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Draft Guidance on Acetylcysteine

October 2024

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Active Ingredient: Acetylcysteine

Dosage Form: Tablet, effervescent

Route: Oral

Strengths: 500 mg, 2.5 gm

Recommended Studies: Two options: (1) One in vivo bioequivalence study with pharmacokinetic endpoints or (2) one in vitro disintegration test

I. Option 1: One in vivo bioequivalence study with pharmacokinetic endpoints:

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 2.5 gm at a dose of 5 gm (2.5 gm x 2) in 300 mL water
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: None

Analyte to measure: Acetylcysteine in plasma

Bioequivalence based on (90% CI): Acetylcysteine

II. Option 2: One in vitro disintegration test

To qualify for a waiver of the in vivo bioequivalence study requirement under 21 CFR §320.22(b)(3), applicants should demonstrate that generic versions of acetylcysteine effervescent tablets are fully dissolved in 200 mL of purified water at the time of administration with six dosage units each of both strengths of the test product and reference listed drug (RLD) by in vitro disintegration testing. Specifications will be determined upon review of the abbreviated new drug application (ANDA). The generic drug product should also contain the same active drug ingredient in the same concentration and dosage form as the RLD and should not contain any excipients that may significantly affect drug absorption and systemic availability.

Waiver request of in vivo testing: 500 mg strength based on (i) acceptable bioequivalence study on the 2.5 gm strength, (ii) acceptable in vitro disintegration testing of both strengths, and (iii) proportional similarity of the formulations between both strengths

Dissolution test method and sampling times: Not applicable

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