

Bon Secours Richmond Health System
Pharmacy & Therapeutics Committee
Azithromycin
2/2002

The MEC has approved the following:

Azithromycin IV is recommended as the preferred IV azalide/macrolide, and is recommended for automatic substitution for erythromycin IV except for the following: patients less than 16 years old, pregnancy, and L&D uses.

Sensitivity of streptococcus pneumoniae is similar for macrolides and azalides (azithromycin, clarithromycin, and erythromycin) for penicillin sensitive, intermediate, and resistant strains with 90%, 70%, and 30% being sensitive, respectively. Cross-resistance occurs to the class.

Dosage Equivalents:

Azithromycin 500 mg IV q24h	Erythromycin 250-500 mg q6h
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Cost Analysis

Drug	Drug Cost	Diluent Cost	Pharmacy/Nursing Labor	Cost Per Day
Azithromycin 0.5gm IV QD	\$18.61	0.55	\$2.78	\$21.94
Erythromycin 0.5gm IV Q6H	\$9.93	6.70	\$11.12	\$27.75
Erythromycin 1 gm IV Q6H	\$18.21	6.70	\$11.12	\$36.03

Pharmacokinetic Profile

	Azithromycin
T1/2	36 hours
Bioavailability	37-52%
Fraction Excreted Unchanged Renal	4.5-12%
Fraction Excreted Unchanged Bowel	65%
Metabolism	35%
Protein Binding	7-50% conc. Dependent
Volume of Distribution	33 l/kg

Assessment:

- Azithromycin is administered once daily versus four times daily for erythromycin.
- Nursing and pharmacy labor is reduced with azithromycin.
- Sensitivity of Streptococcus pneumoniae is similar for macrolides (azithromycin, clarithromycin, and erythromycin) for penicillin sensitive, intermediate, and penicillin resistant strains with 90%, 70%, and 30% being sensitive, respectively. Cross-resistance occurs for the class. Note: greater than 99% of Streptococcus pneumoniae is sensitive to levofloxacin and there is not cross-resistance with penicillin resistant strains. Levofloxacin has a broader spectrum covering Streptococcus pneumoniae (penicillin sensitive and resistant), H. influenzae, Staph. aureus (penicillin sensitive), M. catarrhalis, Klebsiella pneumoniae, and atypical pathogens (Legionella, Mycoplasma, and Chlamydia)
- Azithromycin has a broader spectrum of activity than erythromycin including Mycobacterium avium complex, and Hemophilus influenzae.
- Erythromycin is an inhibitor of cytochrome P-450 enzymes and has clinically significant interactions with: astemizole, cisapride, ciprofloxacin, clozapine, terfenadine, and theophylline. Azithromycin has not been shown to inhibit the cytochrome P-450 system in clinical studies, but there have been case reports of interactions.
- Azithromycin is primarily excreted unchanged via the biliary tract and subsequently eliminated in the stool; very little is excreted unchanged in the urine.
- Community Acquired Bacterial Pneumonia is caused by the following pathogens: S. pneumoniae 25-60%, Chlamydia 5-15%, Legionella 1-16%, Mycoplasma 2-30%, S. aureus 2-10%, H. influenzae 4-15%, and gram negative bacilli 7-18%.
- Erythromycin and azithromycin must be diluted before infusing due to venous irritation to 1-5 mg/ml and 1-2 mg/ml respectively.
- Azithromycin obtains concentrations in tonsillar, pulmonary, prostatic, renal and gynecologic tissues 100 fold higher than serum levels with tissue half-lives of 2-3 days.

References:

- Howard K. Azithromycin Versus Erythromycin For Community-Acquired Pneumonia: A Cost-minimization Analysis. *Am J Health-Syst Pharm* 1999;56:1521-4
- Bartlett J. Community-Acquired Pneumonia in Adults: Guidelines for Management (from the Infectious Disease Society of America). *Clinical Infectious Diseases* 1998;26:811-38.
- Classen D. Clinical and Financial Impact of Intravenous Erythromycin Therapy in Hospitalized Patients. *Ann Pharmacother* 1999;33:669-73
- Stout J. Activity of Azithromycin, Clarithromycin, Roxithromycin, Dirithromycin, Quinupristin/dalfopristin and Erythromycin against Legionella Species by Intracellular Susceptibility Testing in HL-60 Cell. *J Antimicro Chemotherapy*. 1998;41: 289-291.
- Dorn G. Prevalence Of Antimicrobial Resistance Among Respiratory Tract Isolates of Streptococcus pneumoniae in North America: 1997 Results from the SENTR, Antimicrobial Surveillance Program. *Clinical Infectious Disease* 1998;27:764-70
- Aldridge K. A Multicenter Study of the Prevalence and Susceptibility Patterns of Isolates of Streptococcus pneumoniae with Reduced Susceptibility to Penicillin G in Louisiana. *Am J Med Sci* 1998;316: 277-84
- Wintermeyer S. Dirithromycin: A New Macrolide. *Ann Pharmacother* 1996;30:1141-9
- Garey K. Intravenous Azithromycin. *Ann Pharmacother* 1999; 33: 218-28
- File T. A Multicenter, Randomized Study Comparing the Efficacy and Safety of Intravenous and/or Oral Levofloxacin versus Ceftriaxone and/or Cefuroxime Axetil in Treatment of Adults with Community-Acquired Pneumonia. *Antimicrobial Agents and Chemotherapy* 1997;41:1965-72
- The Choice of Antibacterial Drugs. *Medical Letter* 1999;41:95-104