ANDAs 040054/S-015, S-016 and S-017

CHANGES BEING EFFECTED
APPROVAL

Hikma Pharmaceuticals USA Inc.
1809 Wilson Road
Columbus, OH 43228
Attention: Jerald Andry
Senior Director, Drug Regulatory Affairs

Dear Jerald Andry:

This is in reference to your supplemental abbreviated new drug applications (sANDAs) received for review as listed below, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Methotrexate Tablets USP, 2.5 mg.

Supplement	Received Date
S-015	May 18, 2016
S-016	October 31, 2018
S-017	May 21, 2020

Reference is also made to any amendments submitted prior to the issuance of this letter.

These Changes Being Effected supplemental abbreviated new drug applications provide for:

S-015: Revised labeling, carton and container labels to be in accordance with the reference listed drug (RLD), Methotrexate Tablets, NDA 008085/S-066, approved on January 29, 2016.

S-016: Revised labeling to be in accordance with the reference listed drug (RLD), Methotrexate Tablets, NDA 008085/S-068, approved on March 15, 2018.

S-017: Revised labeling to be in accordance with the reference listed drug (RLD), Methotrexate Tablets, NDA 008085/S-071, approved on May 4, 2020.

We have completed the review of these supplemental applications, as amended. They are **approved**, effective on the date of this letter.

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.

If your product is a combination product as defined by 21 CFR 3.2(e) and is comprised of drug and device constituent parts we remind you that you must comply with the postmarking safety reporting requirements for an approved combination product (21 CFR Part 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products

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 https://www.fda.gov/media/71211/download. The SPL will be accessible via publicly available labeling repositories.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions [1] 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.

Sincerely yours,

{See appended electronic signature page}

For Rachel Goehe, Ph.D.
Director
Division of Labeling Review
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

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

Annie Guan

Digitally signed by Annie Guan
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