3 September 2010

Approval of proposal for Roche Oncology and Immunosuppressant Bundle

PHARMAC is pleased to announce the approval of a proposal that was the subject of a consultation letter dated 30 July 2010.

In summary, the effect of the decision is that from 1 October 2010:

1. erlotinib (Tarceva) will be funded for the second line treatment of patients with advanced, unresectable, Non Small Cell Lung Cancer; and
2. funded access to rituximab (Mabthera) will be widened for patients with Non Hodgkins Lymphoma; and
3. funded access to capecitabine (Xeloda) will be widened for patients with colorectal cancer; and
4. funded access to mycophenolate mofetil (Cellcept) will be widened for more transplant recipients and patients with autoimmune diseases that have not responded to other standard immunosuppressant treatments,

This decision is expected to result in approximately 700 new patients having access to these treatments each year.

Further details of the decision and feedback can be found below and on the following pages.

Details of the decision

Tarceva (erlotinib)

- From 1 October 2010 Tarceva will be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule at the following prices and subsidies (ex-manufacturer, excluding GST):

Pharmaceutical	Brand	Form and Strength	Pack Size	Proposed price and subsidy
Erlotinib hydrochloride	Tarceva	Tab 100 mg	30	$3,100.00
Erlotinib hydrochloride	Tarceva	Tab 150 mg	30	$3,950.00

- The listing of Tarceva in Section B of the Pharmaceutical Schedule will be subject to the following Special Authority restriction:

> **Erlotinib - Retail Pharmacy – Specialist - 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 advanced, unresectable, Non Small Cell Lung Cancer (NSCLC); and
> 2. Patient has documented disease progression following treatment with first line platinum based chemotherapy; and
> 3. Erlotinib is to be given for a maximum of 3 months.

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

Renewal application 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.

- Tarceva will be subject to a confidential rebate which would reduce the net price and subsidy paid by the Funder.
- Tarceva will have protection from subsidy reduction and delisting until 31 December 2013.

Mabthera (rituximab)

- From 1 October 2010 the Special Authority criteria applying to the listing of rituximab in Section B of the Pharmaceutical Schedule will be amended to read as follows:

Rituximab – PCT only – Specialist - Special Authority for Subsidy
Initial application — (Post-transplant) 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 B-cell post-transplant lymphoproliferative disorder*; and
2 To be used for a maximum of 8 treatment cycles.

Initial application — (Indolent, Low-grade lymphomas) 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 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 requiring first-line systemic chemotherapy; and
2.2 To be used for a maximum of 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.

Initial application — (Aggressive CD20 positive NHL) 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
1 All of the following:
1.1 The patient has treatment-naive aggressive CD20 positive NHL; and
1.2 To be used with a multi-agent chemotherapy regimen given with curative intent; and
1.3 To be used for a maximum of 8 treatment cycles; or
2 Both:
2.1 The patient has aggressive CD20 positive NHL with relapsed disease following prior chemotherapy; and
2.2 To be used for a maximum of 6 treatment cycles.
Note: 'Aggressive CD20 positive NHL' includes large B-cell lymphoma and Burkitt's lymphoma/leukaemia

Renewal — (Post-transplant) 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 B-cell post-transplant lymphoproliferative disorder*; and
3 To be used for no more than 6 treatment cycles.

Renewal — (Indolent, Low-grade lymphomas) 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 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.

Renewal — (Aggressive CD20 positive NHL) 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 had a rituximab treatment-free interval of 12 months or more; and
2 The patient has relapsed refractory/aggressive CD20 positive NHL; and
3 To be used with a multi-agent chemotherapy regimen given with curative intent; and
4 To be used for a maximum of 4 treatment cycles.

Note: 'Aggressive CD20 positive NHL' includes large B-cell lymphoma and Burkitt's lymphoma/leukaemia

Note: Indications marked with * are Unapproved Indications.

- The confidential rebate currently applying to Mabthera will be increased which will reduce the net price and subsidy paid by the Funder.
- Mabthera will have protection from subsidy reduction and delisting until 31 December 2013.

