Contains Nonbinding Recommendations

Draft Guidance on Acetylcysteine

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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: Acetylcysteine

Dosage Form; Route: Effervescent tablets; oral

Recommended Studies: Two options: in vitro or in vivo studies

I. In Vitro Disintegration Testing

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 all strengths of the test and reference products 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 Reference Listed Drug (RLD) and should not contain any excipients that may significantly affect drug absorption and systemic availability.

II. In Vivo Studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in-vivo
   Strength: 2500 mg at a dose of 5000 mg (2500 mg x 2) in 300 mL water
   Subjects: Healthy males and non-pregnant, non-lactating females, general population.
   Additional Comments: None

2. Type of study: Fed
   Design: Single-dose, two-way crossover in-vivo
   Strength: 2500 mg at a dose of 5000 mg (2500 mg x 2) in 300 mL water
   Subjects: Healthy males and non-pregnant, non-lactating females, general population.
   Additional Comments: None

Analytes to measure (in appropriate biological fluid): Acetylcysteine in plasma

Bioequivalence based on (90% CI): Acetylcysteine

Waiver request of in-vivo testing: 500 mg based on (i) acceptable bioequivalence studies on the 2500 mg strength, (ii) acceptable in vitro disintegration testing of all strengths, and (iii) proportional similarity of the formulations across all strengths.