NOTIFICATION

PHARMAC
Pharmaceutical Management Agency

5 December 2016

Approval of multi-product funding proposal with Roche

PHARMAC is pleased to announce a major funding package following an agreement with Roche Products (NZ) for funding nine medicines covering ten different medical conditions with changes implemented from 1 January 2017. This was the subject of consultation in October 2016, available on PHARMAC's website[1].

This decision will see nearly 2,000 people over five years getting access to medicines they need to treat cancer, respiratory, rheumatology and other diseases. In summary, this decision will result in the following changes from 1 January 2017:

- three new treatments will be funded:
  - obinutuzumab (Gazyva) for chronic lymphocytic leukaemia
  - pertuzumab (Perjeta) for metastatic breast cancer
  - pirfenidone (Esbriet) for idiopathic pulmonary fibrosis

- access to three currently funded treatments will be widened to include seven new therapeutic indications:
  - dornase alfa (Pulmozyme) for children with cystic fibrosis under the age of 5 years
  - 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 idiopathic multicentric Castleman's disease

- contractual terms (including pricing, rebates and protection periods) for five currently funded products will be amended:
  - dornase alfa
  - rituximab
  - tocilizumab
  - trastuzumab (Herceptin)
  - erlotinib (Tarceva)

and from 1 April 2017:

- The subsidy for gefitinib (Iressa, supplied by AstraZeneca) will reduce to the level of the new price for erlotinib via the use of reference pricing.

Further details of this decision can be found on the following pages.

[1] http://www.pharmac.govt.nz/news/consultation-2016-10-11-multi-product-proposal/

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Feedback received

We appreciate all of the feedback that we received and acknowledge the time people took to respond. All consultation responses received were considered in their entirety in making a decision on the proposed changes. Most responses were supportive of the proposals. Issues raised in relation to specific aspects of the proposal are discussed in the relevant proposal sections of this notification letter.

More information

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

Details of the decisions

Oncology/Haematology

Pertuzumab (Perjeta) – *for first-line treatment of HER2-positive metastatic breast cancer*

The proposed terms of listing, including commercial terms and Special Authority criteria, were approved as consulted on without any changes. This means that pertuzumab will be funded from 1 January 2017 for patients with metastatic breast cancer who have not yet commenced treatment for their metastatic disease at 1 January 2017 (regardless of the date of diagnosis) and who meet the required Special Authority criteria.

Following consideration of consultation feedback (see below), pertuzumab will also be funded from 1 January 2017 for patients with metastatic breast cancer who started on pertuzumab in combination with trastuzumab prior to 1 January 2017, providing that the 1 January 2017 criteria were met at the time the patient started on treatment and the patient's disease has not progressed while on pertuzumab.

A Special Authority waiver application will be required to access funding for these patients; further details on this can be found below in the consultation responses summary table.

Consultation feedback

Responses were supportive of the proposal to fund pertuzumab for the first-line treatment of HER2-positive metastatic breast cancer.

Some responders raised a number of issues with the proposal, which fell into five broad themes.

These are outlined below, along with PHARMAC's comments.

