Contains Nonbinding Recommendations

Draft Guidance on Vismodegib

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Capsule; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 150 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional comments:
   1. All the warnings specified in vismodegib labeling should be followed and appropriately incorporated in the bioequivalence (BE) study design and informed consent. Study subjects should be informed about the potential for embrio-fetal toxicity, and appropriate safeguards including adequate contraception should be incorporated in the study protocol.
   2. Vismodegib has a long terminal elimination half-life (>24 hours); therefore adequate washout periods should be ensured between treatments in the crossover studies. A parallel study design may also be considered due to vismodegib's long half-life. For long half-life drug products, an AUC truncated to 72 hours may be used in place of AUC_{0-t} or $AUC_{0-\infty}$. For either a crossover or parallel study, sample collection time should be adequate to cover the duration of gastrointestinal transit of the drug product and absorption of the drug substance.
   3. Sufficient blood samples should be collected in the BE studies to adequately characterize the peak concentration (C_{max}) and time to reach peak concentration (t_{max}).

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2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: 150 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional comments: Same as above

Analytes to measure: Vismodegib (total) in plasma

Bioequivalence based on (90% CI): Vismodegib

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).