

17th August 2012

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Re: Proposal to remove the restrictions applying to azithromycin and list Apotex's brand of azithromycin 250 mg tablets

Dear Greg,

I am writing to you regarding the above proposal and to convey feedback from Paediatric Society members.

With the proposed removal of restrictions on tablets it is also possible azithromycin syrup will be considered for removal of restrictions. Even in the absence of syrup formulations, widening access to azithromycin will impact on infants and children, particularly through changing community resistance patterns of important pathogens.

Internationally widened access of azithromycin has been associated with increasing resistance in group A streptococcus (Gagliotti et al. 2006) and *Streptococcus pneumoniae* (Bergman et al, 2006).

In the New Zealand climate of high burden of disease from both acute GAS and post streptococcal disease (glomerulonephritis and rheumatic fever) increased GAS resistance to macrolides would leave little option for treatment of those with penicillin allergy and sore throat, a vital part of primary prevention of rheumatic heart disease. Similarly with our high burden of disease from acute respiratory infections (secondary to *S.pneumoniae*); we should strive to contain azithromycin for correct indications.

Preferred Azithromycin Indications:

- For children appropriate indications include treatment and prophylaxis of pertussis and possibly treatment of neonatal chlamydia infection.

It has an important role in sexual health, bronchiolitis obliterans, certain cystic fibrosis patients, resistant enteric fever and some mycobacterial infection

Other potential uses for azithromycin which may be inappropriate

- We have some concern that widening access may also result in inappropriate wider use in place of betalactams for indications such as treatment of sore throat, otitis media, acute respiratory infection and suspected, not proven beta-lactam allergy.
- There is increasing support for potential widespread use of azithromycin to prevent exacerbations in chronic lung disease. For children, the prolonged use of azithromycin for respiratory conditions in adults could impact on streptococcal resistance profiles.

We urge you to consider concerns regarding azithromycin widened access and longer term resistance issues and suggest continued restricted indications are appropriate in both in community and hospital.

Yours sincerely,

Dr Emma Best, Paediatric Infectious Diseases Consultant, Starship Children's Hospital
Chair of the **Paediatric Society; Infection and Immunisation Subgroup**

References

1. http://www.heartfoundation.org.nz/shop/product_view/872/algorithm-4-a-guide-for-sore-throat-management
2. Gagliotti et al. Macrolide prescriptions and erythromycin resistance of *Streptococcus pyogenes* Clin Inf Diseases 2006;42 1153
3. ESR national antibiotic resistance 2008 (20% Spn and 5% GAS)
4. Casey and Pichichero. Higher dosages of azithromycin are more effective in treatment of Group A Streptococcal tonsillopharyngitis Clin Inf Dis 2005; 40: 1748-55.
5. Bergman et al, Macrolide and azithromycin use are linked to increased macrolide resistance in Streptococcus pneumoniae, Antimicrob. Agents Chemother. 50 (2006) 3646e3650.
6. Cornick and Bentley. Streptococcus pneumoniae: the evolution of antimicrobial resistance to beta-lactams, fluoroquinolones and macrolides. *Microbes and Infection* 14 (2012) 573e583
7. Wenzel et al. Antibiotic Prevention of Acute Exacerbations of COPD. N Engl.J.Med. 2012;367:340-7

APPENDIX

Specific comments from Paediatric Society members are listed below

A) Respiratory Paediatric SIG – Chairperson

..although I am excited to have the availability of using azithromycin with the severely Bx (bronchiectasis) and especially bronchiolitis obliterans children - but the availability in the general community is a concern as it may limit future effectiveness.

B) Paed Inf Dis Specialist

Community use should still have restrictions. My main concern is that it will be widely used as an easy option for otitis media and other respiratory tract infections in children, with the known risks of increased resistance in Strep pneumo particularly, but also Gp A strep macrolide resistance.

C) General Practitioner; Paediatric Society representative

From a GP perspective I don't have any problems with current restricted use of Azithromycin as outlined (single course for treatment of genital Chlamydia or infant pertussis, bronchiolitis obliterans/CF). I appreciate the concerns re increased resistance. There are already a number of effective alternatives available for otitis media and community treated pneumonia.