Feedback theme	Comment
Requests for patients who were taking pertuzumab before 1 January 2017, and who met the proposed criteria when they started pertuzumab, to have funded access to pertuzumab from 1 January 2017.	Patients who were taking pertuzumab before 1 January 2017, and who met the proposed criteria when they started on pertuzumab and whose disease has not progressed while on pertuzumab, **will be eligible for funded pertuzumab from 1 January 2017**. • Applications for Special Authority waivers will be needed for these patients. • Applicants should manually complete the relevant Special Authority form, state the date that the patient started pertuzumab treatment, and confirm that the criteria that were met at the time and that the patient's disease has not progressed since. • Forms should be sent to waivers@pharmac.govt.nz or faxed to PHARMAC on 04 460-4995. The Special Authority form will be available on PHARMAC's website[2] from Wednesday 7 December **for waiver applications only**. It will also be available in the Special Authority form section of PHARMAC's website from the week before Christmas for regular applications.
Requests for patients who had already started on trastuzumab without pertuzumab before 1 January 2017 to have add-on funded pertuzumab from 1 January 2017.	Pertuzumab will not be funded for this patient group from 1 January 2017. This patient group differs from the Medsafe registered indication – pertuzumab is indicated in combination with trastuzumab and docetaxel for patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for their metastatic disease. We consider that we need clinical advice regarding the use of pertuzumab in patients who have been previously treated with trastuzumab before we could make a funding decision about this. We intend to seek this advice from the Pharmacology and Therapeutics Advisory Committee (PTAC) at its next meeting in February 2017.
Requests for patients who have had previous treatment for metastatic breast cancer, but who are currently off treatment, to have the option of funded pertuzumab from 1 January 2017.	Pertuzumab will not be funded for this patient group from 1 January 2017. As above, use of pertuzumab in this setting would not align with the Medsafe registered indication. We will seek PTAC's advice in February 2017 on the use of pertuzumab in this setting.
Requests for pertuzumab to be funded immediately, or immediately following a decision, rather than from 1 January 2017.	While we acknowledge the desire for eligible patients to start treatment with pertuzumab as soon as possible, the decision is that pertuzumab will be funded from 1 January 2017. We can confirm that any patient who starts on pertuzumab before this date and who met the proposed criteria when they were started pertuzumab and whose disease has not progressed whilst on pertuzumab, will be eligible for funded pertuzumab from 1 January 2017 as explained above.

[2] www.pharmac.govt.nz/news/notification-2016-12-05-multi-product-proposal/

Feedback theme	Comment
Concerns about DHB hospital infusion and related service capacity and the cost of the additional resources needed. Similar concerns were raised about other infusion treatments in the proposal – in particular for obinutuzumab and rituximab.	PHARMAC's assessments and economic analyses include costs to the health system, including costs to DHBs associated with compounding, administration and monitoring. We acknowledge that funding of the additional infusion treatments could result in a budget and resource impact for DHBs due to the service requirements associated with administration and monitoring of patients. We note that this is likely to be low compared with the overall DHB cost of all infusion services. We have provided DHBs with as much information as we can about our estimate of the service impacts of the proposal. We hope this will help DHBs with their budgeting and planning for services to deliver these treatments. We are committed to continuing to engage with various sector stakeholders regarding the impact on services from our funding proposals and decisions.

Obinutuzumab (Gazyva) – *for chronic lymphocytic leukaemia*

The proposed terms of listing, including commercial terms and Special Authority criteria, were approved as consulted on, with some minor changes to the Special Authority wording as explained in the consultation response section.

This means that obinutuzumab will be funded from 1 January 2017 for patients with chronic lymphocytic leukaemia who meet the following Special Authority criteria:

> PCT Only – Specialist – 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 adequate neutrophil and platelet counts (≥1.5 x 10^9/L and platelets ≥75 x 10^9/L) unless the cytopenias are a consequence of marrow infiltration by CLL; and
> 5. Patient has good performance status; and
> 6. Obinutuzumab to be administered at a maximum cumulative dose of 8,000 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. '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.

Consultation feedback

Responses were supportive of the proposal to fund obinutuzumab for chronic lymphocytic leukaemia.

Some responders had a number of queries and suggestions regarding the Special Authority criteria. Two minor suggested changes have been made as outlined below. We consider that clinical advice would be needed for more substantial changes and we would welcome funding submissions if responders consider that further changes are needed.

Feedback theme	Comment
The Special Authority criteria should be amended with regard to the neutrophil and platelet count requirements for patients with bone marrow dysfunction.	The criteria have been amended as requested.
The Special Authority criteria should be amended to include a description of 'good performance status'.	The criteria have been amended as requested.

