DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 205327

ANDA APPROVAL

Osmotica Pharmaceutical US LLC
U.S. Agent for Osmotica Kereskedelmi es Szolgaltato Kft
1904 Eastwood Rd., Lumina Station #2, Suite 205
Wilmington, NC 28403
Attention: Mark S. Aikman, PharmD
Vice President, Drug Safety and Generics Regulatory Affairs

Dear Sir:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on January 18, 2013, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Methylphenidate Hydrochloride Extended-Release Tablets USP, 18 mg, 27 mg, 36 mg, 54 mg, and 72 mg.

Reference is also made to the complete response letter issued by this office on September 16, 2015, and to your amendments received on December 21, 2015; April 20, September 9, September 12, October 14, and November 2, 2016; and January 6, February 16, and March 27, 2017.

Reference is further made to the ANDA Suitability Petition (2005P-0257/CP1) submitted on June 22, 2005, under section 505(j)(2)(C) of the FD&C Act, and approved on November 14, 2005. This petition requested that the U.S. Food and Drug Administration (FDA or the Agency) make a determination as to whether an application for Methylphenidate Hydrochloride Extended-Release Tablets, 72 mg, was suitable for submission as an ANDA. This determination was necessary because the strength proposed in your ANDA differs from the strength of the reference listed drug (RLD), Janssen Pharmaceuticals, Inc.'s (Janssen) Concerta Extended-Release Tablets, 18 mg, 27 mg, 36 mg, and 54 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. **Accordingly the ANDA is approved**, effective on the date of this letter. The Office of Bioequivalence has determined your Methylphenidate Hydrochloride Extended-Release Tablets USP, 18 mg, 27 mg, 36 mg, and 54 mg, to be bioequivalent and, therefore, therapeutically equivalent to the RLD, Janssen's Concerta Extended-Release Tablets, 18 mg, 27 mg, 36 mg, and 54 mg. The Office of Bioequivalence has also determined that your Methylphenidate Hydrochloride Extended-Release Tablets USP, 72 mg, can be expected to have the same therapeutic effect as that of the listed drug product upon which the Agency relied as the basis of safety and effectiveness. 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, Janssen's Concerta Extended-Release Tablets, 18 mg, 27 mg, 36 mg, and 54 mg, 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
6,919,373 (the '373 patent)	January 31, 2018*
6,930,129 (the '129 patent)	January 31, 2018*
8,163,798 (the '798 patent)	January 31, 2018*
8,629,179 (the '179 patent)	January 31, 2018*
9,000,038 (the '038 patent)	January 31, 2018*
9,029,416 (the '416 patent)	July 31, 2017
9,144,549 (the '549 patent)	July 31, 2017

***** with pediatric exclusivity added

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 Methylphenidate Hydrochloride Extended-Release Tablets USP, 18 mg, 27 mg, 36 mg, 54 mg, and 72 mg, under this ANDA. You have notified the Agency that Osmotica Kereskedelmi es Szolgaltato Kft (Osmotica) 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 Osmotica for infringement of the '179 and '798 patents in the United States District Court for the District of Delaware [Alza Corporation and Janssen Pharmaceuticals, Inc. v. Osmotica Kereskedelmi es Szolgaltato Kft and Osmotica Pharmaceutical Corp., Civil Action No. 13-1104-RGA]. You have also notified the Agency that this case was dismissed.

With respect to 180-day generic drug exclusivity, we note that Osmotica was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification for Methylphenidate Hydrochloride Extended-Release Tablets USP, 72 mg. Therefore, with this approval, Osmotica may be eligible for 180 days of generic drug exclusivity for Methylphenidate Hydrochloride Extended-Release Tablets USP, 72 mg. This exclusivity, which is provided for under section 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 Osmotica 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 Osmotica'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 Osmotica begins commercial marketing of Methylphenidate Hydrochloride Extended-Release Tablets USP, 72 mg, or (b) at any time prior to the expiration of the '373,

[1] The Agency notes that the '179 (54 mg strength only), '038, '416, and '549 patents were submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to these patents would not create a statutory stay of approval.

‘129, ‘798, and ‘179 patents if Osmotica has not begun commercial marketing. Please submit correspondence to this ANDA informing the Agency of the date commercial marketing begins.

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 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}

For Vincent Sansone, 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:

USP Apparatus	7 (reciprocating cylinder)
Rotational Speed	30 cycles/min; 2-3 cm amplitude
Temperature	37 ± 0.5°C
Media	Acidified water. Adjust with phosphoric acid to a pH of 3
Volume	50 mL
Specifications	Time (h) Amount Dissolved 1 (b)(4)% - (b)(4)% 4 (b)(4)% - (b)(4)% 10 NLT (b)(4)% Average from 3 to 6 h: (b)(4)%– (b)(4)%/h*

*The average percentage released from 3 to 6 h should be calculated as: (Y - X)/3
Y = cumulative drug released from 0 to 6 h
X = cumulative drug released from 0 to 3 h

Since the FDA-recommended specifications are different from the USP specifications, the test product labeling should state "the USP Dissolution Testing is pending". Following the approval of the application, you may petition the USP for incorporating the FDA-recommended dissolution method and specifications into the USP monograph.

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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