unapproved indication. “Hairy cell leukaemia’ also includes hairy cell leukaemia variant.

Initial application — (Chronic lymphocytic leukaemia) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:
1. The patient has progressive Binet stage A, B or C chronic lymphocytic leukaemia (CLL) requiring treatment; and
2. The patient is rituximab treatment naïve; and
3. Either:
    3.1 The patient is chemotherapy treatment naïve; or
    3.2 Both:
        3.2.1 The patient’s disease has relapsed following no more than three prior lines of chemotherapy treatment; and
        3.2.2 The patient has had a treatment-free interval of 12 months or more if previously treated with fludarabine and cyclophosphamide chemotherapy; and
4. The patient has good performance status; and
5. The patient has good renal function (creatinine clearance ≥ 30 ml/min); and
6. The patient does not have chromosome 17p deletion CLL; and
7. Rituximab to be administered in combination with fludarabine and cyclophosphamide for a maximum of 6 treatment cycles; and
8. It is planned that the patient receives full dose fludarabine and cyclophosphamide (orally or dose equivalent intravenous administration).

Note: 'Chronic lymphocytic leukaemia (CLL)' includes small lymphocytic lymphoma. A line of chemotherapy treatment is considered to comprise a known standard therapeutic chemotherapy regimen and supportive treatments. 'Good performance status' means ECOG score of 0-1, however, in patients temporarily debilitated by their CLL disease symptoms a higher ECOG (2 or 3) is acceptable where treatment with rituximab is expected to improve symptoms and improve ECOG score to <2.

Renewal application – (Chronic lymphocytic leukaemia) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months for applications meeting the following criteria:

All of the following:

1. The patients disease has relapsed following no more than one prior line of treatment with rituximab for CLL; and
2. The patient has had a rituximab treatment–free interval of 36 months or more; and
3. The patient does not have chromosome 17p deletion CLL; and
4. It is planned that the patient receives full dose fludarabine and cyclophosphamide (orally or dose equivalent intravenous administration); and
5. Rituximab to be administered in combination with fludarabine and cyclophosphamide for a maximum of 6 treatment cycles.

Note: 'Chronic lymphocytic leukaemia (CLL)' includes small lymphocytic lymphoma. A line of chemotherapy treatment is considered to comprise a known standard therapeutic chemotherapy regimen and supportive treatments.

- Amendments to the indication of ANCA-associated vasculitis would apply to the listing of rituximab Part II of Section H of the Pharmaceutical Schedule (the Hospital Medicines List; HML) as follows (deletions in strikethrough, additions in bold – amended criteria only shown):

Restricted
Initiation - ANCA associated vasculitis
*Re-assessment required after 4 weeks*
All of the following:

1. Patient has been diagnosed with ANCA associated vasculitis*; and
~~2. Either:~~
   ~~2.1. Patient does not have MPO-ANCA positive vasculitis*; or~~
   ~~2.2. Mycophenolate mofetil has not been effective in those patients who have MPO-ANCA positive vasculitis*; and~~
3. The total rituximab dose would not exceed the equivalent of 375 mg/m$^2$ of body-surface area per week for a total of 4 weeks; and
4. Any of the following:
   4.1. Induction therapy with daily oral or pulse intravenous cyclophosphamide has failed to achieve ~~complete absence~~ **significant improvement** of disease after at least 3 months; or
   4.2. Patient has previously had a cumulative dose of cyclophosphamide >15 g or a further repeat 3 month induction course of cyclophosphamide would result in a cumulative dose >15 g; or
   4.3. Cyclophosphamide and methotrexate are contraindicated; or
   4.4. Patient is a female of child-bearing potential; or
   4.5. Patient has a previous history of haemorrhagic cystitis, urological malignancy or haematological malignancy.

   Note: Indications marked with * are Unapproved Indications.

Continuation - ANCA associated vasculitis
*Re-assessment required after 4 weeks*
All of the following:

1. Patient has been diagnosed with ANCA associated vasculitis*; and
2. Patient has previously responded to treatment with rituximab but is now experiencing an acute flare of vasculitis; and
3. The total rituximab dose would not exceed the equivalent of 375 mg/m$^2$ of body-surface area per week for a total of 4 weeks.

Note: Indications marked with * are Unapproved Indications.

- No other changes to the current funding criteria for rituximab are proposed.
- An amended confidential rebate would apply to Mabthera that would reduce its net price to the Funder.
- Mabthera would have protection from delisting and subsidy reduction until 30 June 2019.

