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Telithromycin

A Viewpoint by Lars Hagberg

Department of Infectious Diseases, Sahlgrenska University Hospital, Gotebörg, Sweden

Ketolides are a novel addition to the macrolide-lincosamide-streptogramin group of antibacterials. They inhibit bacterial growth by interfering with subunits of the ribosome, and are designed for treatment of community-acquired upper and lower respiratory tract infections, including those caused by pathogens resistant to currently used antibacterials and atypical/intracellular pathogens.

Telithromycin is the first of this class to be approved for clinical use with the following indications: community-acquired pneumonia (CAP), acute exacerbations of chronic bronchitis, acute sinusitis and, in Europe, streptococcal tonsillitis. Telithromycin is highly active *in vitro* against respiratory pathogens such as *Streptococcus pneumoniae*, including *mef*(A)- and *erm*(B)-producing strains, *S. pyogenes*, *Staphylococcus aureus*, *Legionella* spp., *Chlamydophila* (previously *Chlamydia*) *pneumoniae*, and *Mycoplasma pneumoniae*. It has lower activity against *Haemophilus influenzae* than amoxicillin, quinolones and tetracyclines, but greater activity than erythromycin. It does not induce the *erm*-encoded modification of the ribosomal binding site in *Streptococcus* spp. (macrolide-lincosamide-streptogramin group B resistance).

The pharmacokinetic profile of telithromycin allows for once-daily oral administration of an 800mg dose. High clinical efficacy has been shown in the treatment of CAP, including patients with *S. pneumoniae* bacteraemia, CAP caused by *mef*(A)- and *erm*(B)-producing *S. pneumoniae*, CAP caused by *H. influenzae* and, in a few patients, mild-to-moderate CAP caused by *Legionella* spp. Telithromycin rapidly penetrates into respiratory and sinus tissues and accumulates intracellularly in polymorphonuclear neutrophils and alveolar macrophages, thus targeting intracellular pathogens such as *Legionella* spp.

Telithromycin is hepatically metabolised and excretion in the urine is limited. It increases plasma concentrations of drugs metabolized by cytochrome P450 3A4 enzymes such as simvastatin and digoxin, but has no clinically significant effect on the pharmacokinetics of warfarin and theophylline. The adverse-effect profile appears to be favourable. The major adverse effect reported is gastrointestinal with diarrhoea, nausea and vomiting, often classified as mild or moderate. As yet, there is no evidence that telithromycin is associated with an excess risk of hepatic adverse events.

Telithromycin is, thus, a promising new agent for first-line empirical treatment of respiratory tract infections in geographical areas with penicillin- and macrolide-resistant respiratory pathogens. ▲