The Clinical Pharmacology of Ziprasidone (Geodon® or Zeldox®) From the Food and Drug Administration (FDA) Reviewer

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Abstract

Ziprasidone (Geodon®), also known at the time of submission to the Food and Drug Administration (FDA) as Zeldox®. It was submitted initially for the treatment of psychiatric disorders e.g., Schizophrenia. However, there was delay on its approval due to increase of QT prolongation, which was discussed at the FDA Advisory Committee. This review focused on the clinical pharmacology and the pharmacokinetics (PK) of the drug, specifically at the time of submission to the FDA and other related updated references. The sponsor (Pfizer) summitted about 40 clinical pharmacology and PK studies including QT prolongation studies. There were four capsules formulation at that time: 20, 40, 60, and 80 mg and one intramuscular (IM) strength in another New Drug Administration (NDA) that came subsequent to oral route. The drug has to be given with food to increase the bioavailability to 60% (two-fold increase). Ziprasidone is extensively metabolized after oral administration with only a small amount excreted in the urine (<1%) or feces (<4%) as unchanged drug. Approximately 20% of the dose is excreted in the urine, with approximately 66% being eliminated in the feces. Some of its metabolites are active. Ziprasidone has very high, sub nanomolar binding affinity for the human serotonin.

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