DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 091059

ANDA APPROVAL/TENTATIVE APPROVAL

Teva Pharmaceuticals USA
425 Privet Road
Horsham, PA 19044
Attention: Scott D. Tomsky
Vice President, Regulatory Affairs, North America, Generics

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated November 18, 2008, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), for Erlotinib Tablets, 25 mg, 100 mg, and 150 mg.

Reference is also made to the Complete Response letter issued by this Office on September 26, 2014, and to your amendment dated October 23, 2014.

The reference listed drug (RLD) upon which you have based your ANDA, Tarceva (erlotinib) Tablets, 25 mg, 100 mg, and 150 mg, of OSI Pharmaceuticals LLC (OSI), is subject to periods of patent protection. The following patents and expiration dates (with pediatric exclusivity added) 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
6,900,221 (the '221 patent)	May 9, 2021
5,747,498 (the '498 patent)	May 8, 2019
7,087,613 (the '613 patent)	May 9, 2021
RE41,065 (the '065 patent)	May 8, 2019

Your ANDA contains paragraph IV certifications to each of the patents 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 Erlotinib Tablets, 25 mg, 100 mg, and 150 mg, under this ANDA.[1] You have notified the agency that Teva Pharmaceuticals USA (Teva) complied with the requirements of section 505(j)(2)(B) of the FD&C Act, and litigation for infringement of the '221, '498, '613, and '065 patents was brought against Teva within the statutory 45-day period in the United States District Court for the District of Delaware [OSI Pharmaceuticals Inc., Pfizer Inc., and Genentech, Inc. v. Teva Pharmaceuticals USA, Inc., Civil Action No. 09-185 (consolidated)]. You have further notified the Agency that the case was dismissed.

[1] The agency notes that the '065 patent was listed in the Orange Book after submission of your ANDA. Litigation, if any, with respect to this patent would not create a statutory stay of approval.

I. Approval of Erlotinib Tablets, 100 mg and 150 mg

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. Approval is granted for your Erlotinib Tablets, 100 mg and 150 mg, effective on the date of this letter. The Division of Bioequivalence has determined your Erlotinib Tablets, 100 mg and 150 mg, to be bioequivalent and, therefore, therapeutically equivalent to the RLD, OSI's Tarceva. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA.

With respect to 180-day generic drug exclusivity, we note that Teva was one of the first ANDA applicants to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Teva may be eligible for 180 days of shared generic drug exclusivity for Erlotinib Tablets, 100 mg and 150 mg. The agency notes that Teva failed to obtain tentative approval of this ANDA within 30 months after the date on which the ANDA was filed. See section 505(j)(5)(D)(i)(IV) of the FD&C Act (forfeiture of exclusivity for failure to obtain tentative approval). The agency is not, however, making a formal determination at this time of Teva's eligibility for 180-day generic drug exclusivity.

At least one first applicant remains eligible for 180 days of generic drug exclusivity for Erlotinib Tablets, 100 mg and 150 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act, will begin to run from the date of the commercial marketing by any first applicant, as identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA informing the agency of the date you begin commercial marketing.

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.

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(s) 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 Erlotinib Tablets, 25 mg

We have completed the review of this ANDA, and based upon the information you have presented to date we have concluded 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 Erlotinib Tablets, 25 mg, at this time because of the exclusivity issue noted below. Therefore, your Erlotinib Tablets, 25 mg, 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) at 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.

We are unable at this time to grant final approval to your Erlotinib Tablets, 25 mg. Prior to the submission of your ANDA, another applicant submitted a substantially complete ANDA

providing for Erlotinib Tablets, 25 mg, and containing a paragraph IV certification. Your ANDA 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 & 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.

To reactivate your ANDA prior to final approval, please submit a "MINOR AMENDMENT – 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 – 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' cGMPs 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.

This drug product may not be marketed without final agency approval under section 505 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 to be approved for marketing under section 505 of the FD&C 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 Jessica Kreger, Regulatory Project Manager, at 240-402-3957.

Sincerely yours,

Carol A. Holquist -S

Digitally signed by Carol A. Holquist -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300052464, cn=Carol A. Holquist -S
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Carol A. Holquist, RPh
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