Draft Guidance on Deutetrabenazine

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

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

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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).