Consultation

PHARMAC
TE PĀTAKA WHAIORANGA

Proposal for funding of oncology, multiple sclerosis and respiratory treatments

7 August 2019

What we're proposing

We are seeking feedback on a proposal to fund three new treatments and widen access to one currently funded treatment through a provisional agreement with Roche Products (NZ) Limited (Roche).

In summary, this proposal would result in the following changes from 1 December 2019:

- Funding of three new treatments:
  - alectinib (Alecensa) for ALK positive advanced non-small cell lung cancer
  - trastuzumab emtansine (Kadcyla) for HER-2 positive metastatic breast cancer
  - ocrelizumab (Ocrevus) for relapsing remitting multiple sclerosis
- Amendment to the listing of pirfenidone (Esbriet) for idiopathic pulmonary fibrosis to:
  - widen access for patients with a forced vital capacity of up to 90%
  - list a new 801 mg tablet presentation

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

Consultation closes at **5.00 pm on Wednesday, 21 August 2019** and feedback can be emailed to consult@pharmac.govt.nz.

To provide feedback

Send us an email: consult@pharmac.govt.nz by **5.00 pm on Wednesday, 21 August 2019**

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.

Alectinib for ALK-positive advanced non-small cell lung cancer

What would the effect be?

Alectinib would be funded for the treatment of anaplastic lymphoma kinase (ALK) locally advanced or metastatic (advanced) non-small cell lung cancer (NSCLC). Evidence indicates that alectinib has activity in CNS disease and provides a significant benefit over chemotherapy.

Funding is proposed for all ALK-positive NSCLC patients and would be funded regardless of histology and for use as a first, second or later line treatment. We estimate that 40 to 70 patients per year would be eligible for treatment under the proposed criteria.

There would be an increase in genetic testing as NSCLC patients would need to be tested for ALK rearrangements to determine eligibility for funded alectinib. Clinical advice indicates this could be around 800 patients per year.

As ALK testing is not routinely undertaken currently it is uncertain what proportion of ALK-positive patients are currently treated with chemotherapy. If this proposal was progressed, patients may receive chemotherapy as a further line of treatment following treatment with alectinib.

Who we think will be interested

- People who have or may develop lung cancer and their whānau
- Oncologists
- Community and hospital pharmacies
- DHBs and genetic testing service providers
- Organisations with an interest in cancer treatment

About alectinib and non-small cell lung cancer

Alectinib is an oral tyrosine kinase inhibitor treatment that targets anaplastic lymphoma kinase (ALK) and is Medsafe approved for use in adult patients with ALK-positive, locally advanced or metastatic (advanced) non-small cell lung cancer (NSCLC).

Patients with ALK-positive NSCLC are more likely to present with advanced disease, more likely to develop central nervous system metastases, and have a poorer prognosis with conventional chemotherapy than patients with NSCLC associated with other oncogenic drivers.

Given alectinib is an orally administered treatment, there may be a reduction in compounding and infusion service requirements if this proposal was progressed.

Information regarding alectinib dosing and administration can be found in the Medsafe datasheet.

Why we're proposing this

A funding application for alectinib for the first-line treatment of ALK-positive advanced NSCLC was considered by the Pharmacology and Therapeutics Advisory Committee (PTAC) in August 2018 and the Cancer Treatments Subcommittee of PTAC (CaTSoP) in April 2019.

PTAC recommended alectinib for funding as a first-line treatment for ALK positive advanced NSCLC with medium priority. CaTSoP recommended that alectinib be funded with high priority for the treatment of ALK-positive advanced NSCLC regardless of histology and line of treatment subject to certain clinical criteria being met.

More information, including links to the PTAC and Subcommittee minutes, can be found in the Application Tracker record for Alectinib for ALK positive advanced NSCLC

Details about our proposal

Alectinib would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 December 2019 at the following price (ex-manufacturer, excluding GST):

Chemical	Formulation	Brand	Pack size	Proposed price and subsidy
Alectinib	Cap 150 mg	Alecensa	224	$7,935.00

A confidential rebate would apply to Alecensa that would reduce the net price to the Funder.

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

Special Authority for Subsidy – Retail Pharmacy - Specialist
Initial application - only from a medical oncologist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:

1. Patient has locally advanced, or metastatic, unresectable, non-small cell lung cancer; and
2. There is documentation confirming that the patient has an ALK tyrosine kinase gene rearrangement using an appropriate ALK test; and
3. Patient has an ECOG performance score of 0-2.

Renewal application - only from a medical oncologist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:
Both:

1. No evidence of progressive disease according to RECIST criteria; and
2. The patient is benefitting from and tolerating treatment.

