NDA 209777/S-016

SUPPLEMENT APPROVAL

Protega Pharmaceuticals LLC
Princeton Innovation Center BioLabs
303A College Road East
Princeton, NJ 08540

Attention: Hafid Touam
Chief Business Officer

Dear Hafid Touam:

Please refer to your supplemental new drug application (sNDA) dated and received April 21, 2026, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for RoxyBond (oxycodone hydrochloride) tablets.

This Prior Approval sNDA provides for proposed modifications to the Opioid Analgesic Risk Evaluation and Mitigation Strategy (OA REMS). This supplement is in response to our February 19, 2026, REMS Modification Notification letter, and is consistent with the requirements of that letter.

We have completed our review of this supplemental application. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The Shared System (SS) OA REMS, of which your drug is a member, was originally approved on July 9, 2012, and the most recent REMS modification was approved on October 31, 2024. The SS REMS consists of a Medication Guide, a disposal requirement, elements to assure safe use, and a timetable for submission of assessments of the REMS.

In order to ensure the benefits of your drug outweigh its risks, we determined that you were required to make REMS modifications. These modifications were outlined in our REMS Modification Notification letter dated February 19, 2026, and included updates to the Patient Guide and REMS website to incorporate updated information regarding FDA-approved opioid overdose reversal agents (naloxone and nalmefene), to conform the approved REMS to the safety labeling changes approved on December 22, 2025.

In addition, the following modifications were communicated during the course of the review:

- The Patient Guide was updated to add established names of drugs that should be avoided when taking opioids.
- The Healthcare Provider and Professional Society/Licensing Board letters were updated to include the risk of death, counseling patients on the importance of opioid overdose reversal agents, and the addition of nalmefene for opioid overdose.
- The REMS document was updated:

    - to distribute Healthcare Provider and Professional Society/Licensing Board letters with updated information related to the safety labeling change
    - to add a new website pop-up, conveying the Patient Guide has been updated with new safety information

Your proposed modified REMS, submitted to Drug Master File (DMF) (b) (4) on April 20, 2026, amended and appended to this letter, is approved.

Furthermore, FDA has updated *FDA's Opioid Analgesic REMS Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain* (FDA Blueprint), March 2026, to incorporate that the risks of nonmedical use, opioid use disorder, overdose, and death can occur at any dosage or duration and persist over the course of therapy. Updated information regarding availability of opioid overdose reversal agents (naloxone and nalmefene) has also been included. As required under the current OA REMS, you must ensure that education based on the FDA Blueprint is made available to healthcare providers who prescribe and healthcare providers involved in the treatment and monitoring of patients who receive OAs.

This shared system REMS, known as the OA REMS, currently includes products listed on the FDA REMS website[1].

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

The timetable for submission of assessments of the REMS remains the same as that approved on October 31, 2024.

There are no changes to the REMS assessment plan described in our November 25, 2025, letter.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, 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 FDCA.

[1] https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use, as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;

b) A determination of the implications of a change in the benefit-risk profile for the current REMS;

c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.

e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.

f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications*, provide a rationale for why the REMS does not need to be modified.

If the methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted methodology, you should update the REMS supporting document to include specific methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted.

Prominently identify the submission containing the methodology with the following wording in bold capital letters at the top of the first page of the submission:

DMF (b) (4) REMS ASSESSMENT METHODOLOGY PROTOCOL REVIEW
(insert concise description of content in bold capital letters, e.g.,
SURVEY METHODOLOGIES, AUDIT PLAN, NONCOMPLIANCE PLAN, DRUG USE STUDY)

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element 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 the REMS assessments 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:

DMF (b) (4) REMS ASSESSMENT

or

NEW SUPPLEMENT FOR NDA 209777/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 209777/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 209777/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 209777/S-000
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

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 REVISIONS FOR DMF (b) (4)

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word and PDF format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word and PDF format are preferred.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

As soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in Structured Product Labeling (SPL) format using the FDA automated drug registration and listing system (eLIST). Content of the REMS document must be identical to the approved REMS document. The SPL will be publicly available.

Information on submitting REMS in SPL format may be found in the guidance for industry *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling.*

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, email Sandrine Ly, PharmD; Safety Regulatory Project Manager, at Sandrine.Ly@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

CDR Mark A. Liberatore, PharmD, MPH, RAC
Deputy Director for Safety
Division of Anesthesiology, Addiction Medicine, and Pain Medicine
Office of Neuroscience
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE:

- REMS

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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