

Draft Guidance on Linagliptin

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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 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: Linagliptin

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in-vivo
Strength: 5 mg
Subjects: Normal healthy males and non-pregnant females, general population.
Additional Comments:

2. Type of study: Fed
Design: Single-dose, two-way crossover in-vivo
Strength: 5 mg
Subjects: Normal healthy males and non-pregnant females, general population.
Additional Comments: Please refer to the Amantadine Hydrochloride Tablet Guidance for additional information regarding fed studies.

Analytes to measure (in appropriate biological fluid): Linagliptin in plasma

Bioequivalence based on (90% CI): Linagliptin

Waiver request of in-vivo testing: Not applicable

Dissolution test method and sampling times: Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please 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 application.

Information Regarding Long Half-Life Drugs

Linagliptin has a long terminal elimination half-life. Please ensure adequate washout periods between treatments in the crossover studies. Please also consider using a parallel study design due to linagliptin's long half-life. For a long half-life drug product, an AUC truncated to 72 hours may be used in place of AUC_{0-t} or AUC_{0-inf} if the drug demonstrates low intrasubject variability in distribution and clearance.