Contains Nonbinding Recommendations

Draft Guidance on Tofacitinib Citrate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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: EQ 10 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional Comments: 1) Study protocol should incorporate appropriate screening and monitoring of subjects as per applicable recommendations from the reference listed drug's label; 2) Prospective study participants should be tested and confirmed negative for latent tuberculosis before enrolling in a bioequivalence study; 3) Enrolled study participants should have normal liver function tests, blood counts, and lipid profiles at baseline prior to study drug administration.

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2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 10 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional Comments: See comments above

Analytes to measure (in appropriate biological fluid): Tofacitinib in plasma

Bioequivalence based on (90% CI): Tofacitinib

Waiver request of in-vivo testing: EQ 5 mg Base based on (i) acceptable bioequivalence studies on the EQ 10 mg Base strength, (ii) proportional similarity of the formulations 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 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).