

*Contains Nonbinding Recommendations*

*Draft – Not for Implementation*

**Draft Guidance on Zolmitriptan**

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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 We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

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**Active Ingredient:** Zolmitriptan

**Dosage Form; Route:** Tablet, orally disintegrating; oral

**Recommended Studies:** Two studies

1. Type of study: Fasting  
Design: Single-dose, two-treatment, two-period crossover in vivo  
Strength: 5 mg  
Subjects: Males and non-pregnant, non-lactating females, general population  
Additional comments: The orally disintegrating tablet should be placed on the tongue, allowed to disintegrate, and swallowed without water. Exclude geriatric subjects due to the greater susceptibility of cardiovascular events and subjects with multiple cardiac risk factors (e.g., diabetes, smoking, obesity). Exclude subjects taking monoamine oxidase-A inhibitors and other medications that may increase the risk for serotonin syndrome.

2. Type of study: Fed  
Design: Single-dose, two-treatment, two-period crossover in vivo  
Strength: 5 mg  
Subjects: Males and non-pregnant, non-lactating females, general population  
Additional comments: See comments above

**Analytes to measure:** Zolmitriptan and its active metabolite, N-desmethylzolmitriptan, 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 area under the curve and maximum concentration.

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

**Waiver request of in vivo testing:** 2.5 mg based on (i) acceptable bioequivalence studies on the 5 mg strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both strengths.

**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 for each of all strengths 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 February 2008; Revised July 2008, September 2008, November 2021

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