Contains Nonbinding Recommendations

Draft Guidance on Selexipag

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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: 0.4 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: For the mitigation of adverse events, the bioequivalence studies should include options for treatment of nausea and vomiting that will not alter the pharmacokinetics (PK) of selexipag and interfere with assessment of bioequivalence.

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 0.4 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: See comments above

Analytes to measure (in appropriate biological fluid): Selexipag and the pharmacologically active metabolite ACT-333679 in plasma

Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and Cmax.

Bioequivalence based on (90% CI): Selexipag

Waiver request of in vivo testing: The 0.2 mg, 0.6 mg, 0.8 mg, 1.0 mg, 1.2 mg, 1.4 mg, and 1.6 mg strengths based on (i) acceptable bioequivalence studies on the 0.4 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths

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