Drug Update

LINEZOLID

Linezolid is a representative member of a new chemical class of synthetic antimicrobial agents called the oxazolidinones.

The oxazolidinones act by protein synthesis inhibition by a unique mechanism and display bacteriostatic activity against many important human pathogens of gram-positive group. Linezolid inhibits protein synthesis by preventing formation of the ribosomal complex that initiates protein synthesis. Its unique binding site located on 23S ribosomal RNA of the 50S subunit and its action at early, ribosome-assembly step of protein synthesis, results in no cross resistance with other drug classes. Linezolid has a wide spectrum of activity against methicillin resistant *Staphylococci*, penicillin resistant *Pneumococci* and vancomycin resistant *Enterococcus fecalis* and *E faecium*. *Mycobacterium tuberculosis* is moderately susceptible with MICs of 2µg/ml. Anaerobes such as *Clostridium*, *Peptostreptococcus* and *Prevotella* species are also susceptible to linezolid. Linezolid is bacteriostatic against most susceptible organisms but displays bactericidal activity against some strains of *Pneumococci*, *Bacteroides fragilis* and *C perfringens*.

Linezolid has near complete oral bioavailability along with favourable pharmacokinetic and toxicity profiles. In clinical trials involving hospitalised patients with skin/soft tissue infections (predominantly *S aureus*), intravenous/oral; linezolid (up to 1250 mg/day) produced clinical success in >83% of individuals. In patients with community-acquired pneumonia, success rates were >94%. Preliminary clinical data also indicate that twice daily intravenous/oral linezolid 600 mg, is as effective as intravenous vancomycin 1 gm in the treatment of patients with hospi-

tal-acquired pneumonia and in those with infections caused by methicillin-resistant *Staphylococci*. Moreover, linezolid 600 mg twice daily produced >85% clinical/microbiological cure in vancomycin-resistant enterococcal infections.

Linezolid is generally well tolerated and gastrointestinal disturbances are the most commonly occurring adverse events. In April 2000, the FDA approved linezolid injection, tablets and oral suspension for the treatment of patients with infections caused by Gram-positive bacteria and the drug shows great promise as an alternative to glycopeptides and streptogramins to treat serious infections due to resistant gram-positive organisms. Following FDA approval, linezolid was launched in May 2000. In various studies linezolid (600-mg twice daily) has had clinical and microbiological cure rates in the range of 85% to 90% in treatment of a variety of infections (soft tissue, urinary tract and bacteraemia) caused by vancomycin-resistant *E faecium*. Therefore, 600-mg twice daily dosage is recommended for treatment of infections caused by *Enterococci*. A 400-mg twice daily dosage regimen is recommended only for treatment of uncomplicated skin and skin-structure infections.

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