



ANDA 203553

ANDA APPROVAL/TENTATIVE APPROVAL

Zydus Pharmaceuticals USA, Inc.
73 Route 31 North
Pennington, NJ 08534
Attention: Srinivas Gurram
Vice President & Head of Regulatory Affairs

Dear Sir:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on February 1, 2012, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Minocycline Hydrochloride Extended-Release Tablets USP, 45 mg, 55 mg, 65 mg, 80 mg, 90 mg, 105 mg, 115 mg, and 135 mg.

Reference is also made to the complete response letter issued by this office on July 15, 2016, and to any amendments thereafter.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, your Minocycline Hydrochloride Extended-Release Tablets, 45 mg, 80 mg, 90 mg, 105 mg, and 135 mg, are **approved**¹, effective on the date of this letter. However, because of the exclusivity issue explained below, we are unable to grant final approval to your Minocycline Hydrochloride Extended-Release Tablets, 55 mg, 65 mg, and 115 mg. Your Minocycline Hydrochloride Extended-Release Tablets, 55 mg, 65 mg, and 115 mg, are **tentatively approved**.

RLD upon which you have based your ANDA, Medicis's Solodyn Extended-Release Tablets USP, 45 mg, 55 mg, 65 mg, 80 mg, 90 mg, 105 mg, 115 mg, and 135 mg, is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Orange Book:

¹ We note that three strengths of the reference listed drug (RLD) upon which you have based this ANDA, Medicis Pharmaceutical Corporation's (Medicis's) Solodyn Extended-Release Tablets USP, 45 mg, 90 mg, and 135 mg, are no longer being marketed in the United States and have been moved to the discontinued section of the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"). In the Federal Register notice of November 12, 2013 (Volume 78, No. 218) the Agency announced its determination that Medicis's Solodyn Extended-Release Tablets USP, 45 mg, 90 mg, and 135 mg, were not withdrawn from sale for reasons of safety or effectiveness. This determination allows the Agency to approved ANDAs for the discontinued strengths of the RLD.

<u>U.S. Patent Number</u>	<u>Expiration Date</u>
5,908,838 (the '838 patent)	February 19, 2018
7,790,705 (the '705 patent)	June 24, 2025
7,919,483 (the '483 patent)	March 7, 2027
8,252,776 (the '776 patent)	June 24, 2025
8,268,804 (the '804 patent)	June 24, 2025
8,722,650 (the '650 patent)	June 24, 2025
9,192,615 (the '615 patent)	November 17, 2031
7,541,347 (the '347 patent)	April 2, 2027
7,544,373 (the '373 patent)	April 2, 2027

The Agency notes that the '650 patent is only listed for the 55 mg, 80 mg, and 105 mg strengths; the '347 and '373 patents are only listed for the 90 mg strength; and the '615 patent is only listed for the 65 mg and 115 mg strengths.

Your ANDA contains paragraph IV certifications to each of the patents² under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Minocycline Hydrochloride Extended-Release Tablets USP, 45 mg, 55 mg, 65 mg, 80 mg, 90 mg, 105 mg, 115 mg and 135 mg, under this ANDA. You have notified the Agency that Zydus Pharmaceuticals USA Inc (Zydus) complied with the requirements of section 505(j)(2)(B) of the FD&C Act and that litigation was initiated within the statutory 45-day period against Zydus for infringement of the '838, '705 and '483 patents in the United States District Court for the District of Delaware [Medicis Pharmaceutical Corporation v. Zydus Pharmaceuticals USA, Inc. and Cadila Healthcare Ltd. D/B/A Zydus Cadila , Civil Action No. 12-00707-LPS] and in the United States District Court for the District of New Jersey [Medicis Pharmaceutical Corporation v. Zydus Pharmaceuticals USA, Inc. and Cadila Healthcare Ltd. D/B/A Zydus Cadila , Civil Action No. 3:12-cv-03368-FLW-LHG]. You have also notified the Agency that the cases were dismissed.

I. Approval of Minocycline Hydrochloride Extended-Release Tablets, 45 mg, 80 mg, 90 mg, 105 mg and 135 mg

The Office of Bioequivalence has determined your Minocycline Hydrochloride Extended-Release Tablets, 45 mg, 80 mg, 90 mg, 105 mg and 135 mg, to be bioequivalent and, therefore, therapeutically equivalent to the RLD, Medicis's Solodyn Extended-Release Tablets, 45 mg, 80 mg, 90 mg, 105 mg and 135 mg, respectively.

