DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 205253

ANDA APPROVAL

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

Dear Sir:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on March 18, 2014, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Trazodone Hydrochloride Tablets USP, 50 mg, 100 mg, 150 mg, and 300 mg.[1]

Reference is also made to the complete response letter issued by this office on April 6, 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, the ANDA is **approved**, effective on the date of this letter. The Office of Bioequivalence has determined your Trazodone Hydrochloride Tablets USP, 50 mg, 100 mg, 150 mg, and 300 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Desyrel Tablets, 50 mg, 100 mg, 150 mg, and 300 mg, of Pragma Pharmaceuticals, LLC (Pragma).

The RLD upon which you have based your ANDA, Pragma's Desyrel Tablets 50 mg, 100 mg, 150 mg, and 300 mg, is subject to a period of patent protection. The following patent and expiration date is currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

U.S. Patent Number	Expiration Date
8,133,893 (the '893 patent)	March 13, 2029

Your ANDA contains a paragraph IV certification to the '893 patent[2] under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Trazodone Hydrochloride Tablets USP, 50 mg, 100 mg, 150 mg, and 300 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.

With respect to 180-day generic drug exclusivity, we note that Zydus was the first ANDA applicant for Trazodone Hydrochloride Tablets USP, 50 mg, 100 mg, 150 mg, and 300 mg, to submit a substantially complete ANDA with a paragraph IV certification to the '893 patent. Therefore, with this approval, Zydus is eligible for 180 days of generic drug exclusivity for Trazodone Hydrochloride Tablets USP, 50 mg, 100 mg, 150 mg, and 300 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 earlier of the court decision or commercial marketing dates identified in section 505(j)(5)(B)(iv) of the FD&C Act.[3] Please submit correspondence to this ANDA informing the Agency of the date the exclusivity begins to run.

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.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[4] 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.

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.

Sincerely yours,

{See appended electronic signature page}

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

[1] We note that the reference listed drug (RLD) upon which you have based this ANDA, Pragma Pharmaceuticals, LLC (Pragma's) Desyrel Tablets, 50 mg, 100 mg, 150 mg, and 300 mg, are no longer being marketed in the United States and are currently listed in the discontinued section of FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"). The Agency has determined that Pragma's Desyrel Tablets, 50 mg, 100 mg, 150 mg, and 300 mg, were not withdrawn from sale for reasons of safety or effectiveness. FDA published this determination in the *Federal Register* (75 FR 11549; March 11, 2010). This determination allows the Agency to approve ANDAs for the discontinued drug products.

[2] The Agency notes that the '893 patent was submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to this patent would not create a statutory stay of approval.

[3] Because another ANDA for Trazodone Hydrochloride Tablets USP, 50 mg, 100 mg, 150 mg, and 300 mg, was filed before the date of enactment of the *Medicare Prescription Drug, Improvement and Modernization Act* (MMA) (Public Law 108-173) on December 8, 2003, this reference to the 180-day exclusivity provision is to the section of the FD&C Act as in effect prior to December 8, 2003. See MMA § 1102(b)(1). This is the case despite the fact that your ANDA was filed after enactment of the MMA.

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

Priya Shah

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