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

Alecensa would have protection from delisting and subsidy reduction until 30 November 2022.

Trastuzumab emtansine for HER2-positive metastatic breast cancer

What would the effect be?

Trastuzumab emtansine would be funded for the second-line treatment of human epidermal growth factor receptor 2 (HER2)- positive metastatic breast cancer. Evidence indicates that there is a survival benefit in those patients previously treated with trastuzumab in the first-line setting.

Funding is proposed for patients who have received prior treatment for their metastatic disease with trastuzumab and a taxane, separately or in combination with pertuzumab.

We estimate that approximately 60 patients per year would be eligible for treatment under the proposed criteria.

This treatment is given by intravenous infusion. We estimate that the impacts to DHB services, if this proposal was progressed, would be:

	FYE 2019*	FYE 2020	FYE 2021	FYE 2022	FYE 2023
Eligible patients	35*	60	60	60	60
Additional infusions	608*	1200	1200	1200	1200
Additional infusion (hours)	612*	1230	1230	1230	1230

*Assumes 7 months of use from 1 December 2019

The above estimated impacts assume a 1.5 hour first infusion and sixteen subsequent 1 hour infusions per patient. This estimate also includes premedication and observation time.

We acknowledge there would also be an impact for pharmacy services from the compounding of trastuzumab emtansine, however this is difficult to quantify.

Who we think will be interested

- People who have or may develop breast cancer and their whānau
- Oncologists
- Community and hospital pharmacies
- DHBs
- Organisations with an interest in cancer treatment

About trastuzumab emtansine and HER2 positive metastatic breast cancer

Trastuzumab emtansine is a HER2-targeted antibody-drug conjugate that contains trastuzumab linked to microtubule inhibitory DM1. It is Medsafe approved as a single agent for the treatment of patients with HER2-positive metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination.

Approximately 10% of patients with breast cancer present with metastatic disease at the time of diagnosis, and the majority of women who relapse after definitive therapy for early stage or locally advanced disease will have metastatic disease. Approximately 20% of breast cancers are HER2 positive. HER2 positivity has an increased risk of disease recurrence and an overall worse prognosis. Five year survival rates for metastatic HER2 positive breast cancer with current treatments are estimated to be approximately 40%.

Trastuzumab emtansine must be reconstituted and diluted prior to administration. It is given by intravenous infusion every three weeks until disease progression or unacceptable toxicity. Further information regarding trastuzumab emtansine dosing and administration can be found in the Medsafe datasheet.

Why we're proposing this

A funding application for trastuzumab emtansine for the second-line treatment of HER2-positive metastatic breast cancer was considered by the Pharmacology and Therapeutics Advisory Committee (PTAC) in November 2017 and the Cancer Treatments Subcommittee of PTAC (CaTSoP) in September 2018.

PTAC and CaTSoP have both recommended that trastuzumab emtansine be funded with medium priority for the treatment of HER-2 positive metastatic breast cancer patients who have received prior treatment with trastuzumab and a taxane, separately or in combination, subject to Special Authority criteria.

The Subcommittee also recommended that funding for patients who have previously received trastuzumab in combination with pertuzumab be deferred pending further evidence to support its use in this setting. However, as PHARMAC has been able to reach suitable commercial arrangements with Roche, funding of trastuzumab emtansine is also proposed for these patients.

More information, including links to the PTAC and Subcommittee minutes, can be found in the Application Tracker record for Trastuzumab emtansine for HER2-positive metastatic breast cancer after prior trastuzumab and a taxane.

Details about our proposal

Trastuzumab emtansine would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 December 2019 at the following price (ex-manufacturer, excluding GST):

Chemical	Formulation	Brand	Pack size	Proposed price
Trastuzumab emtansine	Inj 100 mg vial	Kadcyla	1	$2,320.00
Trastuzumab emtansine	Inj 160 mg vial	Kadcyla	1	$3,712.00
Trastuzumab emtansine	1 mg for ECP	Baxter	1 mg	$23.20*

*1 mg for ECP would be listed at the same price per mg as the vial

A confidential rebate would apply to Kadcyla that would reduce the net price to the Funder.

Trastuzumab emtansine 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.

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

Special Authority for Subsidy – PCT Only - Specialist
Initial application - only from a relevant specialist or medical practitioner or on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:

1. Patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
2. Patient has previously received trastuzumab and a taxane, separately or in combination; and
3. Either
    3.1. The patient has received prior therapy for metastatic disease*; or
    3.2. The patient developed disease recurrence during, or within six months of completing adjuvant therapy*; and
4. Patient has a good performance status (ECOG 0-1); and
5. Patient has left ventricular ejection fraction of 50% or more; and
6. Patient does not have symptomatic brain metastases; and
7. Treatment to be discontinued at disease progression.