Xeloda (capecitabine)

- From 1 October 2010 the Special Authority criteria applying to the listing of Xeloda in Section B of the Pharmaceutical Schedule will be amended to read as follows:

Capecitabine - Retail Pharmacy – Specialist - Special Authority for Subsidy
Initial application 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:
Any of the following:

1 The patient has advanced gastrointestinal malignancy; or
2 The patient has metastatic breast cancer; or
3 The patient has stage III (Dukes' stage C) colorectal*# cancer and has undergone surgery; or
4 All of the following:
    4.1 The patient has stage II (Dukes' stage B) colorectal* cancer and has undergone surgery; and
    4.2 Any of the following:
        4.2.1 the patient has stage T4 disease; or

4.2.2 the patient has vascular invasion; or
4.2.3 Fewer than 10 lymph nodes were examined at resection; or

5 All of the following:
5.1 The patient has locally advanced (clinically or radiologically staged T3/T4: N0,1,2) rectal cancer; and
5.2 Surgery is planned; and
5.3 Capecitabine to be given prior to surgery (neoadjuvant); and
5.4 Capecitabine to be given at a maximum dose of 825 mg/m^2 twice daily in combination with radiation therapy for a maximum of 6 weeks; or

6 Both:
6.1 The patient has poor venous access or needle phobia*; and
6.2 The patient requires a substitute for single agent fluoropyrimidine*.

Renewal 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:
1 The patient requires continued therapy; or
2 The tumour has relapsed and requires re-treatment.
Note indications marked with * are Unapproved Indications, #capecitabine is approved for stage III (Dukes' stage C) colon cancer.

- The confidential rebate currently applying to Xeloda will be increased which will reduce the net price and subsidy paid by the Funder.
- Xeloda will have protection from subsidy reduction and delisting until 31 December 2013.

Cellcept (mycophenolate mofetil)

- From 1 October 2010 the prices and subsidies applying to the listing of Cellcept tablets and capsules in Section B and Part II of Section H of the Pharmaceutical Schedule will be reduced as follows (ex-manufacturer, excluding GST):

Pharmaceutical	Brand	Form and Strength	Pack Size	Current price and subsidy	Proposed price and subsidy
Mycophenolate Mofetil	Cellcept	Tab 500 mg	50	$206.66	$70.00
Mycophenolate Mofetil	Cellcept	Cap 250 mg	100	$206.66	$70.00

- From 1 October 2010 the Special Authority criteria applying to the listing of Cellcept tab 500 mg and cap 250 mg in Section B of the Pharmaceutical Schedule will be amended to read as follows:

Mycophenolate mofetil - Special Authority for Subsidy
Initial application only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid without further renewal unless notified for applications meeting the following criteria:
Either:
1 Transplant recipient; or
2 Both:
Patients with diseases where
2.1 Steroids and azathioprine have been trialled and discontinued because of unacceptable side effects or inadequate clinical response; and

2.2 Either:

Patients with diseases where

2.2.1 Cyclophosphamide has been trialled and discontinued because of unacceptable side effects or inadequate clinical response; or

2.2.2 Cyclophosphamide treatment is contraindicated.

- Cellcept will have protection from subsidy reduction and delisting until 30 June 2012.

Feedback received

We appreciate all of the feedback that we received and acknowledge the time people took to respond. All consultation responses received by 13 August 2010 were considered in their entirety in making a decision on the proposal. Consultation feedback on the proposal was generally supportive; however, some respondents requested changes to the proposed Special Authority and/or access to other patient groups. The following key issues were raised in relation to specific aspects of the proposal:

Theme	Comment
Erlotinib	
The proposed initial 2 months treatment period for erlotinib is too short to adequately assess response to treatment. Recommended that the initial treatment period be extended to 3 months with ongoing treatment beyond 3 months requiring CT scan confirmation of non progression.	We considered that 2 months may indeed be too short. Therefore, the Special Authority for initial application for erlotinib was amended to allow a maximum of 3 rather than 2 months of treatment, and the initial approval period was extended from 3 to 4 months. We considered that although ideally a CT scan should be used to assess treatment response and continuation of treatment in some cases a CT scan may not be available and/or an oncologist may be able to adequately assess treatment response using xray alone. Therefore, the renewal criteria was amended to include a statement that radiological assessment should preferably include a CT scan.
Requests that expensive drugs such as erlotinib should be funded Original Pack (full pack). The drugs should also be supplied in practical pack sizes to help with dispensing.	We consider that the pack size for erlotinib is practical, most patients would be dispensed one pack per month, and a pack contains 30 days of treatment. However, it is not possible to have 'standard' pack sizes for capecitabine, rituximab or mycophenolate as the dosing differs depending on indication, and in the case of capecitabine and rituximab body size. We acknowledge that there are several problems with the current dispensing arrangements for high cost medicine, one of which is the potential for community pharmacies to be left with unsold part-packs. As part of the Pharmaceutical Subsidy Eligibility and Delivery review that was started last year, we are working through these issues and hope to be able to achieve resolution to this problem.
Rituximab	

