DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 203443

Mylan Pharmaceuticals Inc.
Vice President, Regulatory Affairs
Attention: Joseph J. Sobecki
Vice President, Regulatory Affairs
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated September 12, 2011, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Minocycline Hydrochloride Extended-release Tablets, 55 mg (base), 80 mg (base), and 105 mg (base).

Reference is made to the Complete Response letter issued by this office on July 24, 2013, and to your amendments dated September 20, and September 25, 2013; and August 5, August 12, and August 20, 2014.

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. However, we are unable to grant final approval to your Minocycline Hydrochloride Extended-release Tablets, 55 mg (base), at this time because of the exclusivity issue noted below. Therefore, only your Minocycline Hydrochloride Extended-release Tablets, 80 mg (base) and 105 mg (base), are **approved**. The 55 mg (base) strength is **tentatively approved**.

The reference listed drug (RLD), upon which you have based your ANDA, Solodyn, 55 mg (base), 80 mg (base), and 105 mg (base), of Medicis Pharmaceutical Corporation (Medicis), is subject to periods of patent protection. The following patents and their expiration dates are currently listed in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") for this drug product:

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

I. Approval of Minocycline Hydrochloride Extended-release Tablets, 80 mg (base), and 105 mg (base).

With respect to your Minocycline Hydrochloride Extended-release Tablets, 80 mg (base) and 105 mg (base), we have concluded that adequate information has been presented to demonstrate that these strengths are safe and effective for use as recommended in the submitted labeling. Accordingly your Minocycline Hydrochloride Extended-release Tablets, 80 mg (base) and 105 mg (base), are approved, effective on the date of this letter. The Division of Bioequivalence has determined your Minocycline Hydrochloride Extended-Release Tablets, 80 mg (base) and 105 mg (base), to be bioequivalent and, therefore, therapeutically equivalent to the RLD, Solodyn Extended-release Tablets, 80 mg (base) and 105 mg (base), respectively, of Medicis.

Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA. The "interim" dissolution specifications are as follows:

Dissolution Testing should be conducted in:

Medium:	0.1 N HCl
Volume:	900 mL
USP Apparatus:	USP Apparatus I (Basket)
Rotational Speed:	100 rpm

"Interim" Specifications:

Time (Hours)	Percent Dissolved
1	(b) (4)
2	(b) (4)
4	NLT (b) (4)

The "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a "Special Supplement – Changes Being Effected" if there are no revisions to be made to the "interim" specifications, or if the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

Under section 506A of the 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 Act.

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 may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

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

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Office of Prescription Drug Promotion with a completed Form FDA 2253 at the time of their initial use.

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 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.

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 (base).

We are unable to grant final approval to your Minocycline Hydrochloride Extended-release Tablets, 55 mg (base), at this time because prior to the submission of your ANDA, another applicant submitted an ANDA providing for Minocycline Hydrochloride Extended-release Tablets, 55 mg (base), containing a paragraph IV certification. Therefore, your ANDA as it pertains to the 55 mg (base) strength will be eligible for final approval upon the expiration of the 180-day exclusivity identified in section 505(j)(5)(B)(iv) of the Act, or that exclusivity is otherwise resolved.

Your Minocycline Hydrochloride Extended-release Tablets, 55 mg (base), is **tentatively approved**. This determination is based upon information available to the agency at this time (i.e., information in your ANDA and the status of current good manufacturing practice (cGMP) of the facilities used in the manufacturing and testing of the drug product) and is therefore subject to change on the basis of new information that may come to our attention.

To reactivate your ANDA prior to final approval of the 55 mg (base) strength, please submit a "***MINOR AMENDMENT TO ORIGINAL #2 – FINAL APPROVAL REQUESTED***" 90 days prior to the date you believe that your ANDA will be eligible for final approval. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, or a settlement or licensing agreement, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA 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 AMENDMENT TO ORIGINAL #2 – 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 the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your ANDA, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in the status of the manufacturing and testing facilities' cGMP are subject to agency review before final approval of the ANDA will be made. Such changes should be categorized as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The 55 mg (base) strength may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of these strengths before the final approval date is prohibited under section 301 of the Act. Also, until the agency issues the final approval letter, these strengths will not be deemed to be approved for marketing under section 505 of the Act, and will not be listed in the "Orange Book."

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 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.

For further information on the status of this ANDA, or prior to submitting additional amendments, please contact Anh Bui, Project Manager, at 240-402-8900 or via email at YenAnh.Bui@fda.hhs.gov.

Sincerely yours,

{See appended electronic signature page}

CAPT Jason J.Y. Woo, M.D., M.P.H.
Acting Director, Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT L WEST

08/22/2014

Associate Director for Review Quality, for
Jason Woo, M.D., M.P.H.