Health Canada Santé Canada

Date issued October 27, 2006

NOTICE OF DECISION for PrTYGACIL™

On September 14, 2006, Health Canada issued a Notice of Compliance to Wyeth Canada for the drug product Tygacil.

Tygacil contains the medicinal ingredient tigecycline, a glycylcycline, which belongs to the tetracycline class of antibacterials. Tigecycline acts by inhibiting protein synthesis at the level of the bacterial ribosome.

Tygacil is indicated for the treatment of the following infections when caused by susceptible strains of the designated microorganisms in patients 18 years of age and older:

- Complicated skin and skin structure infections caused by *Escherichia coli*, *Enterococcus faecalis* (vancomycin-susceptible strains only), *Staphylococcus aureus* (methicillin-susceptible and -resistant strains), *Streptococcus agalactiae, Streptococcus anginosus, Streptococcus pyogenes* and *Bacteroides fragilis.*

- Complicated intra-abdominal infections caused by *Citrobacter freundii*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Enterococcus faecalis* (vancomycin-susceptible strains only), *Staphylococcus aureus* (methicillin-susceptible strains only), *Streptococcus anginosus* group (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*), *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides vulgatus*, *Clostridium perfringens*, and *Peptostreptococcus micros*.

Tigecycline has decreased *in vitro* activity against *Proteus* spp., *Providencia* spp., and *Morganella* spp. *Pseudomonas aeruginosa* is inherently resistant to tigecycline.

The market authorization was based on submitted data from quality (chemistry and manufacturing) studies, as well as data from non-clinical and clinical studies. Overall, there were four pivotal Phase III double-blind, randomized, multicentre, multinational, active control clinical studies involving 1129 patients with complicated skin infections and 1658 patients with complicated intra-abdominal infections. Cure rates for tigecycline were shown to be non-inferior to the comparators.

Tygacil (50 mg/vial, tigecycline) is presented as sterile, lyophilized powder for intravenous use. The recommended dosage regimen of Tygacil is an initial dose of 100 mg, followed by 50 mg every 12 hours. Intravenous infusions should be administered over approximately 30 to 60 minutes every 12 hours. The recommended duration of treatment is 5 to 14 days. The duration of therapy should be guided by the severity and site of the infection and the patient's clinical and bacteriological progress. Dosing guidelines are available in the Product Monograph.

Tygacil is contraindicated for use in patients who have known hypersensitivity to tigecycline or to the tetracycline class of antibacterials. Tygacil should be administered under the conditions stated in the Product Monograph taking into consideration the potential risks associated with the administration of this drug product. Detailed conditions for the use of Tygacil are described in the Product Monograph.

Based on the Health Canada review of data on quality, safety, and effectiveness, Health Canada considers that the benefit/risk profile of Tygacil is favourable for the indications stated above.

Notices of Decision (NDs) are produced in accordance with the Summary Basis of Decision (SBD) initiative. All NDs will be reproduced within the corresponding SBD, normally available within 5 months of product authorization.