Contains Nonbinding Recommendations

Draft Guidance on Morphine Sulfate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Sustained Release Capsules/Oral

Recommended studies: 3 studies

1. Type of study: Fasting
   Design: Single-dose, two-way, crossover *in-vivo*
   Strength: 100 mg
   Subjects: Normal healthy males and females, general population
   Additional Comments: Please use a narcotic antagonist such as naltrexone if the study involves healthy subjects. You should consult a physician who is an expert in the administration of opioids for an appropriate dose of narcotic antagonist.

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2. Type of study: Fed
   Design: Single-dose, two-way, crossover *in-vivo*
   Strength: 100 mg
   Subjects: Normal healthy males and females, general population
   Additional comments: Please use a narcotic antagonist such as naltrexone if the study involves healthy subjects. You should consult a physician who is an expert in the administration of opioids for an appropriate dose of narcotic antagonist.

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3. Type of study: Sprinkle
   Design: Single-dose, two-way, crossover *in-vivo*
   Strength: 100 mg
   Subjects: Normal healthy males and females, general population
   Additional comments: Please use a narcotic antagonist such as naltrexone if the study involves healthy subjects. You should consult a physician who is an expert in the administration of opioids for an appropriate dose of narcotic antagonist.

Analytes to measure: Morphine and Morphine-6-glucuronide

Bioequivalence based on (90% CI): Morphine

Waiver request of in-vivo testing: 20 mg, 30 mg, 50 mg, and 60 mg based on (i) acceptable bioequivalence studies on the 100 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all 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.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.