NOTIFICATION

PHARMAC
Pharmaceutical Management Agency

12 October 2012

Approval of proposal relating to various Pfizer products: voriconazole, azithromycin, minoxidil, midazolam, sunitinib and dalteparin

PHARMAC is pleased to announce the approval of an agreement with Pfizer New Zealand Limited. This was the subject of a consultation letter dated 30 August 2012 (http://pharmac.govt.nz/?q=various+Pfizer+products%3A+voriconazole). In summary, the effect of the decision is that from 1 November 2012:

- **voriconazole (Vfend)** will be funded for patients with invasive fungal infections;
- **azithromycin granules for oral liquid (Zithromax)** will be funded with a restriction;
- **minoxidil (Loniten)** will be funded for patients with severe refractory hypertension;
- **midazolam injections (Pfizer-midazolam)** will be funded without restriction;
- **dalteparin sodium (Fragmin)** will be funded for venous thromboembolism treatment and prophylaxis in certain clinical situations; and,
- **sunitinib (Sutent)**, will be funded for patients with imatinib refractory, or intolerant, unresectable or metastatic malignant gastrointestinal stromal tumours (GIST).

Details of the proposal

The proposal was accepted with the following amendments due to consultation feedback.

In relation to voriconazole (Vfend):

- The Special Authority has been changed from a one month approval to three months and Clinical Microbiologists have been included as an applicant type.

- This results in the following approved Special Authority:

> **Special Authority for Subsidy**
> **Initial application (invasive fungal infection)** only from a haematologist, infectious disease specialist or clinical microbiologist. Approvals valid for 3 months for applications meeting the following criteria:
> All of the following:
> 1. Patient is immunocompromised; and
> 2. Applicant is part of a multidisciplinary team including an infectious disease specialist; and
> 3. Any of the following:
> 3.1. Patient has proven or probable invasive aspergillus infection; or
> 3.2. Patient has possible invasive aspergillus infection; or
> 3.3. Patient has fluconazole resistant candidiasis; or
> 3.4. Patient has mould strain such as *Fusarium spp*. and *Scedosporium spp.*
>
> **Renewal (invasive fungal infection)** only from a haematologist, infectious disease specialist or clinical microbiologist. Approvals valid for 3 months for applications meeting the following criteria:

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

All of the following:

1. Patient is immunocompromised; and
2. Applicant is part of a multidisciplinary team including an infectious disease specialist; and
3. Any of the following:
   - 3.1. Patient continues to require treatment for proven or probable invasive aspergillus infection; or
   - 3.2. Patient continues to require treatment for possible invasive aspergillus infection; or
   - 3.3. Patient has fluconazole resistant candidiasis; or
   - 3.4. Patient has mould strain such as *Fusarium spp*. and *Scedosporium spp.*

In relation to sunitinib (Sutent):

- The requirement for a renewal every 3 months for GIST has been changed to a renewal approval period of 6 months. The Special Authority criteria for sunitinib from 1 November 2012 will be as follows:

Sunitinib - Retail Pharmacy –Special Authority for Subsidy

Initial application - (RCC) - only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 3 months, for applications meeting the following criteria:

All of the following:

1 The patient has metastatic renal cell carcinoma; and

2 Any of the following:

- 2.1 The patient is treatment naive; or
- 2.2 The patient has only received prior cytokine treatment; or
- 2.3 The patient has only received prior treatment with an investigational agent within the confines of a bona fide clinical trial which has Ethics Committee approval; or
- 2.4 Both:
  - 2.4.1 The patient has discontinued pazopanib within 3 months of starting treatment due to intolerance; and
  - 2.4.2 The cancer did not progress whilst on pazopanib; and

3 The patient has good performance status (WHO/ECOG grade 0-2); and

4 The disease is of predominant clear cell histology; and

The patient has intermediate or poor prognosis defined as:

5 Any of the following:

- 5.1 Lactate dehydrogenase level > 1.5 times upper limit of normal; or
- 5.2 Haemoglobin level < lower limit of normal; or
- 5.3 Corrected serum calcium level > 10 mg/dL (2.5 mmol/L) ; or
- 5.4 Interval of < 1 year from original diagnosis to the start of systemic therapy; or
- 5.5 Karnofsky performance score of ≤ 70; or
- 5.6 ≥ 2 sites of organ metastasis; and

6 Sunitinib to be used for a maximum of 2 cycles.

Initial application - (GIST) - only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 3 months for applications meeting the following criteria:

Both:

1 The patient has unresectable or metastatic malignant gastrointestinal stromal tumour (GIST); and

2 Either:

- 2.1 The patient's disease has progressed following treatment with imatinib; or
- 2.2 The patient has documented treatment-limiting intolerance, or toxicity to, imatinib

