DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 202917

APPROVAL

Sun Pharmaceutical Industries, Inc.
U.S. Agent for Sun Pharma Global FZE
270 Prospect Plains Road
Cranbury, NJ 08512
Attention: Mr. Syed Qadry

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for Metformin Hydrochloride Extended-Release Tablets USP, 500 mg and 1000 mg.

Reference is also made to the tentative approval letter issued by this office on April 10, 2013, and to your amendment dated April 2, 2016.

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 Metformin Hydrochloride Extended-Release Tablets USP, 500 mg and 1g, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Glumetza Extended-Release Tablets, 500 mg and 1g of Santarus, Inc. (Santarus).

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	pH 1.2 Modified Simulated Gastric Fluid per USP less pepsin	
Volume	900 mL	
Temperature	37°C ± 0.5°C	
Apparatus	USP apparatus I (Basket, 40 mesh)	
Speed	100 rpm	
Specification(s) (per time point)	**500 mg and 1000 mg**	
	2 hours	(b) (4) %
	4 hours	(b) (4) %
	8 hours	NLT (b) (4) %
	12 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 Special Supplement – Changes Being Effected when there are no revisions to the "interim" specifications or when 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.

The RLD upon which you have based your ANDA, Santarus's Glumetza Extended-Release Tablets, 500 mg and 1 g, is subject to periods of patent protection. The following patents and expiration dates 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
6,340,475 (the '475 patent)	September 19, 2016 (500 mg strength only)
6,635,280 (the '280 patent)	September 19, 2016 (500 mg strength only)
6,488,962 (the '962 patent)	June 20, 2020
6,723,340 (the '340 patent)	October 25, 2021 (500 mg strength only)
7,780,987 (the '987 patent)	March 23, 2025 (1 g strength only)
8,323,692 (the '692 patent)	March 23, 2025 (1 g strength only)

Your ANDA contains paragraph IV certifications to each of the patents[1] 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 Metformin Hydrochloride Extended-Release Tablets USP, 500 mg and 1 g, under this ANDA. You have notified the agency that Sun Pharma Global FZE (Sun) complied with the requirements of section 505(j)(2)(B) of the FD&C Act, and that litigation was initiated against Sun for infringement of the '475, '280, '962, '340 and '987 patents within the statutory 45-day period in the United States District Court for the District of New Jersey [Depomed Inc. and Valeant International (Barbados) Srl v. Sun Pharma Global FZE, Sun Pharmaceutical, Industries Ltd., and Sun Pharmaceutical Industries Inc., Civil Action No. 11-3553 (JAP)]. You have also notified the agency that this case was dismissed.

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.

[1] The agency notes that the '692 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.

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.

Sincerely yours,

{See appended electronic signature page}

Carol A. Holquist, RPh
Acting Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

Carol Holquist

Digitally signed by Carol Holquist
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