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Draft Guidance on Dextromethorphan Hydrobromide; Quinidine Sulfate

October 2024

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Active Ingredients: Dextromethorphan hydrobromide; Quinidine sulfate

Dosage Form: Capsule

Route: Oral

Strength: 20 mg; 10 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 20 mg; 10 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Females of reproductive potential should use effective contraception during the study. Subjects with any of the following should be excluded:
   a. History of quinidine, quinine or mefloquine-induced thrombocytopenia, hepatitis, or other hypersensitivity reactions.
   b. Known hypersensitivity to dextromethorphan, current use of a monoamine oxidase inhibitor (MAOI) or within 14 days of stopping an MAOI, prolonged QT interval, congenital long QT syndrome, history suggestive of Torsades de Pointes, or heart failure, complete atrioventricular (AV) block without implanted pacemaker, or patients at high risk of complete AV block.
   c. QTc interval of >480 msec by electrocardiogram (ECG) in baseline 12-lead ECG.

Analytes to measure: Dextromethorphan and quinidine in plasma

Bioequivalence based on (90% CI): Dextromethorphan and quinidine

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units for each of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.