

Draft Guidance on Macitentan

This draft guidance, once finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Macitentan

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. **Type of study:** Fasting
Design: Single-dose, two-way crossover in vivo
Strength: 10 mg
Subjects: Healthy males, general population
Additional comments: Due to the risk of teratogenicity of macitentan, the study should be conducted in healthy male subjects. Opsumit (macitentan) was approved with a risk evaluation and mitigation strategy (REMS), which restricts its use. All pertinent elements of the REMS should be incorporated into the protocol and informed consent.

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2. **Type of study:** Fed
Design: Single-dose, two-way crossover in vivo
Strength: 10 mg
Subjects: Healthy males, general population
Additional comments: Same as above
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Analytes to measure (in appropriate biological fluid): Macitentan in plasma

Bioequivalence based on (90% CI): Macitentan

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods Web site available to the public at the following location: <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Conduct comparative dissolution testing on 12 dosage units each of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).