

Draft Guidance on Selegiline Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind the FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want 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, they should provide evidence of high variability in the bioequivalence parameters of AUC and/or C_{max} (i.e., within-subject variability $\geq 30\%$). For detailed information on this approach, see the published book chapter, **Davit B, Conner D. "Reference-scaled average bioequivalence approach." Kanfer I, Shargel L, eds. *Generic Drug Product Development – International Regulatory Requirements for Bioequivalence*. New York, NY: Informa Healthcare, 2010: 271-272.** However, prior to using the alternative approach, the firm is encouraged to submit the study protocols for review by the Division of Bioequivalence.

 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.
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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 C_{max}.

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).