1.0 Introduction

Parkinson disease is recognized as one of the most common neurologic disorders, affecting approximately 1% of individuals older than 60 years. The incidence of Parkinson disease has been estimated to be 4.5-21 cases per 100,000 population per year, and estimates of prevalence range from 18 to 328 cases per 100,000 population, with most studies yielding a prevalence of approximately 120 cases per 100,000 population. The wide variation in reported global incidence and prevalence estimates may be the result of a number of factors, including the way data are collected, differences in population structures and patient survival, case ascertainment, and the methodology used to define cases.82

Improving economy and health in developing countries like India, has increased the life span and changed the emphasis from communicable to noncommunicable diseases. This is likely to increase the prevalence of movement disorders and, age-related diseases like Parkinson’s disease (PD).72 Nearly, 33 million Indians have neurological disorders and they occur twice as often in rural areas.42 In developing countries like India, generic drugs are the answer to better health care for all. India has one of the highest out-of-pocket health care expenditure in the world and despite providing very cheap services (compared to the rate of the countries like USA and UK) it’s still inaccessible to many due to poor purchasing power.62 Neurological disorders like Parkinson’s cause significant morbidity, mortality, disability, socioeconomic losses and reduce the quality of life.72

A generic medicine is a medicine that is developed to be the same as a medicine that has already been authorised (the ‘reference medicine’). A generic medicine contains the same active substance(s) as the reference medicine, and it is used at the same dose(s) to treat the same disease(s) as the reference medicine. However, the name of the medicine, its appearance (such as colour or shape) and its packaging can be different from those of the reference medicine. A generic medicine is marketed in compliance with international patent law. It is identified either by its internationally approved non-proprietary scientific name (INN) or by its own brand name. Generic medicines are widely used in many countries in cost-effective treatment programmes, and are increasingly prescribed by doctors as effective alternatives to higher-priced innovator pharmaceuticals. In India however there were no patent laws till 2005 which meant that anyone could replicate any drug in India without legal ramifications. This led to the trend of branded generic drugs which has 99.5% of the country’s generic drug share.

The key factor in creating a generic medicine is establishing bioequivalence. Bioequivalence means that, when compared scientifically, the generic medicine and the innovator product demonstrate essentially the same rate and extent of biological availability of the active
Bioequivalence is a pharmacokinetics term used to assess the expected in vivo biological equivalence of two proprietary preparations of a drug. If two products are said to be bioequivalent it means that they would be expected to be, for all intents and purposes, the same.

Birkett (2003) defined bioequivalence by stating that, "two pharmaceutical products are bioequivalent if they are pharmaceutically equivalent and their bioavailabilities (rate and extent of availability) after administration in the same molar dose are similar to such a degree that their effects, with respect to both efficacy and safety, can be expected to be essentially the same. Pharmaceutical equivalence implies the same amount of the same active substance(s), in the same dosage form, for the same route of administration and meeting the same or comparable standards." 17

The United States Food and Drug Administration (FDA) has defined bioequivalence as, "the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study." 127

In determining bioequivalence, for example, between two products such as a commercially-available Brand product and a potential to-be-marketeted Generic product, pharmacokinetic studies are conducted whereby each of the preparations are administered in a cross-over study to volunteer subjects, generally healthy individuals but occasionally in patients. Serum/plasma samples are obtained at regular intervals and assayed for parent drug (or occasionally metabolite) concentration. In case, blood concentration levels are neither feasible nor possible to compare the two products (e.g. inhaled corticosteroids), then pharmacodynamic endpoints rather than pharmacokinetic endpoints are used for comparison. For a pharmacokinetic comparison, the plasma concentration data are used to assess key pharmacokinetic parameters such as area under the curve (AUC), peak concentration ($C_{\text{max}}$), time to peak concentration ($T_{\text{max}}$), and absorption lag time ($t_{\text{lag}}$). Testing should be conducted at several different doses, especially when the drug displays non-linear pharmacokinetics.
The FDA considers two products bioequivalent if the T/R ratios and 90% CI’s for pharmacokinetic parameters $C_{\text{max}}$, $\text{AUC}_{(0-t)}$ and $\text{AUC}_{(0-\infty)}$ of the test (e.g. generic formulation) to reference (e.g. innovator brand formulation) lies between 80.00% to 125.00%.