*Rituximab background*

Rituximab is a monoclonal antibody that targets and binds the protein CD20 primarily found on the surface of B lymphocytes and initiates immunologic reactions that mediate B-cell lysis and result in B-cell depletion.

Information relating to the proposed widening of access indications for rituximab is summarised below. More information, including links to PTAC and Subcommittee minutes, can be found in the Application Tracker records for rituximab at http://www.pharmac.govt.nz/patients/ApplicationTracker?SearchTerm=rituximab

Rituximab is currently funded on the Pharmaceutical Schedule under Special Authority for patients with various indications. Note that hairy cell leukaemia and ANCA associated vasculitis are currently unapproved indications and the proposal to widen access to rituximab for these indications is independent of the provisional agreement with Roche.

*Hairy Cell Leukemia (HCL)*

HCL is an uncommon CD20+ indolent B cell malignancy that presents in either classic or variant form with an incidence of approximately 16 patients per year in New Zealand.

PTAC reviewed a clinician application for funding for patients with CD20+ HCL requiring treatment including patients with: residual disease or relapsed disease after purine analogue therapy, those ineligible for purine analogue therapy, or with hairy cell leukaemia variant at its meeting in November 2015. The application was also then reviewed by CaTSoP at its meeting in September 2016. Both committees recommended that rituximab be funded for patients with CD20+ HCL with medium priority.

*Chronic lymphocytic leukaemia (CLL) retreatment*

Access to rituximab was widened from 1 August 2011 to include funding for patients with treatment naïve CLL (first-line) as well as rituximab naïve patients whose CLL disease has relapsed following up to three prior lines of therapy.

The funding of rituximab retreatment for patients with CLL has been considered on a number of occasions by both PTAC and CaTSoP, most recently by CaTSoP in October 2014 and PTAC in May 2015. Funding for rituximab retreatment was recommended with medium priority for patients with CLL and relapsed disease following no more than one prior line of treatment with rituximab, after a rituximab treatment free interval of 36 months or more, and in combination with planned full dose FCR.

*ANCA associated vasculitis*

Access to rituximab was widened from 1 March 2014 in DHB hospitals to include patients with anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis. Currently, patients with MPO-ANCA positive vasculitis are required to trial mycophenolate mofetil before having funded access to rituximab.

The Nephrology Subcommittee considered the available evidence and restrictions for ANCA associated vasculitis at its meeting in December 2014. The Subcommittee recommended that PHARMAC remove the requirement to trial mycophenolate mofetil before accessing rituximab for this indication. We estimate an additional 50 patients per year would access rituximab earlier in their treatment course if the restriction was amended as proposed.

***Tocilizumab (Actemra)***

- Access to tocilizumab (Actemra) would be widened in Part II of Section H of the Pharmaceutical Schedule (the Hospital Medicines List; HML) to include the new indications of polyarticular juvenile idiopathic arthritis and Castleman's disease, and to remove the requirement to trial rituximab prior to tocilizumab in patients with seronegative rheumatoid arthritis, as follows (note that final proposed criteria are shown for rheumatoid arthritis initiation, rather than marked up changes from the current criteria):

Restricted
Initiation – polyarticular juvenile idiopathic arthritis
Rheumatologist
*Re-assessment required after 4 months.*
Either:

1 Both:
  - 1.1 The patient has had an initial Special Authority approval for both etanercept and adalimumab for juvenile idiopathic arthritis (JIA); and
  - 1.2 The patient has experienced intolerable side effects, or has received insufficient benefit from, both etanercept and adalimumab; or

2 All of the following:
  - 2.1 Treatment with a tumour necrosis factor alpha inhibitor is contraindicated; and
  - 2.2 Patient has had severe active polyarticular course JIA for 6 months duration or longer; and
  - 2.3 Patient has tried and not responded to at least three months of oral or parenteral methotrexate (at a dose of 10-20 mg/m² weekly or at the maximum tolerated dose) in combination with either oral corticosteroids (prednisone 0.25 mg/kg or at the maximum tolerated dose) or a full trial of serial intra-articular corticosteroid injections; and
  - 2.4 To be used as an adjunct to methotrexate therapy or monotherapy where use of methotrexate is limited by toxicity or intolerance; and
  - 2.5 Both:
    - 2.5.1 Either:
      - 2.5.1.1 Patient has persistent symptoms of poorly-controlled and active disease in at least 20 swollen, tender joints; or
      - 2.5.1.2 Patient has persistent symptoms of poorly-controlled and active disease in at least four joints from the following: wrist, elbow, knee, ankle, shoulder, cervical spine, hip; and
    - 2.5.2 Physician's global assessment indicating severe disease.

