Contains Nonbinding Recommendations

Draft Guidance on Artemether/Lumefantrine

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablet/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 20 mg/120 mg (Dose= 4 tablets corresponding to a total dose of 80 mg artemether and 480 mg of lumefantrine)
   Subjects: Normal healthy males and non-pregnant females, general population.
   Additional Comments: 1. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. 2. The tablets should be swallowed whole (not crushed).

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 20 mg/120 mg (Dose= 4 tablets corresponding to a total dose of 80 mg artemether and 480 mg of lumefantrine)
   Subjects: Normal healthy males and non-pregnant females, general population.
   Additional Comments: 1. Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. 2. The tablets should be swallowed whole (not crushed).

Analytes to measure (in appropriate biological fluid): Artemether, Dihydroartemisinin (DHA) and Lumefantrine

Please submit the metabolite (DHA) data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and Cmax.

Bioequivalence based on (90% CI): Artemether and Lumefantrine

Waiver request of in-vivo testing: N/A

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 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.