

Contains Nonbinding Recommendations
Draft Guidance on Tolvaptan

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Tolvaptan

Form/Route: Tablet /Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover *in-vivo*
Strength: 30 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments:

-
2. Type of study: Fed
Design: Single-dose, two-way crossover *in-vivo*
Strength: 30 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments
-

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

Bioequivalence based on (90% CI): Tolvaptan

Waiver request of in-vivo testing: 15 mg based on (i) acceptable bioequivalence studies on the 30 mg strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations across both strengths.

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please conduct comparative drug dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.