Renewal – polyarticular juvenile idiopathic arthritis
Rheumatologist
*Re-assessment required after 6 months*
Both:

1 Treatment is to be used as an adjunct to methotrexate therapy or monotherapy where use of methotrexate is limited by toxicity or intolerance; and
2 Either:
  - 2.1 Following 3 to 4 months' initial treatment, the patient has at least a 50% decrease in active joint count and an improvement in physician's global assessment from baseline; or
  - 2.2 On subsequent reapplications, the patient demonstrates at least a continuing 30% improvement in active joint count and continued improvement in physician's global assessment from baseline.

Initiation – idiopathic multicentric Castleman's disease
Haematologist or rheumatologist
*Re-assessment required after 6 months*
All of the following:

1 Patient has severe HHV-8 negative idiopathic multicentric Castleman's disease; and
2 Treatment with an adequate trial of corticosteroids has proven ineffective; and
3 Tocilizumab to be administered at doses no greater than 8 mg/kg IV every 4 weeks.

Continuation – idiopathic multicentric Castleman's disease
Haematologist or rheumatologist
*Re-assessment required after 12 months*
The treatment remains appropriate and the patient has a sustained improvement in inflammatory markers and functional status.

Initiation —Rheumatoid Arthritis
Rheumatologist
*Re-assessment required after 6 months*
Either
1 All of the following:
- 1.1 The patient has had an initial Special Authority approval for adalimumab and/or etanercept for rheumatoid arthritis; and
- 1.2 Either:
  - 1.2.1 The patient has experienced intolerable side effects from adalimumab and/or etanercept; or
  - 1.2.2 The patient has received insufficient benefit from at least a three-month trial of adalimumab and/or etanercept such that they do not meet the renewal criteria for rheumatoid arthritis; and
- 1.3 Either:
  - 1.3.1 The patient is seronegative for both anti-cyclic citrullinated peptide (CCP) antibodies and rheumatoid factor; or
  - 1.3.2 Both:
    - 1.3.2.1 The patient has been started on rituximab for rheumatoid arthritis in a DHB hospital in accordance with the Section H rules; and
    - 1.3.2.2 Either:
      - 1.3.2.2.1 The patient has experienced intolerable side effects from rituximab; or
      - 1.3.2.2.2 At four months following the initial course of rituximab the patient has received insufficient benefit such that they do not meet the renewal criteria for rheumatoid arthritis; or

2 All of the following:
- 2.1 Patient has had severe and active erosive rheumatoid arthritis for six months duration or longer; and
- 2.2 Tocilizumab is to be used as monotherapy; and
- 2.3 Either:
  - 2.3.1 Treatment with methotrexate is contraindicated; or
  - 2.3.2 Patient has tried and did not tolerate oral and/or parenteral methotrexate; and
- 2.4 Either:
  - 2.4.1 Patient has tried and not responded to at least three months therapy at the maximum tolerated dose of cyclosporine alone or in combination with another agent; or
  - 2.4.2 Patient has tried and not responded to at least three months therapy at the maximum tolerated dose of leflunomide alone or in combination with another agent; and
- 2.5 Either:
  - 2.5.1 Patient has persistent symptoms of poorly controlled and active disease in at least 20 active, swollen, tender joints; or
  - 2.5.2 Patient has persistent symptoms of poorly controlled and active disease in at least four active joints from the following: wrist, elbow, knee, ankle, and either shoulder or hip; and
- 2.6 Either:
  - 2.6.1 Patient has a C-reactive protein level greater than 15 mg/L measured no more than one month prior to the date of this application; or
  - 2.6.2 C-reactive protein levels not measured as patient is currently receiving prednisone therapy at a dose of greater than 5 mg per day and has done so for more than three months.

Continuation – Rheumatoid arthritis
Rheumatologist

*Re-assessment required after 6 months*

Either:

1 Following 6 months' initial treatment, the patient has at least a 50% decrease in active joint count from baseline and a clinically significant response to treatment in the opinion of the physician; or

2 On subsequent reapplications, the patient demonstrates at least a continuing 30% improvement in active joint count from baseline and a clinically significant response to treatment in the opinion of the physician.

