Contains Nonbinding Recommendations

Draft Guidance on Paroxetine Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Paroxetine hydrochloride

Dosage Form; Route: Extended release tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover design in vivo
   Strength: EQ 37.5 mg base
   Subjects: Healthy males and females (nonpregnant), general population
   Additional Comments: Other study designs are acceptable if appropriate. Applicants may consider using a reference-scaled average bioequivalence approach for paroxetine. If using this approach, the applicant should provide evidence of high variability (i.e., within-subject variability $\geq$ 30%) in the bioequivalence parameters. For general information on this approach, please refer to the Progesterone Capsule Guidance for additional information regarding highly variable drugs.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover design *in-vivo*
   Strength: EQ 37.5 mg base
   Subjects: Healthy males and females (nonpregnant), general population
   Additional comments: Please see additional comments above.

Analytes to measure: Paroxetine in plasma

Bioequivalence based on (90% CI): Paroxetine

Waiver request of in vivo testing: 12.5 mg and 25 mg based on (i) acceptable bioequivalence studies on the 37.5 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website, available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. 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 abbreviated new drug application (ANDA).

For modified release products, dissolution profiles generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer, water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. The following sampling times are recommended: 1, 2 and 4 hours and every 2 hours thereafter, until at least 80% of the drug is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for twelve tablets. Specifications will be determined upon review of the data submitted in the application.