Renewal – only from a relevant specialist or medical practitioner or on the recommendation of a relevant specialist. Approvals valid for 6 months for applications meeting the following criteria:
Both:

1. The cancer has not progressed at any time point during the previous approval period whilst on trastuzumab emtansine; and
2. Treatment to be discontinued at disease progression.

*Note: Prior or adjuvant therapy includes anthracycline, other chemotherapy, biological drugs, or endocrine therapy.

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

Kadcyla would have protection from delisting and subsidy reduction until 30 November 2022.

Ocrelizumab for relapsing remitting multiple sclerosis

What would the effect be?

Ocrelizumab would be funded for patients with relapsing remitting multiple sclerosis (RRMS), subject to the same funding criteria that apply to currently funded multiple sclerosis (MS) treatments.

There are approximately 1500 people with RRMS currently receiving funding for a MS treatment. This proposal if approved would mean that there would be an additional MS treatment for people with RRMS to choose from (in addition to natalizumab, fingolimod, dimethyl fumarate, teriflunomide, and other treatments). Clinical advice indicates it is likely that some patients who are on natalizumab and at risk for developing progressive multifocal leukoencephalopathy* (PML) may choose to change to ocrelizumab. No increase in the total numbers of patients that receive funding for an MS treatment is expected.

Prevention of relapses and delays in disease progression from treatment with ocrelizumab, or any of the other funded MS treatments, could lead to a reduction in morbidity for people with RRMS. In addition, prevention of relapses and disease progression has the potential to relieve carer burden.

There are potential benefits to the health system where people with RRMS change from natalizumab, as there could be a reduction in use of infusion services. Natalizumab treatment requires 13 x 2 hour infusion sessions per year (26 hours per year), whereas ocrelizumab is administered over a 4 hour infusion session on day 1 and day 15 and then 1 x five hour session every six-months thereafter (13 hours in first year, 10 hours per year ongoing). These estimates also include premedication and observation time. Additional resource would be required for infusion administration for those who change from another MS treatment.

In addition, it is likely that there would be a reduction in MRI scans associated with treatment of ocrelizumab compared to natalizumab. Clinical advice indicates that there would be a reduction in 0.5 MRI scans per year for each person who changes from natalizumab to ocrelizumab.

It is difficult to predict the exact numbers of people who would choose to take up treatment with ocrelizumab; however, we estimate that this could be up to 300 people per year.

*Note: the risk of PML from treatment with ocrelizumab has not been excluded, more details on the safety profile of the treatment are available from the Medsafe website.

Who we think will be interested

- People with multiple sclerosis and their whānau
- Organisations with an interest in multiple sclerosis treatment
- Neurologists
- Community and hospital pharmacies
- DHBs

About ocrelizumab and RRMS

Ocrelizumab is a recombinant humanised monoclonal antibody (IgG1 subtype) that selectively targets CD20-expressing B-cells used for the treatment of adult patients with relapsing remitting MS.

Ocrelizumab is administered by intravenous infusion given 6 monthly. Further information regarding ocrelizumab dosing and administration can be found in the Medsafe datasheet.

Multiple sclerosis (MS) is an autoimmune condition in which the immune system attacks the central nervous system, leading to demyelination. It may cause numerous sensory and physical symptoms, and often progresses to physical and cognitive disability.

Why we're proposing this

A funding application for ocrelizumab for the treatment of RRMS was considered by the Pharmacology and Therapeutics Advisory Committee (PTAC) in February 2018, the Neurological Subcommittee in July 2018 and again by PTAC in November 2018. PTAC recommended that ocrelizumab for the treatment of RRMS be funded if it was cost neutral to the other funded newer MS treatments (natalizumab, fingolimod, dimethyl fumarate and teriflunomide).

A funding application was also received for ocrelizumab for the treatment of primary progressive multiple sclerosis (PPMS) and was considered by PTAC in February 2018. PTAC recommended that funding of ocrelizumab for this indication be declined. The reason for this was primarily around the lack of data to establish both the safety and efficacy of ocrelizumab for people with PPMS. Based on the recommendation to decline from our clinical experts we are not progressing funding of ocrelizumab for PPMS at this time. Should new evidence become available in the future to address these concerns we would be happy to seek an updated review from PTAC.

