

Indiana Medicaid Therapeutics Committee Therapeutic Class Review Summary

Therapeutic Class:

Macrolides

Overview:

Macrolide antibiotics inhibit bacterial protein synthesis by binding to the 50 S ribosomal subunit. Until azithromycin and clarithromycin were released, erythromycin was the only macrolide in widespread clinical use. Erythromycin itself is available in a variety of salts and dosage forms, making it difficult to compare erythromycin products. The oral bioavailability of both azithromycin and clarithromycin are superior to that of erythromycin. Dirithromycin, though now discontinued, has a spectrum of activity similar to erythromycin; however, dirithromycin has greater tissue penetration, a prolonged elimination half-life allowing once-daily dosing, and a lower potential to interact with other drugs metabolized by the cytochrome P450 system.

Despite their significant cost when compared with erythromycin, azithromycin and clarithromycin have earned a solid place in therapy. The activity of erythromycin against gram-positive organisms generally is greater than against gram-negative organisms due to its superior penetration into gram-positive organisms. Both azithromycin and clarithromycin possess greater intrinsic activity against *H. influenzae* than does erythromycin, although other effective antibiotics are less costly. Azithromycin appears to have less gram-positive activity but greater gram-negative activity than erythromycin. Azithromycin and clarithromycin concentrate within macrophages, making them useful against organisms that are taken up by macrophages such as *Mycobacterium avium intracellulare*. Clarithromycin is also approved for treatment of AIDS-related *Mycobacterium avium complex* (MAC). Because of significant tissue concentrations and prolonged elimination, azithromycin has been shown effective as a single-dose treatment for chlamydial infection.

GENERIC NAME	TRADE NAME	MANUFACTURER	GENERIC
Azithromycin	Zithromax®, Z-Pak®, Zmax	Pfizer	Y N (Zmax)
Clarithromycin	Biaxin®, Biaxin XL®	Abbott	Y
Dirithromycin	Dynabac® (PRODUCT DISCONTINUED)	Muro	N
Erythromycin	E-Mycin®, EryPed®, Ery-Tab®, PCE®, Eryc®	Various	Y

Summary:

Clarithromycin has an indication for MAC but also has several drug interactions. Clarithromycin and azithromycin are both available in tablet and suspension dosage forms, and both agents appear to cause fewer gastrointestinal adverse reactions than erythromycin. Macrolide selection for the PDL should take into consideration spectrum of activity, efficacy, cost, and safety.