

Draft Guidance on Dimethyl Fumarate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Delayed Release Capsule/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: 240 mg
Subjects: Healthy males and nonpregnant females, general population
Additional Comments: The product should not be crushed or chewed and the capsule contents should not be sprinkled on food. A recent complete blood cell count (CBC) (i.e. within 6 months) is recommended before initiation of study to identify subjects with pre-existing low lymphocyte counts.

2. Type of study: Fed
Design: Single-dose, two-way crossover in vivo
Strength: 240 mg
Subjects: Healthy males and nonpregnant females, general population
Additional Comments: Please see comment above.

Analytes to measure (in appropriate biological fluid): After oral administration, dimethyl fumarate (DMF) is rapidly and completely hydrolyzed to its active metabolite monomethyl fumarate (MMF) and the plasma DMF concentration is not quantifiable. Thus, analyte to measure is MMF in plasma.

Bioequivalence based on (90% CI): MMF

Waiver request of in vivo testing:

120 mg based on (i) acceptable bioequivalence studies on the 240 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 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.