NOTIFICATION

PHARMAC
Pharmaceutical Management Agency

5 July 2012

Approval of proposal for Tyrosine Kinase Inhibitors for Non Small Cell Lung Cancer

PHARMAC has approved the proposal to fund gefitinib (Iressa) and to amend the Special Authority criteria applying to erlotinib (Tarceva). This was the subject of a consultation letter dated 31 May 2012.

In summary, the effect of the decision is that:

- from 1 August 2012, gefitinib (Iressa) will be funded as a first line treatment for patients with locally advanced, or metastatic, unresectable, non-squamous non small cell lung cancer (NSCLC) expressing activating mutations in Epidermal Growth Factor Receptor (EGFR) tyrosine kinase.
- from 1 January 2014, the funding criteria for erlotinib (Tarceva) will be amended such that it will no longer be funded as a second line treatment option for patients with NSCLC disease known to be negative for activating mutations of EGFR tyrosine kinase.

Patients with advanced non-squamous NSCLC will need to undergo testing for the presence of activating mutations of EGFR tyrosine kinase in order to access funding for tyrosine kinase inhibitors.

Overall, this funding decision is expected to reduce the total number of patients accessing funded tyrosine kinase inhibitors; however, because treatment choices will be targeted to those patients most likely to benefit and funded access to a tyrosine kinase inhibitor will be earlier than is currently funded, it is expected to result in a small increase in overall health gains for NSCLC patients.

Details of the decision

In relation to gefitinib (Iressa):

- Iressa 250 mg tablets will be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 August 2012.

- The following prices and subsidies will apply (all prices are ex-manufacturer and exclude GST):

Brand	Pharmaceutical	Presentation	Pack size	Price and subsidy
Iressa	gefitinib	tab 250 mg	30	$1,700.00

- Iressa will be funded subject to Special Authority criteria as follows:

Gefitinib - Retail Pharmacy – Specialist - Special Authority
Special Authority for Subsidy

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

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:
Either:

1. All of the following:
   1.1 Patient has treatment naïve locally advanced, or metastatic, unresectable, non-squamous Non Small Cell Lung Cancer (NSCLC); and
   1.2 There is documentation confirming that disease expresses activating mutations of EGFR tyrosine kinase; and
   1.3 Gefitinib is to be given for a maximum of 3 months; or
2. The patient received gefitinib treatment prior to 1 August 2012 and radiological assessment (preferably including CT scan) indicates NSCLC has not progressed.

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.

- Gefitinib will be listed on the National Preferred Medicine List (PML) from the date of its implementation (currently estimated to be 1 July 2013). Any restrictions in the PML applying to the prescribing and dispensing of gefitinib will be no more restrictive than those applying to the listing of gefitinib in Section B of the Pharmaceutical Schedule.

- Iressa will have subsidy and delisting protection until 1 January 2015.

In relation to erlotinib (Tarceva):

- Erlotinib hydrochloride (Tarceva) 100 mg and 150 mg tablets will remain listed in Section B and in Part II of Section H of the Pharmaceutical Schedule at the current prices and subsidies.

- Tarceva will remain subject to a confidential rebate which reduces the net price and subsidy paid by the Funder.

- Tarceva will maintain its current subsidy and delisting protection until 31 December 2013.

- The Special Authority criteria applying to all presentations of Tarceva in Section B of the Pharmaceutical Schedule will be amended as follows from 1 January 2014 (additions in bold):

Erlotinib hydrochloride - Retail Pharmacy – Specialist - Special Authority
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 Either:
3.1 All of the following
3.1.1 The patient has non-squamous NSCLC; and

3.1.2 Documentation confirming that disease expresses activating mutations of EGFR tyrosine kinase; and
3.1.3 The patient has not received prior treatment with gefitinib; or

3.2 Insufficient biopsy sample available to determine EGFR mutation status or precise histological type; and

4 Erlotinib is to be given for a maximum of 3 months.

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.

Feedback received

We appreciate all of the feedback that we received and acknowledge the time people took to respond. All consultation responses received by 14 June 2012 were considered in their entirety in making a decision on the proposal. In general, most responders supported the proposal. Key issues raised and PHARMAC comments on these issues are discussed below:

Theme	PHARMAC Comment
A number of laboratory testing/kit providers responded to consultation. They were all supportive of the proposal. The responses mainly focused on their view of the different methods of sampling and EGFR testing and logistical considerations of delivering and funding EGFR testing services in New Zealand	The responses demonstrate that there are a number of parties in NZ who are capable of providing EGFR testing services in New Zealand. Therefore, we consider that the current lack of a national testing service in NZ is not a barrier to DHBs implementing the funding of gefitinib and erlotinib as proposed. These responses have been provided to the National Health Committee (NHC), which is developing advice around EGFR testing. We note that the NHC has recently published a rapid review of EGFR testing for the purposes of seeking feedback from the sector (www.nhc.health.govt.nz)
One responder, who supported the proposal, asked who would fund the EGFR testing	The funding proposal will be cost saving to DHBs even taking into account the costs of funding EGFR testing. Therefore, we consider it would be appropriate for DHBs to fund EGFR testing.

Theme	PHARMAC Comment
Two responders requested that the funding of both gefitinib and erlotinib be extended to all locally advanced, or metastatic, unresectable, NSCLC patients that test positive for EGFR mutations, noting that although EGFR activating mutations are less common in squamous cell carcinomas (3%), they do occur and squamous histology *per se* should not exclude people with them from receiving treatment with an EGFR tyrosine kinase inhibitor.	In populations with low mutation rates there is high risk of EGFR negative patients being falsely reported as positive. We consider that since patients with squamous disease are more likely to be disadvantaged (because of the higher likelihood of a false positive result compared with a true positive result) rather than advantaged by EGFR testing and gefitinib treatment, it would not be appropriate to widen funding for TKIs (and by inference EGFR testing) to squamous NSCLC patients at this time. We would be happy to reconsider funding the Squamous NSCLC group should the specificity and sensitivity of EGFR testing improve to the point where the risk of a false positive result in this population is significantly reduced to a point where these patients are more likely to be advantaged rather than disadvantaged.
One responder considered that EGFR and ALK* testing should be publicly available for all lung cancer cases. **Anaplastic lymphoma kinase tyrosine kinase*	It is our view that where the results of testing are needed for decision making in relation to publically funded treatments for a patient it is appropriate that such testing be provided. However, where the results have no direct effect on a decision in relation publically funded treatment choices for a patient the value of such testing is questionable. Gefitinib and erlotinib funding is to be limited to treatment naïve locally advanced, or metastatic, unresectable, non-squamous NSCLC patients (whose disease expresses activating mutations in EGFR), therefore, we consider that EGFR testing should be limited to this patient group. Currently there are no publically funded ALK-inhibitor treatments, therefore, we do not consider that publically funding ALK testing is appropriate at this time.

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.