Rituximab (Mabthera) *– for re-treatment of relapsed chronic lymphocytic leukaemia*

The proposed terms of listing, including commercial terms and Special Authority criteria, were approved as consulted on without any changes. This means that rituximab will be funded from 1 January 2017 for the re-treatment of relapsed chronic lymphocytic leukaemia for patients who meet the Special Authority criteria.

Consultation feedback

Responses were supportive of the proposal to fund rituximab for re-treatment of relapsed chronic lymphocytic leukaemia. Key issues raised by responders are outlined below, along with PHARMAC's comments.

Feedback theme	Comment
Rituximab should be funded for patients with chronic lymphocytic leukaemia who relapse within 36 months of prior treatment or who develop 17p deletion.	The approved criteria are in line with advice received from PTAC and CaTSoP regarding patients who would benefit most from further rituximab treatment. We welcome a funding application for widened access to rituximab for patients who relapse within 36 months. PTAC and CaTSoP have considered a funding application for rituximab for patients with 17p deletion and recommended it be declined. We welcome further submissions, should new significant evidence become available to support the use of rituximab for patients with 17p deletion CLL.
Measurement of the duration of remission as the interval between retreatment and the end of prior rituximab treatment (rather than the start of prior rituximab treatment).	As noted above, the proposed criteria are in line with clinical advice we received. We note that the definition of remission duration as 'a rituximab treatment-free interval' is consistent with the initial criteria for rituximab for CLL. We note the publication provided by the responder, and we will seek advice on this from CaTSoP at its next meeting.

Rituximab (Mabthera) *– for hairy cell leukaemia*

The proposed terms of listing were approved as consulted on, but some changes to the Special Authority criteria have been made as shown below – this involves an amendment to the current criteria for indolent, low-grade lymphomas rather than a new set of criteria for hairy cell leukaemia.

These changes are in line with recent advice from the Cancer Treatments Subcommittee of PTAC (CaTSoP) and will provide funded access to a wider patient population than the criteria consulted on.

This means that rituximab will be funded from 1 January 2017 for patients with hairy cell leukaemia who meet the following Special Authority criteria (changes from the current criteria for indolent, low-grade lymphomas are shown as additions in bold and deletions in strikethrough):

> PCT Only – Specialist – Special Authority for Subsidy
> Initial application - (Indolent, Low-grade lymphomas **or 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:
> Either:
> 1. Both:
>   1.1. The patient has indolent low grade NHL **or hairy cell leukaemia*** with relapsed disease following prior chemotherapy; and
>   1.2. To be used for a maximum of 6 treatment cycles; or
> 2. Both:
>   2.1. The patient has indolent, low grade lymphoma **or hairy cell leukaemia*** requiring first-line systemic chemotherapy; and
>   2.2. To be used for a maximum of 6 treatment cycles.
>
> Renewal - (Indolent, Low-grade lymphomas **or 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 indolent, low-grade NHL **or hairy cell leukaemia*** with relapsed disease following prior chemotherapy; and
> 3. To be used for no more than 6 treatment cycles.
>
> Note: 'Indolent, low-grade lymphomas' includes follicular, mantle, marginal zone and lymphoplasmacytic/Waldenstrom macroglobulinaemia. ~~Rituximab is not funded for Chronic lymphocytic leukaemia/small lymphocytic lymphoma.~~ ***Hairy cell leukaemia includes hairy cell leukaemia variant *Unapproved indication.**

Consultation feedback

Responses were supportive of the proposal to fund rituximab for patients with hairy cell leukaemia.

Trastuzumab (Herceptin) – *for metastatic breast cancer*

The proposed terms of listing, including commercial terms and the intent of the changes to the initial Special Authority criteria for metastatic breast cancer (ie to allow for the use of trastuzumab in combination with pertuzumab), were approved as consulted on, but there were some changes to the layout of the Special Authority.

