DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

ANDA 065485/S-005 (80 mg and 105 mg)
065485/S-008 (55 mg)

APPROVAL/TENTATIVE APPROVAL

Barr Laboratories, Inc.
425 Privet Road
Horsham, PA 19044
Attention: Rich Leone
Senior Director, Regulatory Affairs, US Generics

Dear Sir:

This is in reference to your supplemental abbreviated new drug application (sANDA) received for review February 9, 2011, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for Minocycline Hydrochloride Extended-Release Tablets, 45 mg, 90 mg, and 135 mg (base).

Reference is also made to your amendments dated March 25, 2011; February 25, and September 22, 2014; and June 16, 2016.

These sANDAs, submitted as a "Prior Approval Supplement," provide for:

> Addition of new strengths, Minocycline Hydrochloride Extended-Release Tablets, 55 mg, 80 mg, and 105 mg (base).

We have completed the review of these sANDAs 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. The Office of Bioequivalence has determined your Minocycline Hydrochloride Extended-Release Tablets, 55 mg, 80 mg, and 105 mg (base), to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Solodyn Extended-Release Tablets, 55 mg, 80 mg, and 105 mg, of Medicis Pharmaceuticals Corporation (Medicis).

However, we are unable to grant final approval to your Minocycline Hydrochloride Extended-Release Tablets, 55 mg, at this time because of the exclusivity issue noted below. Therefore, your sANDA is **approved** insofar as it pertains to Minocycline Hydrchloride Extended-Release Tablets, 80 mg and 105 mg. Your Minocycline Hydrchloride Extended-Release Tablets, 55 mg strength is **tentatively approved**.

The RLD upon which you have based your ANDA, Medicis's Solodyn Extended-Release Tablets, 55 mg, 80 mg, and 105 mg, is subject to periods of patent protection. The following

patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

U.S. Patent Number	Expiration Date
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

Your sANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that each of these patents[1] is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Minocycline Hydrochloride Extended-Release Tablets, 55 mg, 80 mg, and 105 mg under this sANDA. You have notified the agency that Barr Laboratories, Inc. (Barr) complied with the requirements of section 505(j)(2)(B) of the FD&C Act, and that no action for infringement was brought against Barr within the statutory 45- day period.

I. Approval of Minocycline Hdrochloride Extended-Release Tablets, 80 mg and 105 mg.

With respect to your Minocycline Hydrochloride Extended-Release Tablets, 80 mg and 105 mg, dissolution testing should be incorporated into the stability and quality control program using the FDA-recommended method and specification for your application.

Under section 506A of the 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 & 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. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

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

[1] The agency notes that the '483, '776, '804 and '650 patents were submitted to the agency after submission of your sANDA. Litigation, if any, with respect to these patents would not create a statutory stay of approval.

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.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions 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.

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.

With respect to your Minocycline Hydrchloride Extended-Release Tablets, 55 mg, our decision is based upon information currently available to the agency (i.e., date in your sANDA and the status of current good manufacturing practice (cGMP) of the facilities used in the manufacture and testing of the drug product). This decision is subject to change on the basis of new information that may come to our attention.

We are unable to grant final approval to your Minocycline Hydrchloride Extended-Release Tablets, 55 mg. Prior to the submission of you sANDA, another applicant or applicants submitted a substanstially complete ANDA providing for Minocycline Hydrchloride Extended-Release Tablets, 55 mg, and containing a paragraph IV certification. Your ANDA for this strength will be eligible for final approval on the date that is 180 days after the commercial marketing date 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 sANDA will be eligible for final approval. A request for final approval that contains no new data, information, or other changes to the sANDA 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 sANDA 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 sANDA was tentatively approved, i.e.,

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 "MINOR/MAJOR AMENDMENT TO SUPPLEMENT 8 – 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.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your sANDA 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 1 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 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.

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 sANDA or upon submitting an amendment to the sANDA, please contact Stephanie Lim, Regulatory Project Manager, at (240) 402-8998.

Sincerely yours,

{See appended electronic signature page}

Carol A. Holquist, RPh
Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

ENCLOSURE: DISSOLUTION

The "interim" dissolution specifications are as follows:

Dissolution Testing should be conducted in

Medium:	0.1 N HCl
Volume:	900 mL
Apparatus:	USP Apparatus I (Basket)
Speed of Rotation:	100 rpm
Specifications:	1 hour: (b) (4) % 2 hours: (b) (4) % 4 hours: NLT (b) (4) %

The "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data for the first three production size batches. Data should be submitted as a Supplement – Changes Being Effected when there are no revisions to the "interim" specifications or when the final specifications are more stringent than the "interim" specifications. In all other instances, the information should be submitted in a Prior Approval Supplement.

Carol Holquist

Digitally signed by Carol Holquist
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