Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35, Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-1119

Drug Effectiveness Review Project – Literature Scan Summary

Month/Year of Review: January 2015
PDL Class: Macrolide antibiotics , oral

Date of Last Review: January 2013
Source Document: OSU College of Pharmacy, Drug Effectiveness Review Project

Current Preferred Drugs	Current Non-Preferred Drugs
Azithromycin tab (*Zithromax*®)	Azithromycin pckt for susp (*Zithromax*®)
Azithromycin susp, recon	Azithromycin ER susp, recon (*Zithromax*®)
Clarithromycin tab (*Biaxin*®)	Clarithromycin ER tab (*Biaxin XL*®)
	Clarithromycin susp, recon (*Biaxin*®)
	Dirithromycin tab (*Dynabac*®) [DSC]
	Erythromycin (*all formulations*)
	Telithromycin tab (*Ketek*®)

Key: DSC = discontinued product; ER = extended release; pckt = packet; recon = reconstituted; susp = suspension; tab = tablet
Note: Fidaxomicin is a macrolide antibiotic approved to treat diarrhea associated with *Clostridium difficile* and is reviewed separately within the PDL class of antibiotics specifically for *C. diff* infections.

Previous Conclusions and Recommendations:

- Evidence does not support a difference in efficacy or harms between different oral macrolide antibiotics.
- Recommend inclusion of at least one drug from this class. Consider azithromycin or clarithromycin for coverage of *Mycobacterium avium* Complex.

Research Questions:

1. For adults and children with community-acquired pneumonia (CAP), acute bacterial sinusitis, acute exacerbations of chronic bronchitis, otitis media, pharyngitis and *Mycobacterium avium* Complex, do macrolide antibiotics differ in efficacy, safety or adverse events?
2. Are there subgroups of patients based on demographics (age, racial groups, gender), other medications, or co-morbidities, or in pregnancy for which one macrolide is more efficacious or associated with fewer adverse events?

Conclusions and Recommendations:

- Evidence does not support a difference in efficacy or harms between different oral macrolide antibiotics.
- No further review or research needed at this time.
- Evaluate costs in executive session.

Methods:

The DERP scan was used to identify any new comparative research on macrolide antibiotics since the last P&T review in January 2013.[1] An OVID MEDLINE search was also conducted to identify direct comparative studies or systematic reviews of telithromycin with other macrolide antibiotics on clinically relevant outcomes such as mortality or morbidity since the last P&T review in January 2013.

Summary:

No new clinical trials meeting eligibility criteria or systematic reviews were identified by the DERP scan since the last P&T review in July 2013 with the exception one an updated review by the Cochrane Collaboration assessing antibiotics for CAP in children.[2] No new comparative efficacy data on macrolide antibiotics were found by the Cochrane review, but the

review did note that gastrointestinal adverse effects were more commonly reported with erythromycin compared to azithromycin.

The FDA issued a public notification in 2013 that azithromycin can cause abnormal changes in the electrical activity of the heart that may lead to a potentially fatal irregular heart rhythm.[1] Prescribers should consider risk of torsades de pointes with azithromycin when considering treatment options for patients already at risk for cardiovascular events. However, alternative macrolide antibiotics also have the potential for QT prolongation or other significant adverse effects that should be considered when choosing an antibiotic.

No direct comparative studies of telithromycin evaluating clinically relevant outcomes were identified with the OVID MEDLINE. However, one meta-analysis found telithromycin has a similar efficacy and safety profile as clarithromycin for the treatment of community-acquired respiratory tract infections in adolescents and adults.[3] The abstract is presented in the appendix.

References:

1. Holmes R. Drug Class Review on Macrolides, Preliminary Update Scan Report 5, July 2014. Drug Effectiveness Review Project. Pacific Northwest Evidence-based Practice Center, Oregon Health & Science University.
2. Lodha R, Kabra SK, Pandey RM. Antibiotics for community-acquired pneumonia in children. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD004874. DOI: 10.1002/14651858.C D004874.pub4.
3. Li X, Wang F, Yang F, et al. Telithromycin versus clarithromycin for the treatment of community-acquired respiratory tract infections: a meta-analysis of randomized controlled trials. *Chinese Medical Journal*. 2013;126:2179-2185.

Appendix:

Abstract:

Li X, Wang F, Yang F, et al. Telithromycin versus clarithromycin for the treatment of community-acquired respiratory tract infections: a meta-analysis of randomized controlled trials. *Chinese Medical Journal*. 2013;126:2179-2185.

Background The emergence of bacterial resistance to commonly used antibiotics, such as macrolides, is complicating the management of respiratory tract infections (RTIs). Telithromycin, a ketolide antimicrobial structurally related to macrolides, is approved for the treatment of community-acquired RTIs, and shows lower pathogen resistance rates. The purpose of this study was to compare the efficacy and safety of telithromycin with clarithromycin, a macrolide routinely used as therapy for RTIs.
Methods We performed a meta-analysis of relevant randomized-controlled trials (RCTs) identified in PubMed, the Cochrane Library, Embase, CNKI and VIP databases. The primary efficacy outcome was clinical treatment success assessed at the test-of-cure time in the per-protocol population, and the primary safety outcome was drug related adverse effects.
Results Seven RCTs, involving 2845 patients with RTIs, were included in the meta-analysis. Oral telithromycin and clarithromycin showed a similar clinical treatment success in modified intention to treat and per-protocol population (cure and improvement) (odds ratios (ORs): 0.84, 95% confidence intervals (CI): 0.64–1.11 and OR: 1.14, 95% CI: 0.71–1.85, respectively). Similar findings were obtained for secondary efficacy outcomes: clinical treatment success at a late post–therapy visit (OR: 0.92, 95% CI: 0.57–1.48) and microbiological treatment success at the test-of-cure time (OR: 1.14; 95% CI: 0.71–1.85). The safety outcome analysis indicated telithromycin had a similar risk of drug-related adverse effect and serious adverse effect with clarithromycin.
Conclusions Our findings indicate that oral telithromycin and clarithromycin have similar treatment efficacy and adverse effect. The advantages of lower antimicrobial resistance rates, once-daily short-duration dosing and reported lower healthcare costs make oral telithromycin a useful option for the empiric management of mild-to-moderate RTIs.