Theme	Comment
Requests for additional cycles of rituximab treatment to be funded for various NHL patient groups.	The proposed Special Authority criteria for rituximab were based on the recommendations from the Cancer Treatments Subcommittee of PTAC (CaTSoP). We note that in the proposed criteria for rituximab Initial application — (Indolent, Low-grade lymphomas) incorrectly stated 'To be used for a maximum of 4 treatment cycles.', this was corrected to 'To be used for a maximum of 6 treatment cycles', as per the CaTSoP recommendation for this patient group. CaTSoP have considered increasing the number of funded cycles from 6 to 8 in treatment-naïve, rituximab-naïve indolent NHL patients. One study used of R-CVP chemotherapy (rituximab-cyclophosphamide, vincristine and prednisone) which is given for 8 cycles, however, CaTSoP considered that this regimen was not frequently used, or was not as effective, as the more commonly used R-CHOP regimen (rituximab plus cyclophosphamide, doxorubicin and vincristine) which is administered for 6 cycles. In the re-treatment of relapsed aggressive disease setting CaTSoP recommended that rituximab be funded as part of a chemotherapy regimen given with curative intent including a planned stem cell or bone marrow transplant. In this setting rituximab is given for 4 cycles.
How should doctors apply for funding for patients with transformed NHL, i.e those who are initially diagnosed with indolent NHL who then go on to present with aggressive NHL or vice versa?	The new criteria would permit transformed patients to be re-treated through renewal application - in the case of a patient who transformed from indolent to aggressive NHL the doctor would need to make a renewal-aggressive CD20 positive NHL application. In the case of a patient who transforms from aggressive to indolent NHL the doctor would be able to make a renewal-indolent, low grade Lymphoma application.
Rituximab should be funded for patients with Chronic Lymphocytic Leukemia (CLL).	PHARMAC received an application from the supplier Roche for the funding of rituximab for CLL in March 2010. This application is still undergoing clinical assessment and has not yet been prioritised.

Theme	Comment
Rituximab should be funded for maintenance therapy for the management of relapsed NHL.	The issue of maintenance therapy was briefly discussed by CaTSoP in 2007, CaTSoP did not consider it had sufficient information at that time to make a recommendation. We note that the funding of maintenance therapy would likely be a considerable cost and therefore prior to making such a funding decision we would need to carefully consider the relevant evidence, budget impact and cost effectiveness. To date we have not received a specific funding application for rituximab maintenance therapy but we would welcome such an application from clinicians or the supplier.
Capecitabine	
Request that in criterion 4.2.2 for the Capecitabine initial application Special Authority for high risk stage II disease, "serosal cancer deposits" should be removed because under the current colorectal cancer staging system these are considered to represent discontinuous spread via vascular invasion with extra-vascular spread; or a totally replaced lymph node, both cases would be considered node positive stage III disease.	We agreed, therefore, the Special Authority for capecitabine was amended accordingly.

Although no responders to consultation on this Roche proposal specifically commented on the mycophenolate (Cellcept) part of the proposal, PHARMAC received a number of comments in response to a previous consultation on the listing of Douglas' brand of mycophenolate (Myaccord) under the same Special Authority criteria as were proposed for Cellcept. Therefore, we considered these responses as relevant to the consideration of this proposal. Accordingly, some changes were made to the Special Authority criteria that will apply to both Myaccord and Cellcept. For details please of these changes see the notification letter dated 2 September 2010 for the decision on funding Myaccord

(https://pharmac.govt.nz/2010/09/03/2010-08-03%20notification%20of%20decision%20on%20Myaccord%20proposal.pdf).

More information

If you have any questions about this decision, you can call our toll free number (9 am to 5 pm, Monday to Friday) on 0800 66 00 50.