



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-D-1378]

Bioequivalence Recommendations for Clozapine Orally Disintegrating Tablets/Oral; Draft
Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled “Bioequivalence Recommendations for Clozapine,” for the orally disintegrating tablets (ODTs). The recommendations provide specific guidance on the design of bioequivalence (BE) studies to support abbreviated new drug applications (ANDAs) for clozapine ODTs.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on the draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002.

Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance documents.

Submit electronic comments on the draft guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Xiaoqiu Tang, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, rm. 4730, Silver Spring, MD 20993-0002, 301-796-5850.

SUPPLEMENTARY INFORMATION:

I. Background

In the Federal Register of June 11, 2010 (75 FR 33311), FDA announced the availability of a guidance for industry, “Bioequivalence Recommendations for Specific Products,” which explained the process that would be used to make product-specific BE recommendations available to the public on FDA’s Web site at

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

As described in that guidance, FDA adopted this process as a means to develop and disseminate product-specific BE recommendations and provide a meaningful opportunity for the public to consider and comment on those recommendations. This notice announces the availability of one draft BE recommendation for clozapine ODTs.

Clozapine tablets, marketed under the name CLOZARIL, are the subject of new drug application (NDA) 19-758, held by Novartis Pharmaceuticals Corporation and approved by FDA on September 26, 1989. FazaClo ODTs were approved by FDA on February 19, 2004, under

NDA 21-590, currently held by Jazz Pharmaceuticals III International LTD, based upon a finding that FazaClo ODTs were bioequivalent to CLOZARIL immediate-release tablets. FazaClo ODTs are available as yellow, orally disintegrating tablets of 12.5, 25, 100, 150, and 200¹ milligrams (mg) of clozapine for oral administration without water. They are formulated to disintegrate once exposed to saliva and then are easily swallowed.

In June 2005, FDA published a guidance for industry entitled “Clozapine Tablets: In Vivo Bioequivalence and In Vitro Dissolution Testing” (Clozapine Guidance) (70 FR 35447, June 20, 2005), which replaced a 1996 product-specific bioequivalence guidance for clozapine tablets. The 2005 Clozapine Guidance recommends that ANDA applicants employ multiple-dose, steady-state studies to evaluate the bioequivalence of clozapine products.² FDA recommends that such studies be performed only in patients who have not responded well to standard antipsychotic drug treatment and who have been receiving a maintenance dose of an approved clozapine product for at least 3 months. FDA is now issuing a draft guidance for industry on BE recommendations for generic clozapine that applies specifically to the ODTs.

Beckloff Associates, Inc., filed a citizen petition in December 2007, a citizen petition supplement in February 2009, and a second citizen petition in November 2010, requesting that FDA impose certain requirements for bioequivalence testing for ANDAs referencing FazaClo (clozapine) ODTs and modify the Clozapine Guidance (Docket Nos. FDA-2007-P-0188 and FDA-2010-P-0574). FDA is denying these petitions today.

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current

¹ FDA approved the supplemental NDA for the 150 and 200 mg strengths on July 9, 2010.

² The formatting of this guidance was updated in March 2011, but the content is unchanged. The March 2011 version is available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM249219.pdf>.

thinking of FDA on bioequivalence recommendations for clozapine. 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.

II. Comments

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

III. Electronic Access

Persons with access to the Internet may obtain the documents at either <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <http://www.regulations.gov>.

Dated: April 30, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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