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Draft Guidance on Leuprolide Acetate

November 2021

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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In July 2008, FDA issued a draft product-specific guidance for industry on generic leuprolide acetate. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Leuprolide acetate

Dosage Form; Route: Implant; implantation

Recommended Study: One study

1. Type of study: In vivo
   Design: Randomized, single-dose, parallel
   Strength: EQ 65 mg Base
   Subjects: Prostatic carcinoma patients undergoing initial therapy or receiving a stable regimen of leuprolide acetate implant (EQ 65 mg Base)
   Additional Comments: The study should include either exclusively prostatic carcinoma patients undergoing initial therapy, or exclusively prostatic carcinoma patients receiving a stable regimen of leuprolide acetate implant (EQ 65 mg Base). If both types of patients are included in the study, proportions of the patients should be similar for the test and reference groups.

Analyte to measure: Leuprolide in plasma

Bioequivalence based on (90% CI): Leuprolide

The 90% confidence intervals of the following pharmacokinetic (PK) parameters should meet the acceptable limits of [80.00-125.00%]: Log-transformed $AUC_{7\text{-}t}$, $AUC_{0\text{-}t}$, and C_{max}, where $AUC_{7\text{-}t}$ is the area under the plasma-concentration vs. time curve from Day 7 to the last sampling time point with quantifiable concentration, $AUC_{0\text{-}t}$ is the area under the curve from 0 to the last sampling time point with quantifiable concentration, and C_{max} is the maximum plasma concentration.

In addition, for prostatic carcinoma patients undergoing initial therapy, after the PK study is completed, the treatment should not be discontinued or delayed for a second dose.

Waiver request of in vivo testing: Not applicable

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, 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.

Revision History: Recommended July 2008; Revised November 2021

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