More information, including links to the PTAC and Subcommittee minutes, can be found in the Application Tracker record for ocrelizumab for RRMS and ocrelizumab for PPMS

Details about our proposal

Ocrelizumab would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 December 2019 at the following price (ex-manufacturer, excluding GST):

Chemical	Formulation	Brand	Pack size	Proposed price and subsidy
Ocrelizumab	Inj 30 mg per ml, 10 ml vial	Ocrevus	1	$9,346.00

A confidential rebate would apply to Ocrevus that would reduce the net price to the Funder.

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

Special Authority approved by the Multiple Sclerosis Treatment Committee
Notes: Special Authority approved by the Multiple Sclerosis Treatment Assessment Committee (MSTAC). Applications will be considered by MSTAC at its regular meetings and approved subject to eligibility according to the Entry and Stopping criteria (below).
Application details may be obtained from PHARMAC's website http://www.pharmac.govt.nz or:

The coordinator	Phone: 04 460 4990
Multiple Sclerosis Treatment Assessment Committee	Facsimile: 04 916 7571
PHARMAC PO Box 10 254	Email: mstaccoordinator@pharmac.govt.nz
Wellington	

Completed application forms must be sent to the coordinator for MSTAC and will be considered by MSTAC at the next practicable opportunity.
Notification of MSTAC's decision will be sent to the patient, the applying clinician and the patient's GP (if specified).

Entry Criteria

1) Diagnosis of multiple sclerosis (MS) must be confirmed by a neurologist. Diagnosis must include MRI confirmation; and
2) patients must have Clinically Definite Relapsing Remitting MS with or without underlying progression; and
3) patients must have:
   a) EDSS score 0 - 4.0 and:
      - Experienced at least 1 significant relapse of MS in the previous 12 months or 2 significant relapses in the past 24 months; and
      - Evidence of new inflammatory activity on an MR scan within the past 24 months, any of the following:
         i) a gadolinium enhancing lesion; or
         ii) a Diffusion Weighted Imaging positive lesion; or
         iii) a T2 lesion with associated local swelling; or
         iv) a prominent T2 lesion that clearly is responsible for the clinical features of a recent relapse; or
         v) new T2 lesions compared with a previous MR scan; and
4) A significant relapse must:
   a) be confirmed by the applying neurologist or general physician (the patient may not necessarily have been seen by them during the relapse but the neurologist/physician must be satisfied that the clinical features were characteristic and met the specified criteria);
   b) be associated with characteristic new symptom(s)/sign(s) or substantial worsening of previously experienced symptom(s)/sign(s);
   c) last at least one week;
   d) start at least one month after the onset of a previous relapse;
   e) be severe enough to change either the EDSS or at least one of the Kurtzke Functional System scores by at least 1 point;
   f) be distinguishable from the effects of general fatigue; and
   g) not be associated with a fever (T> 37.5°C); and
5) applications must be made by the patient's neurologist or general physician; and
6) patients must have no previous history of lack of response to ocrelizumab; and
7) patients must have not previously had intolerance to ocrelizumab; and
8) patient must not be co-prescribed beta interferon or glatiramer acetate.

Stopping Criteria

Any of the following:

1) Confirmed progression of disability that is sustained for six months. Progression of disability is defined as progress by any of the following EDSS points:
   a) from starting at EDSS 0 increasing to (i.e. stopping on reaching) EDSS 3.0; or
   b) 1.0 to 3.0; or
   c) 1.5 to 3.5; or
   d) 2.0 to 4.0; or
   e) 2.5 to 4.5; or
   f) 3.0 to 4.5; or
   g) 3.5 to 4.5; or
   h) 4.0 to 4.5.

2) increasing relapse rate over 12 months of treatment (compared with the relapse rate on starting treatment) (see note); or
3) intolerance to ocrelizumab; or
4) non-compliance with treatment, including refusal to undergo annual assessment.

Note: Switching between natalizumab, fingolimod, dimethyl fumarate, teriflunomide and ocrelizumab is permitted provided the EDSS stopping criteria are not met. Switching to interferon or glatiramer acetate is only permitted provided the EDSS stopping criteria are not met and both fingolimod and natalizumab are either not tolerated or treatment with both agents would be clinically inappropriate. Continued relapses on treatment would be expected to lead to a switch of treatment provided the stopping criteria are not met. If a relapse has resulted in an increased EDSS score that potentially may lead to discontinuation of treatment according to stopping criteria, a period of 6 months is allowed from the start of the relapse for recovery to occur.

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

Ocrevus would have protection from delisting and subsidy reduction until 30 November 2022.