In addition, similar changes were approved for the renewal criteria for the indication of early breast cancer, which provide for the use of trastuzumab in metastatic breast cancer where the patient has previously been treated with trastuzumab for early breast cancer. The latter changes were not included in the consultation letter but are necessary to allow the concomitant use of pertuzumab in this patient group.

This means that from 1 January 2017 the Special Authority for trastuzumab (Herceptin) will be amended to allow for the use of pertuzumab with trastuzumab in patients who have not previously received treatment for their metastatic disease as outlined below. Similar changes will apply to the hospital restrictions.

The initial Special Authority criteria for trastuzumab for the indication of metastatic breast cancer will be replaced with the following criteria from 1 January 2017:

> 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:
> 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 The patient has not previously received lapatinib treatment for HER-2 positive metastatic breast cancer; or
> 2.2 Both:
> 2.2.1 The patient started lapatinib treatment for metastatic breast cancer but discontinued lapatinib within 3 months of starting treatment due to intolerance; and
> 2.2.2 The cancer did not progress whilst on lapatinib; and
> 3. Either:
> 3.1 Trastuzumab will not be given in combination with pertuzumab; or
> 3.2 All of the following:
> 3.2.1 Trastuzumab to be administered in combination with pertuzumab; and
> 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
> 3.2.3 The patient has good performance status (ECOG grade 0-1); and
> 4. Trastuzumab not to be given in combination with lapatinib; and
> 5. Trastuzumab to be discontinued at disease progression.

The renewal Special Authority criteria for trastuzumab for the indication of early breast cancer will be replaced with the following criteria from 1 January 2017:

> Renewal– (early 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 patient received prior adjuvant trastuzumab treatment for early breast cancer; and
> 3. Any of the following:
> 3.1 The patient has not previously received lapatinib treatment for HER-2 positive metastatic breast cancer; or
> 3.2 Both:
> 3.2.1 The patient started lapatinib treatment for metastatic breast cancer but discontinued lapatinib within 3 months of starting treatment due to intolerance; and
> 3.2.1.1 The cancer did not progress whilst on lapatinib; or
> 3.3 The cancer has not progressed at any time point during the previous 12 months whilst on trastuzumab; and
> 4. Either:

4.1 Trastuzumab will not be given in combination with pertuzumab; or
4.2 All of the following:
4.2.1 Trastuzumab to be administered in combination with pertuzumab; and
4.2.2 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
4.2.3 The patient has good performance status (ECOG grade 0-1); and

5. Trastuzumab not to be given in combination with lapatinib; and
6. Trastuzumab to be discontinued at disease progression.

Note: *For patients with relapsed HER-2 positive disease who have previously received adjuvant trastuzumab for early breast cancer.

Consultation feedback

No responses relating to this part of the proposal were received.

Erlotinib (Tarceva) – *for non-small cell lung cancer*

The proposed terms of listing, including commercial terms and changes to the Special Authority restrictions, were approved as consulted on without any changes.

This means that from 1 April 2017 the criteria for erlotinib will be amended to allow patients currently on funded gefitinib to change to funded erlotinib for reasons other than intolerance. Note that this will only be implemented if gefitinib is not fully funded at 1 April 2017 (see 'Reference pricing gefitinib (Iressa)' section below).

Consultation feedback

No responses relating to this part of the proposal were received.

Reference pricing gefitinib (Iressa) – *for non-small cell lung cancer*

The proposed reduction in subsidy for gefitinib to the level of the new subsidy for erlotinib, via the application of reference pricing, was approved as consulted on without any changes.

This means that from 1 April 2017, if the supplier of gefitinib (AstraZeneca) does not reduce the price to match the new subsidy, a manufacturer's surcharge will apply to gefitinib and patients will need to change to erlotinib in order to remain on a fully funded product. The manufacturer's surcharge is likely to be in the region of a $1,000 per month cost to patients, taking into account GST and other pharmacy/wholesaler markups.

