Draft Guidance on Benznidazole

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in-vivo
   Strength: 100 mg
   Subjects: Non-pregnant, non-lactating females, general population.
   Additional Comments:
   1. The study drug products should be administered with intact tablets.
   2. Females of reproductive potential should not be pregnant or lactating, and should practice abstention or use effective contraception up to five days after the final dose.

2. Type of study: Fed
   Design: Single-dose, two-way crossover in-vivo
   Strength: 100 mg
   Subjects: Non-pregnant, non-lactating females, general population.
   Additional Comments: See above

Submission of a Bio-Investigational New Drug Application (IND) is required prior to the conduct of a bioequivalence study for a cytotoxic drug product. (See 21 C.F.R § 320.31).

Analyte to measure (in appropriate biological fluid): Benznidazole in plasma

Bioequivalence based on (90% CI): Benznidazole

Waiver request of in-vivo testing: 12.5 mg strength based on (i) acceptable bioequivalence studies on the 100 mg strength, (ii) proportional similarity of the formulations 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 web site, 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 the test and reference

Recommended Sept 2018
products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).

Since Benznidazole Tablets 100 mg are functionally scored tablets, additional dissolution testing should be conducted on split tablet portions test (i.e. halves and quarters). Dissolution data on split tablet portions should meet finished-product release requirements. For additional information on the evaluation of scored tablets, refer to the FDA Guidance on Tablet Scoring1.