DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 091640

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 December 16, 2009, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Mesalamine Delayed-Release Tablets USP, 1.2 g.

Reference is also made to the complete response letter issued by this office on December 14, 2016, and to your amendment received on February 23, 2017.

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 Mesalamine Delayed-Release Tablets USP, 1.2 g, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Lialda Delayed-Release Tablets, 1.2 g, of Shire Development LLC (Shire). Your dissolution testing should be incorporated into the stability and quality control program using the FDA-recommended method and specification for your application (see enclosure).

The RLD upon which you have based your ANDA, Shire's Lialda Delayed-Release Tablets, 1.2 g, 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
6,773,720 (the '720 patent)	June 8, 2020

Your ANDA contains a paragraph IV certification to the '720 patent 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 Mesalamine Delayed-Release Tablets USP, 1.2 g, 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 '720 patent in the United States District Court for the District of Delaware [Shire Development Inc., Shire Pharmaceutical Development Inc., Cosmo Technologies Limited, and Giuliani International Limited v. Cadila Healthcare Limited (d/b/a Zydus Cadila) and Zydus Pharmaceuticals (USA) Inc., Civil Action No. 1:10-cv-00581]. You have also notified the Agency that on September 16, 2016, the court entered a final judgment of non-infringement in Zydus' favor. You have further notified the Agency that the case was appealed to the United States Court of Appeals for the Federal Circuit and on May 9, 2017, the court affirmed the decision of the district court.

With respect to 180-day generic drug exclusivity, we note that Zydus was the first ANDA applicant for Mesalamine Delayed-Release Tablets USP, 1.2 g, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Zydus may be eligible for 180 days of generic drug exclusivity for Mesalamine Delayed-Release Tablets USP, 1.2 g. This exclusivity, which is provided for under 505(j)(5)(B)(iv) of the FD&C Act, would begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). The Agency notes that Zydus failed to obtain tentative approval of this ANDA within 30 months after the date of 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 Zydus's eligibility for 180-day generic drug exclusivity. It will do so only if a subsequent paragraph IV applicant becomes eligible for full approval (a) within 180 days after Zydus begins commercial marketing of Mesalamine Delayed-Release Tablets USP, 1.2 g, or (b) at any time prior to the expiration of the '720 patent if Zydus has not begun commercial marketing. Please submit correspondence to this ANDA informing the Agency of the date commercial marketing begins.

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. 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

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.

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}

Heidi Lee, PharmD
Acting 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:

Method	**Acid Stage A**: 750 mL of 100 mM HCl (Acid Stage A) **Buffer Stage B**: 950 mL of Phosphate buffer, pH 6.4 (Buffer Stage B: A+ 200 mL 200 mM Na_3PO_4) **Buffer Stage C**: 960 mL of Phosphate buffer, pH 7.2 (Buffer Stage C: B + 9 mL 2M NaOH adjusting pH with 2M NaOH or 2M HCl)
Apparatus	USP apparatus 2 (Paddle)
Speed	100 rpm
Specifications	**Acid stage A:** NMT (b)(4)% in 2 hours **Buffer stage B:** NMT % in 1 hour **Buffer stage C:** 1 hour: NMT (b)(4)% 2 hours: (b)(4)% 6 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.

Heidi Lee

Digitally signed by Heidi Lee
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