Contains Nonbinding Recommendations

Draft Guidance on Deutetrabenazine

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in-vivo
   Strength: 12 mg
   Subjects: Males and non-pregnant, non-lactating females, general population.
   Additional Comments: None

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2. Type of study: Fed
   Design: Single-dose, two-way crossover in-vivo
   Strength: 12 mg
   Subjects: Males and non-pregnant, non-lactating females, general population.
   Additional Comments: None

Analytes to measure (in appropriate biological fluid): Deutetrabenazine and its active metabolites, α- and β- dihydrotetrabenazine (HTBZ), in plasma using an achiral assay.

Bioequivalence based on (90% CI): Deutetrabenazine.

If deutetrabenazine plasma concentrations can be reliably measured and its pharmacokinetics accurately determined, 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, which it is not possible to measure deutetrabenazine in plasma accurately and reliably, analyze the metabolite using the confidence interval approach.

Waiver request of in-vivo testing: 6 mg and 9 mg strengths based on (i) acceptable bioequivalence studies on the 12 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 products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).