



ANDA 090713

ANDA APPROVAL

Teva Pharmaceuticals USA, Inc.
425 Privet Road
Horsham, PA 19044
Attention: Cory Wohlbach
Senior Director, Regulatory Affairs, US Generics

Dear Sir:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on August 20, 2008, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Palonosetron Hydrochloride Injection, 0.075 mg (base)/1.5 mL and 0.25 mg (base)/5 mL single-use vials.

Reference is also made to the tentative approval letter issued by this office on October 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 Palonosetron Hydrochloride Injection, 0.075 mg (base)/1.5 mL and 0.25 mg (base)/5 mL single-use vials, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Aloxi Injection, 0.075 mg (base)/1.5 mL and 0.25 mg (base)/5 mL single-use vials, of Helsinn Healthcare SA (Helsinn).

The RLD upon which you have based your ANDA, Helsinn's Aloxi Injection, 0.075 mg (base)/1.5 mL and 0.25 mg (base)/5 mL single-use vials, is subject to periods of patent protection. The following patents and expiration dates (with pediatric exclusivity added) are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

<u>U.S. Patent Number</u>	<u>Expiration Date</u>
7,947,724 (the '724 patent)	July 30, 2024
7,947,725 (the '725 patent)	July 30, 2024
7,960,424 (the '424 patent)	July 30, 2024
8,518,981 (the '981 patent)	July 30, 2024
8,598,218 (the '218 patent)	July 30, 2024
8,598,219 (the '219 patent)	July 30, 2024 (0.25 mg/5 mL only)
8,729,094 (the '094 patent)	July 30, 2024 (0.25 mg/5 mL only)
9,066,980 (the '980 patent)	July 30, 2024 (0.25 mg/5 mL only)
9,125,905 (the '905 patent)	July 30, 2024 (0.25 mg/5 mL only)
9,173,942 (the '942 patent)	July 30, 2024
9,439,854 (the '854 patent)	July 30, 2024
9,457,020 (the '020 patent)	July 30, 2024
9,457,021 (the '021 patent)	July 30, 2024 (0.25 mg/5 mL only)

Your ANDA contains paragraph IV certifications to each of the patents¹ 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 Palonosetron Hydrochloride Injection, 0.075 mg (base)/1.5 mL and 0.25 mg (base)/5 mL single-use vials, under this ANDA.

You have notified the Agency that the United States District Court for the District of New Jersey [Helsinn Healthcare S.A. and Roche Palo Alto LLC v. Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries, Ltd., Civil Action No. 11-3962(MLC)(DEA)] issued a Final Judgment on November 16, 2015, in which the court determined that the asserted claims of the '724, '725, and '424 patents are valid and infringed by Teva Pharmaceuticals USA, Inc.'s (Teva's) Palonosetron Hydrochloride Injection, 0.075 mg (base)/1.5 mL and 0.25 mg (base)/5 mL single-use vials, and the '219 patent is valid and infringed by Teva's Palonosetron Hydrochloride Injection, 0.25 mg (base)/5 mL single-use vials. The court ordered that pursuant to 35 U.S.C. 271(e)(4)(A), "the effective date of any final approval of ANDA No. 090713 by the FDA shall be no earlier than July 30, 2024, the expiration of the '724, '725, '424 and '219 patents, including pediatric exclusivity." You have further notified the Agency that this case was appealed to the Court of Appeals for the Federal Circuit, and on May 1, 2017, the court reversed the district court decision.² The Court of Appeals for the Federal Circuit issued a mandate in accordance with the May 1, 2017, judgment on January 29, 2018, and on February 6, 2018, the district court vacated its November 16, 2015, Final Judgment.

With respect to 180-day generic drug exclusivity, we note that Teva was one of the first ANDA applicants with a substantially complete ANDA for Palonosetron Hydrochloride Injection, 0.075 mg (base)/1.5 mL and 0.25 mg (base)/5 mL single-use vials, to submit a paragraph IV certification. Therefore, with this approval, Teva may be eligible for 180 days of shared generic drug exclusivity for Palonosetron Hydrochloride Injection, 0.25 mg (base)/5 mL single-use vials, and is eligible for 180 days of shared generic drug exclusivity for Palonosetron Hydrochloride Injection, 0.075 mg (base)/1.5 mL single-use vials. The Agency notes that Teva failed to obtain tentative approval of the 0.25 mg (base)/5 mL strength single-use vials, within the relevant time period after the date on 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 Teva's eligibility for 180-day exclusivity for the 0.25 mg (base)/5 mL strength.

At least one first applicant remains eligible for 180 days of generic drug exclusivity for Palonosetron Hydrochloride Injection, 0.25 mg (base)/5 mL single-use vials.³ This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act, will begin to run from the date of the commercial marketing by any first applicant, as identified in section 505(j)(5)(B)(iv) of the FD&C Act. Please submit correspondence to this ANDA notifying the Agency within 30 days of the date of the first commercial marketing of this drug product or the RLD. If you do not notify the Agency within 30 days, the date of first commercial marketing will be deemed to be the date of the drug product's approval. See 21 CFR 314.107(c)(2).

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 506l of the FD&C Act. The Agency 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 506l(b) of the FD&C Act, you are required to notify the Agency 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 provisions⁴ 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
Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

¹ The Agency notes that the ‘724, ‘725, ‘424, ‘981, ‘218, ‘219, ‘094, ‘980, ‘905, ‘942, ‘854, ‘020 and ‘021 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.

² *Helsinn Healthcare S.A. v. Teva Pharmaceuticals USA, Inc.*, 855 F.3d 1356 (2017).

³ See also draft guidance for industry on *180-Day Exclusivity: Questions and Answers*, Q. 42, at 26 (Jan. 2017).

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

Digitally signed by Priya Shah

Date: 3/23/2018 08:32:25AM

GUID: 5256c7080002b0e78814870319c70608