



July 7, 2006

The FDA Commissioner
c/o Division of Dockets Management
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, MD 20852

Dear Commissioner:

This correspondence is in reference to Docket No. 2006P-0124 entitled "Stay any approvals of an Abbreviated New Drug Application (ANDA) for Vancocin Capsules." While I am generally very much in favor and support the use of generic drugs for clinical use in the United States, I must express my concern with respect to the level of evidence needed to assure bioequivalence for oral vancomycin tablets. As a practicing infection disease physician and infection control officer, my colleagues and I have witnessed a significant increase in severe and fulminant *Clostridium difficile* associated diarrhea over the last two to three years. There is a national epidemic of this particularly virulent strain of *C. difficile*. One of the mainstays of treatment for this disease entity is the oral administration of vancocin tablets. Because of limited absorption of this complex glycopeptide antibiotic, vancomycin retains excellent antibacterial levels within the gastrointestinal tract. Vancomycin is highly active against *Clostridium difficile* and is one of the few drugs that is capable of eliminating this organism from the alimentary tract. The intravenous formulation of this drug does not attain high levels within the lumen of the GI tract and is not an effective treatment for *C difficile* associated diarrhea. The treatment of choice for severe fulminant *C. difficile* diarrhea remains oral administration of vancomycin in combination with other intravenous antibiotics (mentronidazole) and other supportive care strategies. The bioavailability of vancomycin within the gastrointestinal tract is absolutely critical to the treatment of this infection.

I am greatly concerned that an ANDA for this particular indication may allow generic drugs to the market with uncertain bio-availability, pharmacokinetics, pharmacodynamics, with variable distribution within the body in seriously ill patients. Unless therapeutic equivalence to oral vancocin tablets is specifically tested, it is possible that they will be insufficient to be released within the lumen of the GI tract in a patient with severe diarrhea with an increased intestinal transit time. This may result in insufficient drug levels within the lumen of the intestine and would therefore fail to effectively treat *C. difficile* lumen associated diarrhea.

Alternately, if the drug formulations generate high concentrations of vancomycin that would be absorbed across the diseased alimentary tract of patients with severe colitis, this may result in high levels of vancomycin within the bloodstream. As patients with *C. difficile* diarrhea of the fulminant variety often have acute renal failure, this may impair the clearance of any orally absorbed vancomycin resulting in potential toxic levels within the blood of patients with severe disease.

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The risk of inadequate levels within the GI tract or excess levels in the bloodstream with generic alternatives to the current oral vancomycin tablets needs to be carefully considered. In light of increasing prevalence of vancomycin resistance among enterococci and of vancomycin resistance in *Staphylococcus aureus*, detailed knowledge of the pharmacokinetics of oral vancomycin are of great importance in clinical medicine today.

I respectfully request you reconsider the ANDA for generic equivalence to oral vancomycin tablets. At the very least some pharmacokinetic and pharmacodynamic studies in actual patients with severe *C difficile* diarrhea should be performed. Preferably, some limited comparative studies with generic alternatives to the current formulation of oral vancomycin should be performed in patients to assure the safety and efficacy of this critically important antibiotic.

Thank you for your attention to this important clinical matter. Please contact me directly should you have additional questions or concerns about this correspondence.

Respectfully submitted,


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