*Contains Nonbinding Recommendations*

*Draft - Not for Implementation*

**Draft Guidance on Midostaurin**

**May 2022**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in FDA guidances means that something is suggested or recommended, but not required.

In September 2018, FDA issued a draft product-specific guidance for industry on generic midostaurin. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

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**Active Ingredient:** Midostaurin

**Dosage Form; Route:** Capsule; oral

**Recommended Studies:** Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 25 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Ensure adequate washout periods between treatments in the crossover study due to the long terminal elimination half-life of the active metabolite of midostaurin, CGP52421. Alternatively, a parallel study design may be considered. Female subjects of reproductive potential and male subjects with female partners of reproductive potential should use effective contraception during the study and for 4 months after the last dose.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 25 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: See comments above.

**Analytes to measure:** Midostaurin and its active metabolites, CGP52421 (7-hydroxylation, epimer 1 and epimer 2 in total) and CGP62221 (O-demethylation), in plasma
Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolites, 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 $C_{max}$.

**Bioequivalence based on (90% CI):** Midostaurin

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

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**Revision History:** Recommended September 2018; Revised May 2022

**Unique Agency Identifier:** PSG_207997