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Draft Guidance on Sildenafil Citrate

October 2024

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Active Ingredient: Sildenafil citrate

Dosage Form: Tablet

Route: Oral

Strengths: EQ 20 mg Base, EQ 25 mg Base, EQ 50 mg Base, EQ 100 mg Base

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 100 mg
   Subjects: Healthy males
   Additional comments: None

Analytes to measure: Sildenafil and active metabolite, piperazine N-desmethyl-sildenafil in plasma

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 C_{max}.

Bioequivalence based on (90% CI): Sildenafil

Waiver request of in vivo testing: EQ 20, mg Base, EQ 25 mg Base and EQ 50 mg Base based on (i) acceptable bioequivalence study on the EQ 100 mg Base strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

Note: Sildenafil tablets, EQ 20 mg Base, and sildenafil tablets, EQ 25 mg Base, EQ 50 mg Base and EQ 100 mg Base are the subject of two separate reference products. Two separate applications must be submitted comparing to the appropriate reference listed drug (RLD).[1] An applicant may request a waiver of in vivo bioequivalence testing for the EQ 20 mg Base strength provided that it (1) submits an abbreviated new drug application (ANDA) containing acceptable in vivo studies on the EQ 100 mg Base strength; (2) cross-references the ANDA for the 100 mg Base strength; and (3) meets the criteria of 21 CFR § 320.22(d) (2) Refer to the most recent version of the Guidance for Industry, *Variations in Drug Products that May Be Included in a Single ANDA.*[a]

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units for each of all strengths of the test product and RLD.[1] Specifications will be determined upon review of the ANDA.

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[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions.*