

## Draft Guidance on Ledipasvir; Sofosbuvir

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

**Dosage Form; Route:** Tablet; oral

**Recommended Studies:** Two in vivo studies

1. Type of study: Fasting  
Design: Single-dose, two-treatment, two-period crossover or parallel group study  
Strength: 90 mg; 400 mg  
Subjects: Healthy males and nonpregnant females, general population  
Additional comments:
  - a. Female subjects should not be pregnant or lactating, and, if applicable, should practice abstinence or contraception during the study.
  - b. Ensure adequate washout periods between treatments in the crossover studies due to ledipasvir's long terminal elimination half-life.
  - c. For long half-life drug products with low intra-subject variability in distribution and clearance, an AUC truncated to 72 hours may be used in place of  $AUC_{0-t}$  or  $AUC_{0-\infty}$ .
  - d. For either a crossover or parallel study, sample collection time should be adequate to ensure completion of gastrointestinal transit of the drug product and absorption of the drug substance. Collect sufficient blood samples in the bioequivalence studies to adequately characterize the peak concentration ( $C_{max}$ ) and time to reach peak concentration ( $t_{max}$ ).
  
2. Type of study: Fed  
Design: Single-dose, two-treatment, two-period crossover in vivo  
Strength: 90 mg; 400 mg  
Subjects: Healthy males and nonpregnant females, general population  
Additional comments: Same as comments above

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**Analytes to measure (in appropriate biological fluid):** Ledipasvir and sofosbuvir in plasma

**Bioequivalence based on (90% CI):** Ledipasvir and sofosbuvir

**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 all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).