Contains Nonbinding Recommendations

Draft Guidance on Everolimus

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet for oral suspension; oral

Recommended Study: Two studies

1. **Type of study:** Fasting
   Design: Single-dose, 2-way, crossover design in vivo
   Strength: 5 mg
   Subjects: Males and females (non-pregnant), general population
   Additional Comments: 1) Women of childbearing potential should be advised to use an effective method of contraception while using everolimus tablet for oral suspension and for up to 8 weeks after ending treatment. 2) Females should not be breastfeeding. 3) Study subjects should have normal baseline renal and liver function.

2. **Type of study:** Fed
   Design: Single-dose, 2-way, crossover design in vivo
   Strength: 5 mg
   Subjects: Males and females (non-pregnant), general population
   Additional comments: Please see additional comments above.

Analytes to measure (in appropriate biological fluid): Everolimus in whole blood

Bioequivalence based on (90% CI): Everolimus

Waiver request of in vivo testing: 2 mg and 3 mg based on (i) acceptable bioequivalence studies on the 5 mg strength, (ii) proportional similarity of all strengths, and (iii) acceptable in vitro dissolution testing across 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 all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).