Changes to the note in the Special Authority Criteria for all MS treatments

Should the proposal be approved for ocrelizumab from 1 December 2019 the note in the Special Authority Criteria for the Multiple Sclerosis Treatments natalizumab, fingolimod, dimethyl fumarate and teriflunomide, would be amended as follows (additions in bold, deletions in strikethrough):

Switching between natalizumab, fingolimod, dimethyl fumarate**,** ~~and~~ teriflunomide **and ocrelizumab** is permitted provided the EDSS stopping criteria are not met. Switching to inferferon or glatiramer acetate is only permitted provided the EDSS stopping criteria are not met and both fingolimod and natalizumab are either not tolerated or treatment with both agents would be clinically inappropriate.

Continued relapses on treatment would be expected to lead to a switch of treatment provided the stopping criteria are not met. If a relapse has resulted in an increased EDSS score that potentially may lead to discontinuation of treatment according to stopping criteria, a period of 6 months is allowed from the start of the relapse for recovery to occur.

Pirfenidone for idiopathic pulmonary fibrosis

What would the effect be?

Funded access to pirfenidone would be widened to include patients with less severe disease. The restrictions would be amended to increase the upper limit of forced vital capacity (FVC) from 80% predicted to 90% predicted.

This amendment would mean pirfenidone would have the same access criteria as nintedanib (Ofev), which is another currently funded treatment for idiopathic pulmonary fibrosis; and would allow patients to access funded pirfenidone earlier than under the current criteria.

Treatment with antifibrotic agents, such as pirfenidone and nintedanib, slows the rate of disease progression and decline in lung function.

The listing of the new 801 mg tablet presentation would reduce the number of tablets per dose for patients.

Who we think will be interested

- People with idiopathic pulmonary fibrosis and their whānau
- Respiratory clinicians
- Community and hospital pharmacies
- DHBs

About pirfenidone and idiopathic pulmonary fibrosis

Pirfenidone is an antifibrotic indicated for the treatment of idiopathic pulmonary fibrosis. The recommended dose of pirfenidone is 801 mg three times a day, following the initial 14 day titration period. Information regarding pirfenidone dosing and administration can be found on the Medsafe datasheet.

Idiopathic pulmonary fibrosis is a progressive and severe interstitial lung disease affecting mostly the elderly population, with a median survival duration of 2-3 years after diagnosis.

Why we're proposing this

In May 2018, PTAC recommended that the access criteria for pirfenidone be widened to increase the upper FVC limit to 90% predicted with high priority based on evidence to support the benefit of patients being treated earlier.

More information, including links to the PTAC and Subcommittee minutes, can be found in the Application Tracker record for Pirfenidone –widening access

Details about our proposal

A new 801 mg tablet presentation of pirfenidone would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 December 2019 at the following price (ex-manufacturer, excluding GST):

Chemical	Formulation	Brand	Pack size	Proposed price and subsidy
Pirfenidone	Tab 801 mg	Esbriet	90	$3,645.00

A confidential rebate would apply to pirfenidone (both the currently listed 276 mg capsule and the new 801 mg tablet presentation) that would reduce the net price to the Funder.

Access to pirfenidone (Esbriet) would be widened in Section B of the Pharmaceutical Schedule from 1 December 2019 to include patients with a forced vital capacity of up to 90% as follows (deletions in strikethrough, additions in bold):

Initial application – (idiopathic pulmonary fibrosis) only from a respiratory physician. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:

1. Patient has been diagnosed with idiopathic pulmonary fibrosis by a multidisciplinary team including a radiologist; and
2. Forced vital capacity is between 50% and ~~80~~**90**% predicted; and
3. Pirfenidone is to be discontinued at disease progression (See Note); and
4. Pirfenidone is not to be used in combination with subsidised nintedanib; and
5. Any of the following:
   - 5.1. The patient has not previously received treatment with nintedanib; or
   - 5.2. Patient has previously received nintedanib, but discontinued nintedanib within 12 weeks due to intolerance; or
   - 5.3. Patient has previously received nintedanib, but the patient's disease has not progressed (disease progression defined as 10% or more decline in predicted FVC within any 12 month period since starting treatment with nintedanib).

Renewal application – (idiopathic pulmonary fibrosis) only from a respiratory physician. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:

1. Treatment remains clinically appropriate and patient is benefitting from and tolerating treatment; and
2. Pirfenidone is not be used in combination with subsidised nintedanib; and
3. Pirfenidone is to be discontinued at disease progression (See Note).

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

The same change would be applied to the restrictions 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 28 February 2021.