



ANDA 211594

**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 May 23, 2018, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Buprenorphine Buccal Film, 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, and 900 mcg.

Reference is also made to the tentative approval letter issued by this office on February 4, 2021, 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 Buprenorphine Buccal Film, 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, and 900 mcg, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Belbuca Buccal Film, 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, and 900 mcg, of BioDelivery Sciences International, Inc. (BDSI).

The RLD upon which you have based your ANDA, BDSI's Belbuca Buccal Film, 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, and 900 mcg, 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>
8,147,866 (the '866 patent)	July 23, 2027
9,655,843 (the '843 patent)	July 23, 2027

9,901,539 (the '539 patent) December 21, 2032

Your ANDA contains paragraph IV certifications to each of the patents 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 Buprenorphine Buccal Film, 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, and 900 mcg, under this ANDA. You have notified the Agency that Alvogen Malta Operations Ltd. (Alvogen) complied with the requirements of section 505(j)(2)(B) of the FD&C Act. Litigation was initiated within the statutory 45-day period against Alvogen for infringement of the '866, '843, and '539 patents in the United States District Court for the District of Delaware [BioDelivery Sciences International, Inc. and Arius Two, Inc. v. Alvogen PB Research & Development LLC, Alvogen Malta Operations Ltd., Alvogen Pine Brook LLC, Alvogen, Inc., and Alvogen Group, Inc., Civil Action No. 18-01395]. Although this litigation remains ongoing, the 30-month period identified in section 505(j)(5)(B)(iii) of the FD&C Act, during which FDA was precluded from approving your ANDA, has expired.

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 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) of the FD&C Act]. 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) of the FD&C Act 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 June 14, 2018.

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>. Other products may be added in the future if additional NDAs or ANDAs are approved.

The Opioid Analgesic REMS consists of a Medication Guide and Elements to Assure Safe Use (ETASU).

Your REMS must be fully operational before you introduce your drug product into interstate commerce.

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) of the FD&C Act 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 211594 REMS ASSESSMENT  
CROSS REFERENCE TO THE REMS DMF**

*or*

**NEW SUPPLEMENT FOR ANDA 211594/S-000  
CHANGES BEING EFFECTED IN 30 DAYS  
PROPOSED MINOR REMS MODIFICATION  
CROSS REFERENCE TO THE REMS DMF**

*or*

**NEW SUPPLEMENT FOR ANDA 211594/S-000  
PRIOR APPROVAL SUPPLEMENT  
PROPOSED MAJOR REMS MODIFICATION  
CROSS REFERENCE TO THE REMS DMF**

*or*

**NEW SUPPLEMENT FOR ANDA 211594/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 211594  
CROSS REFERENCE TO THE REMS DMF**

The Opioid Analgesic REMS uses a Type V DMF for shared system REMS submissions. Please refer to the draft guidance for industry *Use of a Drug Master File for Shared System REMS Submissions*,<sup>1</sup> for instructions on how to submit and reference the shared system REMS DMF.

## **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 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 506I(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: <https://www.fda.gov/media/128163/download>).

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 <https://www.fda.gov/media/73013/download>. Information and Instructions for completing the form can be found at <https://www.fda.gov/media/132152/download>. For more information about submission of promotional materials to the Office of Prescription

Drug Promotion (OPDP), see <https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/opdp-ectd>.

### **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 1<sup>st</sup> 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 or active pharmaceutical ingredients 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.

We remind you that you must continually monitor available labeling resources such as DRUGS@FDA for changes to your reference listed drug's labels and labeling and make any necessary revisions to your labels and labeling. More information on post-approval labeling changes may be found in the guidance for industry titled "Changes to an Approved NDA or ANDA" at <https://www.fda.gov/media/71846/download>.

Sincerely yours,

*{See appended electronic signature page}*

For Edward M. Sherwood  
Director  
Office of Regulatory Operations  
Office of Generic Drugs  
Center for Drug Evaluation and Research

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<sup>1</sup> We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance web page at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

<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

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