- No other changes to the current funding criteria for tocilizumab are proposed.
- An amended confidential rebate would apply to Actemra that would reduce its net price to the Funder.
- Actemra would have protection from delisting and subsidy reduction until 31 December 2019.

*Tocilizumab background*

Tocilizumab is a recombinant humanised monoclonal antibody that binds specifically to both soluble and membrane-bound interleukin (IL)-6 receptors, thereby inhibiting IL-6 receptor-mediated signalling. IL-6 has been implicated in the pathogenesis of diseases including rheumatoid arthritis and juvenile idiopathic arthritis. It is administered by intravenous infusion in hospital. It is currently funded for systemic juvenile idiopathic arthritis, rheumatoid arthritis and adult onset Still's disease, subject to clinical criteria being met.

Information relating to the new proposed indications for tocilizumab is summarised below. More information, including links to PTAC and Subcommittee minutes, can be found in the Application Tracker records for tocilizumab at http://pharmac.govt.nz/patients/ApplicationTracker?SearchTerm=tocilizumab

Note that Castelman's disease is currently an unapproved indication and widening access to tocilizumab for this indication is proposed independent of the provisional agreement with Roche.

*Polyarticular juvenile idiopathic arthritis (JIA)*

PTAC reviewed an application to fund tocilizumab for polyarticular JIA at its meeting in August 2015 and recommended that access to tocilizumab be widened to include polyarticular JIA, subject to clinical criteria being met, with a medium priority.

*Castleman's disease*

In February 2015 PTAC reviewed a clinician application to fund of tocilizumab for the treatment of Castleman's disease. The Committee recommended that access to tocilizumab be widened to include HIV/HHV-8 negative idiopathic multicentric Castleman's disease with a low priority, subject to restrictions. The proposal would result in a second biologic treatment option being funded for this patient group: siltuximab (Sylvant) was funded for the same patient group from 1 June 2016.

*Rheumatoid arthritis*

The Rheumatology Subcommittee of PTAC (in October 2015) and PTAC (in November 2015) reviewed a clinician application to amend the hospital restrictions for tocilizumab for rheumatoid arthritis to remove the requirement to trial rituximab in patients with rheumatoid arthritis seronegative for both anti-cyclic citrullinated peptide (CCP) antibodies and

rheumatoid factor (RF). Both the Subcommittee and PTAC recommended that this amendment be made only if this would be cost-neutral to the status quo hospital expenditure on rituximab and tocilizumab for this patient group.

### *Trastuzumab (Herceptin)*

- Access to trastuzumab (Herceptin) would be amended in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 January 2017 for the indication of metastatic breast cancer, to allow for the use of trastuzumab in combination with pertuzumab as follows (amended criteria only shown):

> TRASTUZUMAB – PCT only - Specialist
> Special Authority for Subsidy
> Initial application - (metastatic breast cancer) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months for applications meeting the following criteria:
> ~~Either:~~ **Any of the following:**
> 1. All of the following:
>  1.1. The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
>  1.2. The patient has not previously received lapatinib treatment for HER-2 positive metastatic breast cancer; and
>  1.3. Trastuzumab not to be given in combination with lapatinib; and
>  1.4. Trastuzumab to be discontinued at disease progression; or
> 2. All of the following:
>  2.1. The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
>  2.2. The patient started lapatinib treatment for metastatic breast cancer but discontinued lapatinib within 3 months of starting treatment due to intolerance; and
>  2.3. The cancer did not progress whilst on lapatinib; and
>  2.4. Trastuzumab not to be given in combination with lapatinib; and
>  2.5. Trastuzumab to be discontinued at disease progression; or
> **3. All of the following:**
>  **3.1. The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and**
>  **3.2. Either:**
>  **3.2.1. Patient is chemotherapy treatment naïve; or**
>  **3.2.2. Patient has not received prior treatment for their metastatic disease and has had a treatment free interval of at least 12 months between prior (neo)adjuvant chemotherapy treatment and diagnosis of metastatic breast cancer; and**
>  **3.3. The patient has good performance status (ECOG grade 0-1); and**
>  **3.4. Trastuzumab to be administered in combination with pertuzumab; and**
>  **3.5. Trastuzumab to be discontinued at disease progression.**
>
> Renewal- (metastatic breast cancer) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months for applications meeting the following criteria:
> All of the following:
> 1. The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
> 2. The cancer has not progressed at any time point during the previous 12 months whilst on trastuzumab; and
> 3. Trastuzumab not to be given in combination with lapatinib; and
> 4. Trastuzumab to be discontinued at disease progression.