² The agency notes that the '804 patent was submitted to the Agency after submission of your ANDA for the 45 mg, 55 mg, 65 mg, 80 mg, 90 mg, 105 mg, 115 mg, and 135 mg strengths; the '776 patent was submitted to the Agency after submission of your ANDA for the 45 mg, 55 mg, 65 mg, 80 mg, 90 mg, 105 mg and 135 mg strengths; the '650 patent was submitted to the Agency after submission of your ANDA for the 55 mg, 80 mg, and 105 mg strengths; and the '615 patent was submitted to the Agency after submission of your ANDA for the 65 mg and 115 mg strengths. Litigation, if any, with respect to the '804 patent for the 45 mg, 55 mg, 65 mg, 80 mg, 90 mg, 105 mg, 115 mg, and 135 mg strengths; the '776 patent for the 45 mg, 55 mg, 65 mg, 80 mg, 90 mg, 105 mg and 135 mg strengths; the '650 patent for the 55 mg, 80 mg, and 105 mg strengths; and the '615 patent for the 65 mg and 115 mg strengths would not create a statutory stay of approval.

Under section 506A of FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Office of Generic Drugs should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Office of Generic Drugs in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. [As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.].

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling materials prior to publication or dissemination. Please note that these submissions are voluntary. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert (PI), Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

You must also submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For

more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>. The SPL will be accessible via publicly available labeling repositories.

II. Tentative Approval of Minocycline Hydrochloride Extended-Release Tablets, 55 mg, 65 mg and 115 mg

We are unable to grant final approval to your ANDA at this time. Prior to the submission of your ANDA for the 55 mg and 65 mg strengths and your amendment for the 115 mg strength, another applicant or applicants submitted a substantially complete ANDA providing for Minocycline Hydrochloride Extended-Release Tablets USP, 55 mg, 65 mg, and 115 mg, and containing a paragraph IV certification. Your ANDA insofar as the 55 mg, 65 mg, and 115 mg strengths will be eligible for final approval on the date that is 180 days after the commercial marketing date of each strengths, respectively, identified in section 505(j)(5)(B)(iv) of the FD&C Act.

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

RESUBMISSION

To request final approval, please submit an amendment titled “FINAL APPROVAL REQUESTED” with enough time to permit FDA review prior to the date you believe that your ANDA will be eligible for final approval. A request for final approval that contains no new data, information, or other changes to the ANDA generally requires a period of 90 days for Agency review. Accordingly, such a request for final approval should be submitted no later than 90 days prior to the date on which you seek approval. A request for final approval that contains substantive changes to this ANDA or changes in the status of the manufacturing and testing facilities’ compliance with cGMPs will be classified and reviewed according to OGD policy in effect at the time of receipt. Applicants should review available agency guidance for industry related to amendments under the generic drug user fee program to determine the duration of Agency review needed to review the changes submitted. The submission of multiple

amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The amendment requesting final approval should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, settlement or licensing agreement, or other information described in 21 CFR 314.107, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, e.g., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a “FINAL APPROVAL REQUESTED.”

In addition to the amendment requested above, the Agency may request, at any time prior to the date of final approval, that you submit an additional amendment containing information as specified by the Agency. Failure to submit either or, if requested, both types of amendments described above may result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final Agency approval under section 505(j) of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the FD&C Act. Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under section 505(j) of the FD&C Act, and will not be listed in the Orange Book. Should you believe that there are grounds for issuing the final approval letter, you should amend your ANDA accordingly.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions³ with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that

³ Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self-identification or fee payment.

Additionally, we note that the failure of any facility referenced in the application to self-identify and pay applicable fees means that FDA will not consider the GDUFA application review goal dates to apply to that application.

The Electronic Common Technical Document (eCTD) is CDER's standard format for electronic regulatory submissions. Beginning May 5, 2017, ANDAs must be submitted in eCTD format and beginning May 5, 2018, drug master files must be submitted in eCTD format. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit: www.fda.gov/ectd.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Kevin Denny, Regulatory Project Manager, at (240) 402-8919.

Sincerely yours,

{See appended electronic signature page}

Vincent Sansone, PharmD
Acting Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research



Vincent
Sansone

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