Pharmacokinetic Evaluation of Two Brands of Linezolid Tablets in Healthy Human Volunteers

P. Parameshwar1,*, Y.N. Rao2, J.C. Shobha3, Y.N. Reddy4, V.M. Reddy1
1Srikrupa Institute of Pharmaceutical Sciences, Medak, India.
2Donbosco PG College of Pharmacy, Guntur, India.
3Nizam’s Institute of Medical Sciences, Hyderabad, India.
4University College of Pharmaceutical Sciences, Warangal, India.

ABSTRACT: The aim of a randomized, balanced, two treatment, two-period, two-sequence, single-dose, crossover pilot bioavailability and bioequivalence study conducted in 12 healthy adult male volunteers under fasting conditions was to compare steady state pharmacokinetics of Linezolid 600mg tablets of Dr.Reddy’s Laboratories Ltd, and Zyvox® (Linezolid) 600mg tablets of Pharmacia & Upjohn Company, USA. The subjects were dosed once during the study and the pre-dose blood samples were collected within 1 hr prior to dosing. The concentrations of Linezolid from the blood samples were quantified by validated HPLC method and pharmacokinetic parameters were computed. 90% Confidence intervals of reference Vs test for Cmax lower limit 87.23 and upper limit 109.24, AUC 0-t lower limit 86.20 and upper limit 109.17, AUC 0-α lower limit 85.48 and upper limit 111.54. Analysis of variance (ANOVA) did not show significant difference to these parameters. Based on the results obtained, both the formulations have exhibited the same rate and extent of absorption, indicating switch ability in clinical practice.

KEY WORDS: Linezolid; single dose; pharmacokinetics; statistics

Introduction

Linezolid chemically (S)-N-[(3-fluoro-4-(morpholin-4-yl)phenyl)-2-oxo-1,3-oxazolidin-5-yl]methyl]acetamide and it is the first oxazolidinone antibiotic to be approved in the USA and other countries worldwide; it is available in both intravenous and oral dosage forms. The drug has substantial antimicrobial activity against Gram-positive bacteria, such as *Staphylococci*, *streptococci* and *enterococci*. This includes activity against methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *enterococci* (VRE). Linezolid uniquely inhibits the formation of the bacterial protein synthesis initiation complex, possibly by distorting the binding site for initiator t-RNA (Noskin, G. A, et al., 1999). Ensuring uniformity in standards of quality, efficacy and safety of pharmaceutical products is the fundamental responsibility of central drug standards organization. Reasonable assurance has to be provided that various products, containing same ingredients marketed by different licenses are clinically equivalent and interchangeable. Accordingly, the bioavailability of an active substance from a pharmaceutical product should be known and reproducible. In most cases, it is cumbersome and unnecessary to assess this by clinical studies, bioavailability and bioequivalence data is therefore, required to be furnished with applications for new drugs as required under the Schedule Y, depending on the type of application being submitted. Both bioavailability and bioequivalence focus on the release of a drug substance from its dosage form and subsequent absorption into the systemic circulation. For this reason, similar approaches of measuring bioavailability should generally be followed in demonstrating bioequivalence (Slatter, J. G et al., 2001).

Methods and Materials

These studies were performed in accordance with good clinical practice guidelines. The study protocols were reviewed and approved by the institutional review board of the participating institution (Nizam’s Institute of Medical Sciences).