- No other changes to the current funding criteria for trastuzumab are proposed.

- An amended confidential rebate would apply to Herceptin that would reduce its net price to the Funder.

- Herceptin would have protection from delisting and subsidy reduction until 31 December 2018.

***Erlotinib (Tarceva)***

- The price and subsidy for erlotinib (Tarceva) would be reduced in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 January 2017 as follows (ex-manufacturer, excluding GST):

| Presentation | Pack size | Current price and subsidy | Proposed price and subsidy |
|---|---|---|---|
| Tab 100 mg | 30 | $1,000.00 | $764.00 |
| Tab 150 mg | 30 | $1,500.00 | $1,146.00 |

- Tarceva would have protection from delisting and subsidy reduction until 31 December 2019.

- Tarceva would cease to have Sole Subsidised Supply status in the community, and would cease to have Hospital Supply Status in DHB hospitals, from 1 January 2017.

- The Special Authority criteria for erlotinib would be amended as outlined below from 1 April 2017, but only if the proposal to apply reference pricing to gefitinib (see below) is approved AND the supplier of gefitinib did not reduce its price to match the new subsidy:

Special Authority for Subsidy
Initial application only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 4 months for applications meeting the following criteria:
All of the following:

1. Patient has locally advanced or metastatic, unresectable, non-squamous Non Small Cell Lung Cancer (NSCLC); and
2. There is documentation confirming that the disease expresses activating mutations of EGFR tyrosine kinase; and
3. Any of the following:
    - 3.1 Patient is treatment naive; or
    - 3.2 Both:
        - 3.2.1 Patient has documented disease progression following treatment with first line platinum based chemotherapy; and
        - 3.2.2 Patient has not received prior treatment with gefitinib; or
    - 3.3 Both:
        - 3.3.1 The patient has discontinued gefitinib within 12 weeks of starting treatment due to intolerance; and
        - 3.3.2 The cancer did not progress while on gefitinib; ~~and~~ **or**
    - **3.4 Both:**
        - **3.4.1 Patient has had treatment with gefitinib prior to 1 April 2017; and**
        - **3.4.2 Patient's disease has not progressed; and**
4. Erlotinib is to be given for a maximum of 3 months.

Renewal only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months where radiological assessment (preferably including CT scan) indicates NSCLC has not progressed.

***Reference pricing gefitinib***

- The subsidy for gefitinib (Iressa) would be reduced in Section B of the Pharmaceutical Schedule via the application of reference pricing to the new proposed subsidy for erlotinib (see above) from 1 April 2017 as follows (ex-manufacturer, excluding GST):

| Presentation | Pack size | Current price and subsidy | Proposed subsidy (price) |
|---|---|---|---|
| Tab 250 mg | 30 | $1,700.00 | $1,146.00<br>($1,700.00) |

- No changes to the current funding criteria for gefitinib are proposed.

- If the supplier of gefitinib did not reduce its price to match the new proposed subsidy, patients would need to change to erlotinib to remain on a fully funded product. This would also require clinicians to apply for a new Special Authority for erlotinib for their patients. Amendments to the erlotinib Special Authority to allow for this are proposed (see above).

*Reference pricing gefitinib and erlotinib background*

Gefitnib and erlotinib are both currently funded as first-line treatments for patients with advanced or metastatic non-small cell lung cancer with activating epidermal growth factor receptor (EGFR) tyrosine kinase mutations.

Funding of gefitinib and erlotinib has been considered by both PTAC and CaTSoP on a number of occasions, most recently by PTAC at its meeting in May 2013. The Committee considered that erlotinib (150 mg daily) and gefitinib (250 mg daily) have the same or similar effect and could be considered under the same therapeutic sub-group which would allow for reference pricing between the two chemicals.

More information, including links to PTAC and Subcommittee minutes, can be found in the Application Tracker records for gefitinib and erlotinib at
http://www.pharmac.govt.nz/patients/ApplicationTracker?SearchTerm=gefitinib
http://www.pharmac.govt.nz/patients/ApplicationTracker?SearchTerm=erlotinib