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Draft Guidance on Leuprolide Acetate

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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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This is a new draft product-specific guidance for industry on generic leuprolide acetate.

Active Ingredient: Leuprolide acetate

Dosage Form; Route: Powder; subcutaneous

Recommended Study: One study

1. Type of study: Bioequivalence study with pharmacokinetic (PK) endpoints
Design: Single-dose, randomized, parallel, in-vivo
Strength: 7.5 mg
Subjects: Prostatic carcinoma patients undergoing initial therapy or receiving a stable regimen of leuprolide acetate (7.5 mg) via subcutaneous injection
Additional comments: The test and reference groups should be balanced with respect to patient disease progression and treatment history. The same injection site should be used for test and reference products, which should be pre-specified prior to conducting the study. The study should include exclusively prostatic carcinoma patients undergoing initial therapy or exclusively those receiving a stable regimen of leuprolide acetate (7.5 mg) via subcutaneous injection route. If both types of patients are included in the study, proportions of the patients should be similar between test and reference groups.

Analyte to measure: Leuprolide in plasma

Bioequivalence based on (90% CI): Leuprolide

The 90% confidence intervals of the following PK parameters should meet the acceptable limits of [80.00-125.00]: Log-transformed AUC_{7-t} , AUC_{0-t} , and C_{max} , where AUC_{7-t} is the area under the plasma-concentration vs. time curve from 7 days to the last sampling time point, AUC_{0-t} is the area under the curve from 0 to the last sampling time point, and C_{max} is the maximum plasma concentration. Note that the last sampling time point 't' equals the dosing interval of the product used in the in vivo PK study.

In addition, for prostate 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 applicant should develop and validate a method to determine in vitro drug release. Conduct comparative dissolution testing on 12 dosage units of the test and reference product. Specifications will be determined upon review of the abbreviated new drug application.

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