Contains Nonbinding Recommendations

Draft Guidance on Sildenafil Citrate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 100 mg
   Subjects: Normal, healthy males
   Additional comments:

---

2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 100 mg
   Subjects: Normal, healthy males
   Additional comments:

Analytes to measure (in appropriate biological fluid): Sildenafil and active metabolite, piperazine N-desmethylsildenafil in plasma.

Bioequivalence based on (90% CI): Sildenafil

Please submit the metabolite data 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: 20, mg, 25 mg and 50 mg based on (i) acceptable bioequivalence studies on the 100 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

Please note that Sildenafil Tablets, 20 mg, and Sildenafil Tablets, 25 mg, 50 mg and 100 mg are the subject of two separate reference products. Two separate applications must be submitted comparing to the appropriate reference products. An applicant may request a waiver of in vivo bioequivalence testing for the 20 mg strength provided that it (1) submits an ANDA containing acceptable in vivo studies on the 100 mg strength; (2) cross-references the ANDA for the 100-mg strength; and (3) meets the criteria of 21 CFR § 320.22(d) (2).. Please refer to the Guidance for Industry, *Variations in Drug Products that May Be Included in a Single ANDA* located at: http://www.fda.gov/cder/guidance.

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.