Contains Nonbinding Recommendations

Draft Guidance on Quinine Sulfate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Capsules/Oral

Recommended study: 1 study

Type of study: Steady-state
Design: Two-arm, parallel in vivo study with pharmacokinetic endpoints.
Strength: 324 mg [Dose: 648 mg (two capsules) every 8 hours for 7 days]
Subjects: Adult patients with uncomplicated *P. falciparum* malaria for whom quinine sulfate is a reasonable treatment option.
Additional comments: Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study. Subjects with any of the following should be excluded:

- Prolongation of QTc interval (>480 msec), ventricular arrhythmia, atrial fibrillation, atrial flutter or bradycardia in baseline 12-lead ECG.
- History of glucose-6-phosphate dehydrogenase (G6PD) deficiency, myasthenia gravis, optic neuritis, prolongation of the QT interval, ventricular arrhythmias, thrombocytopenia, atrial fibrillation or flutter, uncorrected hypokalemia, or bradycardia.
- Known hypersensitivity to quinine, mefloquine or quinidine.

Analytes to measure (in appropriate biological fluid): Quinine in plasma on 7th day of dosing

Bioequivalence based on (90% CI): Quinine

Waiver request of in-vivo testing: Not Applicable

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.

Risk Evaluation and Mitigation Strategy (REMS): This drug product has an innovator developed REMS. Any ANDA citing the innovator drug product will also be required to have a REMS. Please refer to 73 FR 16313: March 27, 2008 and Section 505-1 of the Food, Drug and Cosmetic Act.