NDA 213978

NDA APPROVAL

Oyster Point Pharma Inc.
Attention: Loni da Silva, MS, RAC
Vice President and Head of Regulatory Affairs
202 Carnegie Center
Suite 109
Princeton, NJ 08540

Dear Ms. Da Silva:

Please refer to your new drug application (NDA) dated and received December 17, 2020, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TYRVAYA (varenicline solution) nasal spray, 0.6 mg/mL. This new drug application provides for the use of TYRVAYA (varenicline solution) nasal spray for the treatment of signs and symptoms dry eye disease.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (Prescribing Information, Patient Package Insert, and Instructions for Use) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As.*[2] The SPL will be accessible via publicly available labeling repositories.

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain*

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 213978**." Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for TYRVAYA (varenicline solution) nasal spray shall be 12 months from the date of manufacture when stored at 20°C-25 °C.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable. We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable. There are too few children with dry eye syndrome to perform an adequate study.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4139-1 Provide a release test method and verification data for activation force.

The timetable you submitted on August 25, 2021, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 12/2021
Study/Trial Completion: 2/2022
Final Report Submission: 4/2022

4139-2 Develop and validate a new analytical method that is sufficiently sensitive to measure (b) (4) in the drug product at the Acceptable Intake (AI) limits in the FDA guidance. Generally, sensitive methods with limits of quantitation (LOQ) in the parts-per-billion (ppb) range are needed to meet the low AI recommended for (b) (4). The (b) (4) should include those identified in the submitted (b) (4) Risk Assessment (b) (4) and those in the FDA guidance (b) (4). Submit data from confirmatory testing using the new method. Confirmatory testing should include aged samples of the three drug product registration lots. Propose a (b) (4) control strategy for your commercial drug product quality program based on the results of confirmatory testing. This

may include routine release and stability testing for [redacted] (b) (4) until sufficient data are available to support discontinuation. Submit new method, data and [redacted] (b) (4) control strategy in a Prior-Approval supplement.

The timetable you submitted on August 25, 2021, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 9/2021
Study/Trial Completion: 12/2022
Final Report Submission: 1/2022

4139-3 Improve Pump Delivery (PD) and Delivered Dose Uniformity (DDU) performance in varenicline nasal spray to meet FDA[3] and USP[4] guidelines. This includes determining the root cause of low dose failures, reported in release, stability, dosing orientation and freeze/thaw studies submitted in your NDA, and implementing corrective actions to your analytical methods or container closure system. Depending on the root cause, additional one-time studies such as In-Use Testing may be needed to demonstrate PD and DDU performance through end of life of the unit (15 days/60 doses) at expiry. We note that the manufacturer's Certificate of Analysis for your model pump [redacted] (b) (4) specifies a dose volume acceptance criteria of mean [redacted] (b) (4) % and single values [redacted] (b) (4) %, which do not meet FDA guidelines for pump delivery. We also note that your actuation method, with and without the compensator, also does not meet guidelines for PD and DDU performance. Submit PD and DDU method validation studies and data from confirmatory testing which meet guidelines. Confirmatory testing should include aged samples of the three drug product registration lots. Submit method validations, additional studies and data in a Prior-Approval supplement.

The timetable you submitted on August 25, 2021, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 12/2021
Study/Trial Completion: 2/2022
Final Report Submission: 4/2022

Submit nonclinical and chemistry, manufacturing, and controls protocols, and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your

[3] Guidance for Industry "Nasal Spray and Inhalation Solution, Suspension and Spray Drug Products – Chemistry, Manufacturing and Controls Documentation" (2002).
[4] USP <601> Aerosols, Nasal Sprays, Metered-Dose Inhalers, and Dry Powder Inhalers.

annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," **or** "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[5]

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[6] Information and Instructions for completing the form can be found at FDA.gov.[7]

[5] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[7] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

REPORTING REQUIREMENTS

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

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.[8]

If you have any questions, call Dheera Semidey, Regulatory Project Manager, at 301-796-3009.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Director
Division of Ophthalmology
Office of Specialty Medicine
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
  - Instructions for Use
- Carton and Container Labeling

[8] https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products

---

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/

WILEY A CHAMBERS
10/15/2021 02:33:43 PM