

Draft Guidance on Sitagliptin Phosphate; Metformin Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover *in vivo*
Strength: 50 mg /1000 mg
Subjects: Normal healthy males and females, general population.
Additional Comments: Females should not be pregnant or lactating, and if applicable, should practice abstinence or contraception during the study.
The drug products should be administered with 240 mL of a 20% glucose solution in water, followed by 60 mL of the glucose solution administered every 15 minutes for up to 4 hours after dosing.

2. Type of study: Fed
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 50 mg /1000 mg
Subjects: Normal healthy males and females, general population
Additional comments: Please see comments above

Analytes to measure: Sitagliptin and metformin in plasma.

Bioequivalence based on (90% CI): Sitagliptin and metformin

Waiver request of in-vivo testing: 50 mg/500 mg based on (i) acceptable bioequivalence studies on the 50 mg /1000 mg strength, (ii) acceptable dissolution testing across all strengths, and (iii) proportional similarity in the formulations across all strengths.

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.fda.gov/cder/ogd/index.htm>. 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.