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 AUC0-t or AUC0-inf if the drug demonstrates low intrasubject variability in distribution and clearance.