Note that the recommended daily dose of erlotinib is 150 mg taken at least one hour before or two hours after ingesting food; whereas the recommended dose of gefitinib is one 250 mg tablet once a day, taken with or without food***. It will be very important for clinicians to highlight this difference to any patients changing from gefitinib to erlotinib.***

Consultation feedback

Responses noted or supported the proposal; one responder had queries of a commercial nature and we have communicated with this responder separately.

Respiratory

Pirfenidone (Esbriet) *– for idiopathic pulmonary fibrosis*

The proposed terms of listing, including commercial terms and Special Authority criteria, were approved as consulted on without any changes. This means that pirfenidone will be funded from 1 January 2017 for patients with idiopathic pulmonary fibrosis who meet the Special Authority criteria.

Consultation feedback

Responses were supportive of the proposal to fund pirfenidone for idiopathic pulmonary fibrosis. Key issues raised by responders are outlined below, along with PHARMAC's comments.

Feedback theme	Comment
A diagnosis of idiopathic pulmonary fibrosis should be made by a multidisciplinary team, not just a respiratory physician.	We agree that diagnosis by a multidisciplinary team is important. We note that the Special Authority criteria do not require the diagnosis to be made by respiratory physician; however, the Special Authority funding application can only be made by a respiratory physician.
Queries as to whether the National Institute for Health and Care Excellence (NICE) treatment guidelines, on which the Special Authority criteria were based, had been reviewed recently.	NICE's 2013 technology appraisal guidance was reviewed by NICE in 2016 following feedback from the supplier. The review considered including people with a forced vital capacity (FVC) above 80% predicted and removing the stopping criteria, but no changes to the NICE criteria were recommended.
Objections to the use of FVC measures in both the initial and renewal criteria.	We note that pirfenidone is a very expensive treatment and would be the first funded treatment in New Zealand for a condition that is challenging to diagnose. We recognise that there are concerns regarding the use of lung function measures for both starting and stopping criteria. At this early stage we have followed the NICE UK treatment guidelines and the Global Lung Initiative definition of disease decline. We are open to amending the criteria as appropriate, following clinical review by the relevant clinical advisory committees. We intend to seek updated clinical advice once New Zealand has some experience with funded pirfenidone and following the availability of a Statement for Treatment from the Thoracic Society of Australia and New Zealand.

Dornase alfa (Pulmozme) *– for patients with cystic fibrosis under the age of 5 years*

The proposed terms of listing, including commercial terms and Special Authority criteria, were approved as consulted on without any changes. This means that dornase alfa will be funded from 1 January 2017 for patients with cystic fibrosis under the age of 5 years who meet the Special Authority criteria, on application to the Cystic Fibrosis Panel.

Consultation feedback

Responses were generally supportive of the proposal to fund dornase alfa for patients with cystic fibrosis under the age of 5 years. One responder raised an issue which is outlined below, along with PHARMAC's comments.

Feedback theme	Comment
Applicants (applying for dornase alfa Special Authorities for these younger children) should not be restricted to specialist physicians/paediatricians.	There is no restriction on the type of clinician that can apply for the Special Authority – applications could be made by any prescriber type; all applications are assessed by the Cystic Fibrosis Panel.

Rheumatology/Immunosuppressants

Rituximab (Mabthera) *– for patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis*

The proposed hospital restrictions were approved as consulted on without any changes. This means that from 1 January 2017 patients with myeloperoxidase (MPO)-ANCA positive vasculitis will no longer be required to trial mycophenolate mofetil before having funded access to rituximab.

Consultation feedback

Responses were supportive of the proposal to remove the requirement to try mycophenolate mofetil prior to rituximab in patients with MPO-ANCA. Key issues raised by responders are outlined below, along with PHARMAC's comments.

