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Draft Guidance on Mycophenolate Mofetil

February 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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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 November 2019, FDA issued a draft product-specific guidance for industry on generic mycophenolate mofetil. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Mycophenolate mofetil

Dosage Form; Route: For suspension; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 200 mg/mL [Recommended dose: 1000 mg (5 mL)]
   Subjects: Healthy males, and healthy females not of reproductive potential
   Additional comments: Male subjects with female partners of reproductive potential should use effective contraception during the study and for 90 days after the last dose. Male subjects should not donate semen during the study and for 90 days after the last dose. Subjects should not donate blood during the study and for 6 weeks after the last dose. Subjects should not receive any live attenuated vaccines while participating in the study.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 200 mg/mL [Recommended dose: 1000 mg (5 mL)]
Subjects: Healthy males, and healthy females not of reproductive potential
Additional comments: See comments above.

Analytes to measure: Mycophenolate mofetil, and the active metabolite, mycophenolic acid 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): Mycophenolate mofetil

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

Product-specific testing conditions for in vitro feeding tube studies: The approved labeling for the reference product states that the product may be administered by a nasogastric (NG) tube. Using the constituted suspension product, conduct the in vitro feeding tube studies including comparative recovery testing and sedimentation volume and redispersibility testing. For general procedures of in vitro feeding tube studies, refer to the most recent version of the FDA guidance for industry on *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations*.[a]

Testing tube: NG tube (8 French; minimum 1.7 mm interior diameter)

Testing strength: 200 mg/mL [Recommended quantity: 1500 mg (7.5 mL)]

Incubation times: 0 and 15 minutes

Additional Information:

Device:

This product is a drug-device combination product. Refer to the most recent version of the FDA guidance for industry on *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA.*[a] An ANDA for a proposed generic drug-device combination product should include complete comparative analyses.

Revision History: Recommended June 2010; Revised February 2014, October 2017, November 2019, February 2022

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[a] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents