

Draft Guidance on Tolvaptan

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 45 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: Tolvaptan Tablets are approved with a Risk Evaluation and Mitigation Strategy (REMS) with an Elements to Assure Safe Use (ETASU), which restricts its use. All pertinent elements of the REMS must be incorporated into the protocol and informed consent.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 45 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above

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

Bioequivalence based on (90% CI): Tolvaptan

Waiver request of in vivo testing: 15 mg, 30 mg, 60 mg, and 90 mg, based on (i) acceptable bioequivalence studies on the 45 mg strength (ii) proportionally similar 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 for each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.