



ANDA 206986

**ANDA APPROVAL**

Alvogen PB Research and Development LLC  
U.S. Agent for Alvogen Malta Operations Ltd.  
44 Whippany Road  
Suite 300  
Morristown, NJ 07960  
Attention: Patricia Jaworski  
Vice President - Regulatory Affairs

Dear Madam:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on April 17, 2014, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Hydrocodone Bitartrate Extended-Release Capsules, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, and 50 mg.

Reference is also made to the tentative approval letter issued by this office on May 25, 2017, the complete response letter issued by this office on October 3, 2019, 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 meets the requirements for approval under the FD&C Act. Accordingly, the ANDA is **approved**, effective on the date of this letter. We have determined your Hydrocodone Bitartrate Extended-Release Capsules, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, and 50 mg, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Zohydro ER Capsules, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, and 50 mg, of Persion Pharmaceuticals LLC (Persion).

The RLD upon which you have based your ANDA, Persion's Zohydro ER Capsules, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, and 50 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>U.S. Patent Number</u>	<u>Expiration Date</u>
9,132,096 (the '096 patent)	September 12, 2034
9,265,760 (the '760 patent)	July 25, 2033
9,326,982 (the '982 patent)	July 25, 2033
9,333,201 (the '201 patent)	July 25, 2033
9,339,499 (the '499 patent)	July 25, 2033
9,421,200 (the '200 patent)	July 25, 2033
9,433,619 (the '619 patent)	July 25, 2033
9,452,163 (the '163 patent)	September 12, 2034
9,486,451 (the '451 patent)	September 12, 2034
9,610,286 (the '286 patent)	July 25, 2033
9,713,611 (the '611 patent)	September 12, 2034
10,028,946 (the '946 patent)	July 25, 2033
10,092,559 (the '599 patent)	September 12, 2034
10,322,120 (the '120 patent)	July 25, 2033
10,456,393 (the '393 patent)	July 25, 2033

Your ANDA contains paragraph IV certifications to each of the patents<sup>1</sup> 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 Hydrocodone Bitartrate Extended-Release Capsules, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, and 50 mg. You have notified the Agency that Alvogen Malta Operations Ltd. complied with the requirements of section 505(j)(2)(B) of the FD&C Act.

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.

## **RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS**

Section 505-1 of the FD&C Act authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a)]. In accordance with section 505-1(i) of the FD&C Act, a drug that is the subject of an ANDA under section 505(j) is subject to certain elements of the REMS required for the applicable listed drug.

The details of the REMS requirements were outlined in our REMS Notification letter dated October 15, 2015. In that letter, you were also notified that pursuant to section 505-1(i) of the FD&C Act, a drug that is the subject of an ANDA and the listed drug it references must use a single, shared system for elements to assure safe use (ETASU), unless FDA waives that requirement.

Your final proposed REMS referenced in Drug Master File (DMF) (b) (4); is approved, and will be posted on the FDA REMS website: <http://www.fda.gov/remis>.

The REMS consists of a Medication Guide and ETASU.

Your REMS must be fully operational before you introduce **hydrocodone bitartrate** into interstate commerce.

The Opioid Analgesic REMS uses a shared system for the ETASU. This shared system REMS Program currently includes the products listed on the FDA REMS website, available at <http://www.fda.gov/remis>. Other products may be added in the future if additional NDAs or ANDAs are approved.

Under section 505-1(g)(2)(C) of the FD&C Act, FDA can require the submission of a REMS assessment if FDA determines an assessment is needed to evaluate whether the REMS should be modified to ensure the benefits of the drug outweigh the risks or to minimize the burden on the healthcare delivery system of complying with the REMS.

We remind you that you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FD&C Act.

We also remind you that section 505-1(f)(8) of the FD&C Act prohibits holders of an approved covered application from using any element to assure safe use to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing a REMS assessment or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

**ANDA 206986 REMS ASSESSMENT  
CROSS REFERENCE TO THE REMS DMF**

**NEW SUPPLEMENT FOR ANDA 206986/S-000  
CHANGES BEING EFFECTED IN 30 DAYS  
PROPOSED MINOR REMS MODIFICATION  
CROSS REFERENCE TO THE REMS DMF**

*or*

**NEW SUPPLEMENT FOR ANDA 206986/S-000  
PRIOR APPROVAL SUPPLEMENT  
PROPOSED MAJOR REMS MODIFICATION  
CROSS REFERENCE TO THE REMS DMF**

*or*

**NEW SUPPLEMENT FOR ANDA 206986/S-000  
PRIOR APPROVAL SUPPLEMENT  
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING  
CHANGES SUBMITTED IN SUPPLEMENT XXX  
CROSS REFERENCE TO THE REMS DMF**

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

**REMS REVISION FOR ANDA 206986  
CROSS REFERENCE TO THE REMS DMF**

The **Opioid Analgesic** REMS uses a Type V DMF for shared system REMS submissions. Please refer to the *Use of a Drug Master File for Shared System REMS Submissions: Guidance for Industry*, for instructions on how to submit and reference the Shared System REMS (SSR) DMF.

**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 provisions<sup>2</sup> 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 <https://www.fda.gov/media/71211/download>. The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

*{See appended electronic signature page}*

For Vincent Sansone, PharmD  
CAPT, USPHS  
Deputy Director  
Office of Regulatory Operations  
Office of Generic Drugs  
Center for Drug Evaluation and Research

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<sup>1</sup> The Agency notes that the '096, '760, '982, '201, '499, '200, '619, '163, '451, '286, '611, '946, '599, '120, and '393 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.

<sup>2</sup> Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).



Catherine  
Poole

Digitally signed by Catherine Poole

Date: 1/21/2020 10:00:14AM

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