CONSULTATION

PHARMAC
Pharmaceutical Management Agency

26 February 2015

Proposal to fund abiraterone, list additional presentations of epoetin alfa and reduce expenditure on methylphenidate hydrochloride extended release and topiramate

PHARMAC is seeking feedback on a provisional agreement with Janssen-Cilag Pty Ltd. In summary, this proposal is, from 1 May 2015, to:

- Fund abiraterone acetate (Zytiga) 250 mg tablets for patients with metastatic castration resistant prostate cancer;
- List two additional presentations of epoetin alfa (Eprex) – Inj 8,000 iu in 0.8 ml syringe and Inj 40,000 iu in 1 ml syringe; and
- Reduce the net cost of methylphenidate hydrochloride extended-release tablets (Concerta) and topiramate tablets and sprinkle capsules (Topamax).

Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **5pm Thursday, 12 March 2015** to:

Jackie Evans
Senior Therapeutic Group Manager
PHARMAC
PO Box 10 254
Wellington 6143

Email: jackie.evans@pharmac.govt.nz

Fax: 04 460 4995

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.

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

Details of the proposal

In relation to Zytiga

- Abiraterone acetate (Zytiga) 250 mg tablets would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 May 2015. The following price and subsidy would apply (all prices are ex-manufacturer and exclude GST):

Chemical	Presentation	Brand	Pack size	Price/Subsidy
Abiraterone acetate	Tab 250 mg	Zytiga	120	$4,276.19

- Confidential rebates would apply to Zytiga, reducing its net price to the Funder and/or DHB Hospitals.

- Abiraterone acetate (Zytiga) would be listed in Section B of the Pharmaceutical Schedule subject to Special Authority criteria as follows:

Abiraterone acetate – Retail Pharmacy - Specialist - Special Authority for Subsidy

Initial Application

Applications only from a Medical Oncologist, Radiation Oncologist or Urologist or any other medical practitioner on the recommendation of a Medical Oncologist, Radiation Oncologist or Urologist. Approvals valid for 6 months for applications meeting the following criteria:

All of the following:

1. Patient has prostate cancer; and
2. Patient has metastases; and
3. Patient's disease is castration resistant; and
4. Either:
   - 4.1. All of the following:
     - 4.1.1. Patient is symptomatic; and
     - 4.1.2. Patient has disease progression after anti-androgen therapy withdrawal; and
     - 4.1.3. Patient has good performance status (ECOG performance score of 0-1); and
     - 4.1.4. Patient has not had prior treatment with taxane chemotherapy; or
   - 4.2. All of the following:
     - 4.2.1. Patient's disease has progressed following prior chemotherapy containing a taxane; and
     - 4.2.2. Patient has not had prior treatment with abiraterone.

Renewal Application

Applications only from a Medical Oncologist, Radiation Oncologist or Urologist or any other medical practitioner on the recommendation of a Medical Oncologist, Radiation Oncologist or Urologist. Approvals valid for 6 months for applications meeting the following criteria:

All of the following:

1. No evidence of clinical disease progression;
2. No initiation of taxane chemotherapy with abiraterone; and
3. The treatment remains appropriate and the patient is benefiting from treatment.

- Abiraterone acetate (Zytiga) would be listed in Part II of Section H of the Pharmaceutical Schedule, subject to restrictions similar to the proposed Special Authority criteria above for Section B.

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

In relation to Eprex

- Two additional presentations of epoetin alfa (Eprex) would be listed in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 May 2015 as follows (all prices are ex-manufacturer and exclude GST):

Chemical	Presentation	Brand	Pack size	Price/Subsidy
Epoetin alfa [erythropoietin alfa]	Inj 8,000 iu in 0.8 ml , syringe	Eprex	6	$352.69
Epoetin alfa [erythropoietin alfa]	Inj 40,000 iu in 1 ml syringe	Eprex	1	$263.45

- The subsidy rules that currently apply to the other strengths of Eprex would also apply to these new listings, including Special Authority, wastage claimable and Sole Subsidised Supply.

- Confidential rebates would also apply to these presentations of Eprex, reducing its net price to the Funder and/or DHB Hospitals.

In relation to Concerta

- There would be no change to the listings of methylphenidate hydrochloride extended-release tablets (Concerta) in Section B and in Part II of Section H of the Pharmaceutical Schedule.

- From 1 July 2015 new confidential rebates would apply to all strengths of Concerta, reducing its net price to the Funder and/or DHB Hospitals.
- Concerta would have protection from subsidy reduction and delisting until 30 June 2018.

In relation to Topamax

- There would be no change to the listings of topiramate (Topamax) tablets and sprinkle capsules in Section B and in Part II of Section H of the Pharmaceutical Schedule.

- From 1 July 2015 new confidential rebates would apply to all strengths of Topamax, reducing its net price to the Funder and/or DHB Hospitals.
- Topamax would have protection from subsidy reduction and delisting until 30 June 2018.

