

Draft Guidance on Riociguat

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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: Riociguat

Dosage Form; Route: Tablet; oral

Recommended Studies: Two in vivo studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 2.5 mg
Subjects: Normal healthy males, general population
Additional Comments: Due to the risk of teratogenicity of riociguat, the study should be conducted in healthy male volunteers. Adempas® (Riociguat) Tablet was approved with a Risk Evaluation and Mitigation Strategy (REMS). All pertinent aspects of the REMS must be incorporated into the protocol and informed consent.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 2.5 mg
Subjects: Normal healthy males, general population
Additional comments: Same as comments above

Analytes to measure (in appropriate biological fluid): Riociguat

Bioequivalence based on (90% CI): Riociguat

Waiver request of in vivo testing: 0.5 mg, 1.0 mg, 1.5 mg, and 2.0 mg tablets based on i) acceptable bioequivalence studies on the 2.5 mg strength, ii) proportional similarity of formulations across all strengths, and iii) acceptable dissolution among all strengths.

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website 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 all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).