

Contains Nonbinding Recommendations

Draft Guidance on Leflunomide

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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: Leflunomide

Form/Route: Tablets/Oral

Recommended studies: 3 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover *in-vivo*
Strength: 100 mg
Subjects: Normal healthy males and females, general population.
Additional Comments:

2. Type of study: Fasting
Design: Single-dose, two-way crossover *in-vivo*
Strength: 20 mg
Subjects: Normal healthy males and females, general population.
Additional comments: Only female subjects who are unable to bear children should be included in the study and male subjects wishing to father a child during the study should be excluded from the study. Since the half-life of the metabolite A77 1726 is very long, you may consider bioequivalence studies with parallel designs.

3. Type of study: Fed
Design: Single-dose, two-way crossover *in-vivo*
Strength: 20 mg
Subjects: Normal healthy males and females, general population.
Additional comments: Please see comment above.

Analytes to measure: Please measure only the leflunomide's metabolite, A77 1726, in plasma

Bioequivalence based on (90% CI): The metabolite of leflunomide, A77 1726

Waiver request of in-vivo testing: 10 mg based on (i) acceptable bioequivalence studies on the 20 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all 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.fda.gov/cder/ogd/index.htm>. Please find the dissolution information for this product at this website. Please 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 application.