Contains Nonbinding Recommendations

Guidance on Pilocarpine Hydrochloride

This guidance represents 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: Pilocarpine Hydrochloride

Form/Route: Tablet /Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover *in-vivo*
   Strength: 7.5 mg
   Subjects: Normal healthy males and females, general population
   Additional Comments:

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover *in-vivo*
   Strength: 7.5 mg
   Subjects: Normal healthy males and females, general population
   Additional comments:

Analytes to measure (in appropriate biological fluid): Pilocarpine and the metabolite, pilocarpic acid in plasma.

Pilocarpine has been shown to be unstable in heparinized plasma and convert to pilocarpic acid during storage. Therefore, you should pay attention to the stabilization of pilocarpine and separation of the drug from its metabolites in the assay development and validation. Recent literature states that the use of EDTA as an anticoagulant during blood sampling may be helpful in stabilizing pilocarpine. The stability of pilocarpine in plasma samples and the assay specificity of pilocarpine, especially in relation to its metabolites and plasma endogenous components, should be clearly demonstrated in the assay method validation report submitted to the FDA.

Bioequivalence based on (90% CI): Pilocarpine.
If pilocarpine can be reliably measured, a confidence interval approach for bioequivalence determination should be used for pilocarpine. If pilocarpine cannot be reliably measured, a confidence interval approach for bioequivalence determination should be used for pilocarpic acid

Waiver request of in-vivo testing: 5 mg based on (i) acceptable bioequivalence studies on the 7.5 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

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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.