Background

Prostate Cancer

Prostate cancer is the most commonly registered cancer in New Zealand men accounting for around 1/3 of all cancer registrations, and is the third most common cause of cancer death after lung cancer and bowel cancer. Approximately 3,000 men present with prostate cancer each year and around 600 men die each year of the disease. Whilst prostate cancer registrations are significantly lower for Māori men than for non-Māori, Māori men have prostate cancer mortality rates almost twice that of non-Māori. Mortality rates for prostate cancer also show a general increase with increasing deprivation.

The clinical behavior of prostate cancer ranges from a microscopic, well-differentiated tumor that may never be clinically significant to aggressive, high grade cancer that ultimately causes metastases, morbidity, and death.

Prostate cancer is characterised by androgen-stimulated growth and early treatment options include surgery, radiation therapy and androgen blockade, comprising testicular suppression with gonadotropin-releasing hormone (GnRH) agonists and testosterone blockade with agents such as flutamide and bicalutamide. Castration-resistant prostate cancer (CRPC) is defined by disease progression despite androgen-blockage therapy. Prostate cancer deaths are typically the result of metastatic castration-resistant prostate cancer (mCRPC), and historically survival for men with mCRPC is very poor with median survival less than two years.

Current treatment options for patients with mCRPC are limited. Docetaxel chemotherapy can improve overall survival in mCRPC, however, few patients in NZ (<5%) currently receive this treatment mainly because of its toxicity. Currently funded treatments, including chemotherapy, and the proposed treatment, abiraterone, are not curative.

Abiraterone

Abiraterone inhibits an enzyme which is expressed in testicular, adrenal, and prostatic tumor tissues leading to decrease circulating levels of testosterone.

Abiraterone is indicated in combination with prednisone or prednisolone for:

- the treatment of patients with metastatic castration resistant prostate cancer (mCRPC) who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy (ADT) in whom chemotherapy is not yet clinically indicated (see Clinical Trials section).
- the treatment of patients with metastatic advanced prostate cancer (castration resistant prostate cancer, mCRPC) who have received prior chemotherapy containing a taxane.

The recommended dosage of abiraterone is 1000 mg (four 250 mg tablets) as a single daily dose abiraterone should be taken at least two hours after eating and no food should be eaten for at least one hour after taking abiraterone. Treatment with abiraterone is continued until disease progression.

Key evidence for abiraterone comes from two phase III trials in men with metastatic, castration resistant prostate cancer, one in patients who had received prior docetaxel and the other in patients with chemotherapy-naïve disease. In men who had previously been treated with a docetaxel-containing chemotherapy abiraterone significantly improved overall survival by around 5 months compared with placebo, improvements were also seen in time to progression, radiologic progression-free survival, and response rate.

In men who had not received prior chemotherapy abiraterone significantly improved overall survival by around 4 months, however, these results were confounded by cross-over whereby nearly half of the patients on placebo received abiraterone on disease progression. Abiraterone improved progression free survival by around 8 months in this patient population.

Side effects that are more common with abiraterone include fluid retention and hypokalemia. Non-specific cardiac abnormalities, abnormal liver function tests, and hypertension may also be more common in patients treated with abiraterone. Caution is required in treating patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalemia or fluid retention, e.g., those with heart failure, recent myocardial

infarction or ventricular arrhythmia. Blood pressure, serum potassium and fluid retention should be monitored at least monthly in patients receiving abiraterone.

The Pharmacology and Therapeutics Advisory Committee (PTAC) and the Cancer Treatments Subcommittee of PTAC (CaTSoP) have provided advice on the funding of abiraterone. In summary, PTAC recommended that abiraterone should be funded for taxane naïve and taxane-pretreated patients with low priority, relevant PTAC and CaTSoP minutes can be found here:

http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=809

It is anticipated that, if funded as proposed, approximately 800 patients would access funded abiraterone in the first year rising to approximately 1000 patients per year from year 2 onwards.

Epoetin alfa

Janssen-Cilag's brand of epoetin was awarded Sole Subsidised Supply Status (the only funded brand of epoetin in the community) and Hospital Supply Status (the only available brand of epoetin in DHB hospitals, subject to a 5% DV limit) from 1 March 2015 to 28 February 2018.

PHARMAC received clinical requests for the funding of two additional presentations. We received feedback that an 8,000 iu presentation would be desirable as an increasing number of patients are on that dose and are currently requiring multiple injections. A 40,000 iu presentation was also sought because patients who were receiving epoetin for the myelodysplasia indication require higher doses.

Methylphenidate hydrochloride extended release tablets and topiramate

Methylphenidate hydrochloride extended release tablets (Concerta) are currently funded for treatment of attention deficit and hyperactivity disorder (ADHD), subject to Special Authority and Hospital Medicines List (HML) restrictions.

Topiramate (Topamax) tablets and sprinkle capsules are currently listed on the Pharmaceutical Schedule under the Control of Epilepsy subheading.