Contains Nonbinding Recommendations

Draft Guidance on Ivosidenib

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 250 mg
   Subjects: Healthy males
   Additional comments: Elderly subjects and subjects with risk factors for prolonged QTc interval and Torsades de Pointes should be excluded from the study. Subjects should be appropriately monitored for electrocardiogram changes during the study. Ensure adequate washout periods between treatments in the crossover studies due to ivosidenib's long terminal elimination half-life or consider using a parallel study design.

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 250 mg
   Subjects: Healthy males
   Additional comments: See comments above. In addition, the fed study should be conducted with a low-fat meal (400-500 total calories), with approximately 25 percent of total calories from fat (11-14 g).

Analyte to measure (in appropriate biological fluid): Ivosidenib in plasma

Bioequivalence based on (90% CI): Ivosidenib

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 for each of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.