NOTIFICATION

PHARMAC
Pharmaceutical Management Agency

19 October 2012

Approval of proposal to amend the restrictions applying to azithromycin and list Apotex's brand of azithromycin 250 mg tablets

PHARMAC is pleased to announce that the approval of an agreement with Apotex NZ Limited. This was the subject of a consultation letter dated 30 August 2012 (http://pharmac.govt.nz/2012/08?q=azithromycin). In summary, the effect of the decision is that:

- Apo-Azithromycin 250 mg tablets will be listed in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 December 2012
- A restriction will apply to all dispensings of azithromycin 250 mg tablets in the community from 1 December 2012;
- The restriction applying to the community dispensing of azithromycin 500 mg tablets will be amended from 1 December 2012.

Background

- In July 2012 PHARMAC consulted upon removing the restrictions relating to the prescribing of azithromycin tablets http://pharmac.govt.nz/2012/07/04.Whilst there was general support for the removal of restrictions, several responses to consultation noted concerns that azithromycin would be used for its anti-inflammatory properties or as a prophylactic in chronic obstructive pulmonary disease and that such use may increase azithromycin resistant micro-organisms in the population.
- Following this feedback PHARMAC amended the proposal and issued the second consultation letter dated 30 August 2012 (see above link). The revised proposal included 5 day treatment length restrictions on the prescribing of azithromycin tablets that could be waived by endorsement for specified uses, in order to encourage appropriate prescribing. This proposal has now been approved.

Details of the decision

- Azithromycin 250 mg tablets (Apo-Azithromycin) will be funded in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 December 2012 as follows (prices ex-man, ex-GST):

Chemical	Presentation	Brand	Pack size	Price and subsidy
Azithromycin	Tablet 250 mg	Apo-Azithromycin	30	$10.00

- The following funding restriction will apply to all community dispensings of azithromycin 250 mg tablets

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

Maximum of 5 days treatment per prescription; can be waived by endorsement for the following patients:

For Endorsement, Patient has either:

i. Received a lung transplant and requires treatment or prophylaxis for bronchiolitis obliterans syndrome*; or

ii. Cystic fibrosis and has chronic infection with Pseudomonas aeruginosa or Pseudomonas related gram negative organisms*.

*Indications marked with * are Unapproved Indications

- The following funding restriction will apply to all community dispensings of azithromycin 500 mg tablets

a) Maximum of 5 days treatment per prescription; can be waived by endorsement for the following patients:

For Endorsement, Patient has either:

iii. Received a lung transplant and requires treatment or prophylaxis for bronchiolitis obliterans syndrome*; or

iv. Cystic fibrosis and has chronic infection with Pseudomonas aeruginosa or Pseudomonas related gram negative organisms*.

*Indications marked with * are Unapproved Indications

b) Maximum of 8 available on PSO

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. The following issues were raised in relation to specific aspects of the proposal:

Theme	Comment
Queried whether this proposal allows two 1 gram doses a week apart (with other antibiotics) for the treatment of pelvic inflammatory disease as per recommended guidelines.	Yes, the intent is to limit the number of doses a patient can have (i.e. total 5 days treatment), so two doses of 1 gram would be funded.
The proposed restriction needs to include treatment of a bronchiolitis obliterans syndrome (BOS) in stem cell transplant patients as well as lung transplant patients.	We sought advice on this matter from the Anti-Infective Subcommittee of PTAC at its 22 February 2012 meeting; it recommended that funding of BOS following stem cell/bone marrow transplantation be declined. The relevant minute can be found at the following link: http://pharmac.govt.nz/?q=2012-02+Anti-Infective PHARMAC would welcome a further application from clinicians or suppliers if there is further evidence to consider.
A study just published in the Lancet from an Auckland/Hamilton group shows azithromycin works in non Cystic Fibrosis (CF) bronchectasis so this should be funded as well as CF.	PHARMAC has not had advice on this study from its clinical advisors to date. We will seek advice from the Anti-Infective Subcommittee as to whether the bronchiectasis indication should be widened.

Theme	Comment
Queried the rationale for listing azithromycin for patients with Cystic fibrosis and chronic infection with Pseudomonas aeruginosa when pseudomonas is likely to be resistant to azithromycin.	In patients with Cystic fibrosis who have chronic colonisation with P. aeruginosa, azithromycin is not being used for its direct antimicrobial effect. The Cystic Fibrosis Panel considered that *in vitro* studies suggest that azithromycin, and other macrolide agents to varying degrees, may act by decreasing the production of bacterial virulence factors and allow other antibiotics to act more effectively against the Pseudomonas aeruginosa infection and, may modulate the host inflammatory response. PHARMAC has been funding azithromycin for this indication via Special Authority since 1 July 2009.
The use of BPAC journal does not meet the needs of prescribers who are not subscribers of this journal. PHARMAC must ensure appropriate education is provided to all antimicrobial prescribers.	PHARMAC will also consider other avenues by which to disseminate this information. BPAC articles are freely available on-line for access by any interested party. We would encourage all prescribers to consider this website for their educational purposes and would recommend that Infectious Disease Specialists refer their colleges to this site when the articles are published.
PHARMAC should monitor azithromycin usage and significant variances in usage should be correlated with infectious disease epidemiology and antimicrobial resistance treads to inform the need for further prescriber education or alteration of prescriber restrictions.	We regularly provide updates to the Anti-infective Subcommittee of PTAC highlighting prescribing trends nationally and by DHB region. As a result of this reporting the Subcommittee has recently recommended restrictions for quinolone antibiotics and PHARMAC are currently consulting on re-implementing restrictions on these pharmaceuticals.
It is necessary to monitor the development of antimicrobial resistance after a change in prescriber restrictions. In terms of azithromycin this should include Streptococcus pneumonia, Streptococcus pyogenes, Staphylococcus aureus and possibly helicobacter pylori.	PHARMAC has discussed monitoring of azithromycin resistance with ESR. Available data will be monitored by PHARMAC and included in our reporting to the Anti-Infective Subcommittee of PTAC.
Recent studies have associated azithromycin 5 day courses with significant increased risk of cardiovascular endpoints including death when compared to amoxicillin or quinolones, therefore, treatment with azithromycin should be limited to minimum effective duration in patients for whom there are no funded alternatives.	We agree that appropriate prescribing is important for antibiotics (as it is for all prescription medications) and would encourage clinicians to consider the safest, most effective funded treatment options available for their patients. PHARMAC will work with BPAC to ensure relevant information regarding this risk is included in any article.

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.