TIGECYCLINE (TYGACIL™)

Tigecycline is the first glycylcycline, a new type of antibiotic that exhibits potent activity against a variety of resistant bacteria.

Tigecycline exhibits potent activity against a broad spectrum of bacteria, including strains that have become resistant to commonly used antibiotics such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE). Tigecycline was developed to circumvent two major resistance mechanisms, efflux pumps and ribosomal protection, which have limited the use of tetracyclines. Efflux pumps cause the antibiotic to be quickly pumped out of the bacteria, significantly decreasing the antibiotic's effectiveness. Ribosomal protection blocks antibiotics from interfering with bacterial protein synthesis.

Glycylcyclines do not share characteristics common to penicillins, cephalosporins, or fluoroquinolones, thus tigecycline is therefore not affected by most mechanisms that limit the activity of these classes of antibiotics. Glycylcyclines work by binding to the ribosome (the cell structure in which proteins are manufactured) with an affinity five times higher than that of tetracycline. Tigecycline binds to additional sites of the ribosome in a manner not seen before, interfering with the mechanism of ribosomal protection proteins.

Tigecycline has been approved for use in the Canada for the treatment of complicated intra-abdominal infections (cIAI) and complicated skin and skin structure infections (cSSSI) in adults.

Tigecycline provides clinicians with a broad-spectrum option that can be used empirically, that is, at the onset of treatment when the specific bacteria present are not yet known.

Tigecycline is administered intravenously. The recommended dosage regimen is a 100mg initial dose followed by 50 mg every 12 hours. Tigecycline, used as a single agent, does not require dosage adjustments in patients with impaired renal function or with mild-to-moderately impaired liver function. In clinical trials, tigecycline provided comparable clinical cure rates in cSSSI to vancomycin and aztreonam, a combination treatment. Overall, the clinical cure rate in cSSSI in clinically evaluable patients was 86.5 per cent for tigecycline as a single agent, compared with 88.6 per cent for vancomycin and aztreonam in combination. Tigecycline cure rates for complicated soft tissue infections, including abscesses, infected ulcers, and burns, were comparable to cure rates for vancomycin and aztreonam in combination. Tigecycline showed comparable clinical cure rates for MRSA strains, to combination treatment. The clinical cure rate for MRSA was 78.4% with tigecycline, while the cure rate for the combination treatment was 76.5%.

In the treatment of complicated intra-abdominal infections (cIAI), monotherapy with tigecycline provided clinical cure rates comparable to imipenem in combination with cilastatin, a commonly used treatment for cIAI. Overall, the clinical cure rates in cIAI in microbiologically evaluable patients were 86.1% for tigecycline compared to 86.2% for imipe-

nem/cilastatin. Tigecycline cure rates for complicated appendicitis, perforation of the intestines, and other cIAI were comparable to cure rates for imipenem/cilastatin. Tigecycline clinical cure rates for Escherichia coli and *Bacteroides fragilis,* two difficult-to-treat infections, were comparable to cure rates for imipenem/cilastatin.

References:

1. Zhanel GG, Homenuik K, Nichol K, Noreddin A, Vercaigne L, Karlowsky J, Embil J, Gin AS and Hoban DJ. The glycylcyclines: A critical review. Drugs 2004; 64(1);63-88.

2. Zhanel GG, Karlowsky, JAK, Rubinstein E, Hoban DJ. A review of tigecycline: A novel glycylcycline. Expert Reviews in Antiinfective Therapy 2006; 4:9-25.