Renewal - (RCC) - only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 3 months for applications meeting the following criteria:

Both:

1 No evidence of disease progression; and

2 The treatment remains appropriate and the patient is benefiting from treatment.

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

The patient has responded to treatment or has stable disease as determined by Choi's modified CT response evaluation criteria as follows:

1. Any of the following:
   - 1.1 The patient has had a complete response (disappearance of all lesions and no new lesions), or
   - 1.2 The patient has had a partial response (a decrease in size of >/= 10% or decrease in tumour density in Hounsfield Units (HU) of >/= 15% on CT and no new lesions and no obvious progression of non measurable disease), or
   - 1.3 The patient has stable disease (does not meet criteria the two above) and does not have progressive disease and no symptomatic deterioration attributed to tumour progression; and
2. The treatment remains appropriate and the patient is benefiting from treatment.

Notes:

RCC - Sunitinib treatment should be stopped if disease progresses.

Poor prognosis patients are defined as having at least 3 of criteria 5.1-5.6. Intermediate prognosis patients are defined as having 1 or 2 of criteria 5.1-5.6.

GIST - It is recommended that response to treatment be assessed using Choi's modified CT response evaluation criteria (J Clin Oncol, 2007, 25:1753-1759). Progressive disease is defined as either: an increase in tumour size of >/= 10% and not meeting criteria of partial response (PR) by tumour density (HU) on CT; or: new lesions, or new intratumoral nodules, or increase in the size of the existing intratumoral nodules.

In relation to minoxidil (Loniten):

- The renewal requirement consulted upon has been removed meaning that initial applications would be for lifetime approval unless notified.

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 September 2012 were considered in their entirety in making a decision on the proposed changes. Most responses were supportive of the proposal, and the following issues were raised in relation to specific aspects of the proposal:

Theme	Comment
Voriconazole	
Voriconazole may be a good treatment option in patients with suspected or proven fungal meningitis who are not immunocompromised, as well as those who are immunocompromised.	There have been no applications for voriconazole funding for this indication (under NPPA or EC), but PHARMAC will seek the advice of the Anti-Infective Subcommittee as to whether fungal meningitis should be included in the Special Authority.
A patient having a proven/probable invasive fungal infection, particularly a patient with an underlying blood disorder which is usually post-transplant, is certainly going to require more than 1 months treatment with voriconazole.	PHARMAC have amended the proposed Special Authority approval period to three months from the originally proposed one month period.
We need voriconazole funded for prophylaxis in the really high risk patients as per e.g. the UK guidelines, as well as treatment of established systemic fungal disease. The cost of treating established disease is very high and the prognosis poor.	PHARMAC staff have received an application for posaconazole for prophylaxis of Invasive fungal infection and have received advice from the Anti-Infective Subcommittee and PTAC that this should be funded for patients at high risk. PHARMAC staff note that voriconazole is not indicated for prophylaxis of fungal infections. PHARMAC would welcome an application for voriconazole for prophylaxis for high risk patients.
Dalteparin	
Listing dalteparin does not address the current issues with enoxaparin dispensing namely community pharmacies being reluctant to stock it given its high cost and the risk of being left with unused opened packs. It is also unlikely to result in any savings given the market familiarity with enoxaparin.	We acknowledge that there are some issues with the dispensing of enoxaparin. The listing of dalteparin provides another option for patients at risk of thrombosis
Midazolam	
Suggests that Pfizer-midazolam in plastic ampoules are only listed in the higher strength 15mg/3ml because it is the strength used for the treatment of status epilepticus. This would avoid the lower strength from being dispensed in error for this indication.	Both strengths of Pfizer-midazolam have been listed in Section B since 2007 and we have not been informed of any issue regarding dispensing errors. Such dispensing issues are not just limited to midazolam and it should be part of good pharmacy practice to have practices in place to prevent such errors for all medicines dispensed.
Sunitinib	
The stipulation that a patient must have a CT scan every 3 months for ongoing sunitinib funding will be difficult and costly and will impact radiology capacity. Would it be possible to extend this, in most cases asymptomatic patients would be routinely scanned every 6-12 months.	PHARMAC note that sunitinib is a very expensive treatment; therefore, it is important that patients discontinue treatment if they are not benefitting. However, we agree that on balance the requirement for a disease assessment (including a CT as outlined in the Choi's methodology) every 3 months for renewal would be burdensome, therefore have amended the renewal approval period to 6 months.

Theme	Comment
General	
Support listing of azithromycin, minoxidil, midazolam and sunitinib. Notes that the pack sizes and prices for voriconazole and dalteparin place a fiscal risk on pharmacy with part packs being left. The Guild would like PHARMAC to initiate a system where pharmacies could claim for wastage.	PHARMAC is doing some work around the distribution of medications with a high cost and these medications could be included in this process.

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.