Feedback theme	Comment
The cumulative dose of cyclophosphamide in criterion 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") should be adjusted for the paediatric/adolescent cohort, using a g/m^2 cut-off, as opposed to total dose, because of male fertility concerns; recommended cut-off at 4 g/m^2 (not the 15 g cut-off).	The original 15 g limit relates to haematological and urological toxicities, not the impact on fertility. Fertility is addressed in criterion 4.4 (where part of the eligibility criteria is that "Patient is a female of child-bearing potential; or"), and access to rituximab in this setting is limited to females of child-bearing potential. This is as per PTAC's advice at the time. PTAC noted that extending this to include males at risk of fertility issues would pose a significant financial risk. As such, we consider that the limit proposed does not align with the intent of criterion 4.2. We intend to seek clinical advice on this from PTAC when it next meets in February 2017.

Tocilizumab (Actemra) *– for patients with polyarticular juvenile idiopathic arthritis (pJIA), idiopathic multicentric Castleman's disease (iMCD) and rheumatoid arthritis*

The proposed terms of listing, including commercial terms and hospital restrictions, were approved as consulted on, with one minor change to the criteria for iMCD to permit 3-4

weekly dosing of tocilizumab at 8 mg/kg rather than requiring a minimum of 4-weekly dosing intervals.

This means that from 1 January 2017 tocilizumab will be funded for patients with pJIA and iMCD who meet the hospital restrictions and the requirement to trial rituximab prior to tocilizumab in patients with seronegative rheumatoid arthritis will be removed.

Consultation feedback

Responses were generally supportive of the proposals for tocilizumab for patients with pJIA, iMCD and seronegative rheumatoid arthritis. Key issues raised by responders are outlined below, along with PHARMAC's comments.

Theme	Comment
Treatment of pJIA with tocilizumab should be started by a "paediatric rheumatologist or rheumatologist on the recommendation of a paediatric rheumatologist", rather than by a "rheumatologist", because these patients should be under the care of the multi-disciplinary NZ Paediatric Rheumatology Service.	We note that all paediatric rheumatologists are rheumatologists, and we consider that it is up to the clinician to determine the best point of care for their patients. We also note that it is possible for a patient to be over the age of 18 years and have a diagnosis of pJIA (from when they were younger), in which case it would be unlikely that they would remain under the care of the NZ Paediatric Rheumatology Service.
Patients with pJIA should be required to trial etanercept or adalimumab but not both.	The approved criteria for pJIA, which require a trial of both etanercept and adalimumab, are in line with those recommended by PTAC. In particular, we note that the Committee considered that it would be reasonable to require a trial of both etanercept and adalimumab prior to accessing tocilizumab, taking into account the clinical benefits and risks of the treatments and the costs associated with community TNF alpha inhibitors and tocilizumab. We note that if it was not possible or clinically appropriate to trial a second TNF inhibitor, an HML waiver could be sought.
In the indication of iMCD, more frequent dosing should be permitted (ie more frequent than 8 mg/kg every 4 weeks), as this is occasionally needed to maintain efficacy.	After considering this feedback, we have changed the criteria to permit 3-4 weekly dosing in this indication.

Theme	Comment
One responder considered that tocilizumab should not be funded for iMCD because it is an unregistered indication, the supporting data is poor and there is already a funded alternative treatment (ie. siltuximab) which is registered for iMCD and has better supporting data. If tocilizumab is funded, it should be restricted to second-line use following siltuximab.	We received separate feedback (during consultation on PHARMAC's proposal to fund siltuximab) that agents such as siltuximab may lose their efficacy in a significant number of patients, for example because of development of anti-drug antibodies. Given the potential for an interfering anti-drug antibody to develop against siltuximab, with resulting loss of efficacy, responders asked that PHARMAC remain open to funding the use of alternative therapies that target the IL-6/IL-6 receptor pathway. Further, we note that PTAC has recommended that tocilizumab be funded for iMCD (with a low priority). We consider that restricting tocilizumab to second-line use following siltuximab is unnecessary, taking into account the relative cost of the two treatments and the likelihood that clinicians in the first instance would opt for the registered product with the better evidence base.