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Telithromycin

A Viewpoint by Arthur L. Barry

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Telithromycin represents the first compound of a new class of antibacterial agents, the ketolides. Like erythromycin and other macrolides, the ketolides have a 14-membered lactone ring. However, the L-cladinose moiety has been replaced with a 3-keto structure; hence the name ketolides. The macrolides and ketolides are similar in that their spectrum of activity is directed primarily against Gram-positive cocci. However, the ketolide telithromycin is also active against many macrolide-resistant strains that are becoming increasingly common among species of important respiratory pathogens.

Erythromycin-resistant *Streptococcus pneumoniae* strains are increasing in prevalence, especially among penicillin-resistant strains. About half of all penicillin-resistant pneumococci are also resistant to erythromycin and other macrolides. Such strains are often resistant to multiple antibiotics and can cause serious therapeutic problems if they are involved in life-threatening infections. Telithromycin remains active against such multiply-resistant pneumococci as well as against macrolide-susceptible strains.

Group A haemolytic streptococci (GAS) remain susceptible to benzylpenicillin but patients who cannot be given penicillins are often treated with erythromycin. Unfortunately, erythromycin-resistant GAS are now becoming an important problem in some countries. In North America, about 2 to 4% of all GAS are resistant to the macrolides, but the prevalence can be much higher in some local areas. Telithromycin is currently effective against erythromycin-resistant strains of GAS.

Among *Staphylococcus aureus* isolates, there are different mechanisms of resistance that can result in different levels of resistance to the macrolides and lincosamides. Some staphylococci are resistant to erythromycin and other macrolides but susceptible to the lincosamide clindamycin as well as to telithromycin. Other macrolide-resistant staphylococci that are also resistant to clindamycin are also telithromycin resistant. Consequently, telithromycin resistance among staphylococci is limited to clindamycin-resistant strains. Among methicillin-susceptible *S. aureus* isolates, clindamycin resistance occurs at a prevalence of about 3%. However, about 42% of methicillin-resistant staphylococci are resistant to clindamycin, erythromycin and telithromycin. For treating nosocomial staphylococcal infections in institutions where methicillin-resistant *S. aureus* strains are endemic, telithromycin may not be the drug of choice. However, resistant strains are uncommon in community-acquired infections and, consequently, telithromycin should prove to be an effective alternative to the macrolides, especially in communities with a high prevalence of erythromycin-resistant strains.

Because of its favourable pharmacokinetic properties and lack of serious adverse effects, telithromycin appears to be a useful agent for treating community-acquired infections in this era of increasing antibiotic resistance. ▲