Contains Nonbinding Recommendations

Draft Guidance on Tetrabenazine

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in-vivo
   Strength: 25 mg
   Subjects: Males and non-pregnant females aged 18 - 45 years, general population
   Additional Comments:

2. Type of study: Fed
   Design: Single-dose, two-way crossover in-vivo
   Strength: 25 mg
   Subjects: Males and non-pregnant females aged 18 - 45 years, general population
   Additional Comments:

Analytes to measure (in appropriate biological fluid): Tetrabenazine and its active metabolite, HTBZ, in plasma using an achiral assay.

Bioequivalence based on (90% CI): Tetrabenazine. If tetrabenazine plasma concentrations can be reliably measured and its pharmacokinetics accurately determined, please analyze the data for the parent compound using the confidence interval approach. The data for the active metabolite can be used as supportive evidence. However, if you demonstrate, using state of the art assay methods, that it is not possible to measure tetrabenazine in plasma accurately and reliably, please analyze the metabolite using the confidence interval approach.

Waiver request of in-vivo testing: 12.5 mg based on (i) acceptable bioequivalence studies on the 25 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across both 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 all strengths of the test and

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