Contains Nonbinding Recommendations

Guidance on Selegiline Hydrochloride

This guidance represents the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Selegiline hydrochloride

Dosage Form; Route: Capsule; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 5 mg
   Additional comments: Applicants may consider using a reference-scaled average bioequivalence approach for selegiline. If using this approach, you should provide evidence from your bioequivalence study of high variability in the bioequivalence parameters of AUC and/or Cmax (i.e., within-subject variability ≥ 30%). For information on this approach, see the FDA guidance on Progesterone.

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2. Type of study: Fed
   Design: Partial or fully replicated crossover design in vivo
   Strength: 5 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional comments: See additional comments above.

Analytes to measure (in plasma): Selegiline and its metabolite N-desmethylselegiline in plasma

Bioequivalence based on (90% CI): Selegiline

The metabolite data should be submitted as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and Cmax.

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website, available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and

reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).