NDA 219209

NDA APPROVAL

Vertex Pharmaceuticals Inc
50 Northern Avenue
Boston, MA 02210

Attention: Cassidy Kelley
Sr. Manager, Regulatory Strategy

Dear Cassidy Kelley:

Please refer to your new drug application (NDA) dated and received May 30, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Journavx (suzetrigine) tablets, 50 mg.

This NDA provides for the use of Journavx for the treatment of moderate to severe acute pain in adults.

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.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 (text for the Prescribing Information and Patient Package Insert) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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.

CARTON AND CONTAINER LABELING

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 *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 219209**." 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 Journavx (suzetrigine) tablets shall be 24 months from the date of manufacture when stored at 20-25°C (68 to 77°F), with excursions permitted between 15-30°C (59 to 86°F).

ADVISORY COMMITTEE

Your application for Journavx was not referred to an FDA advisory committee because outside expertise was not necessary; there were no controversial issues that would benefit from advisory committee discussion.

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 deferring submission of your pediatric studies according to the timetables listed below, because this product is ready for approval for use in adults and the pediatric studies have not been completed.

[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.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FDCA. These required studies are listed below.

4787-1 Conduct a juvenile animal study in the rodent model to characterize the impact of suzetrigine on the developing brain and reproductive tissues to support clinical studies in pediatric patients from 3 to less than 12 years of age.

Draft Protocol Submission:	06/2025
Final Protocol Submission:	09/2025
Study Completion:	09/2026
Final Report Submission:	03/2027

4787-2 Conduct a juvenile animal study in the rodent model to characterize the impact of suzetrigine on the developing brain to support clinical studies in pediatric patients from birth to less than 3 years of age.

Draft Protocol Submission:	03/2027
Final Protocol Submission:	06/2027
Study Completion:	06/2028
Final Report Submission:	12/2028

4787-3 Conduct a randomized, controlled study evaluating the pharmacokinetics, safety, and efficacy of Journavx in pediatric patients aged 12 to less than 17 years with moderate to severe acute pain.

Draft Protocol Submission:	03/2025
Final Protocol Submission:	09/2025
Study Completion:	06/2027
Final Report Submission:	12/2027

4787-4 Conduct a randomized, controlled study evaluating the pharmacokinetics, safety, and efficacy of Journavx in pediatric patients aged 6 to less than 12 years with moderate to severe acute pain.

Draft Protocol Submission:	09/2027
Final Protocol Submission:	03/2028
Study Completion:	03/2030
Final Report Submission:	09/2030

4787-5 Conduct a randomized, controlled study evaluating the pharmacokinetics, safety, and efficacy of Journavx in pediatric patients aged 1 to less than 6 years with moderate to severe acute pain.

Draft Protocol Submission:	06/2029
Final Protocol Submission:	12/2029
Study Completion:	12/2031
Final Report Submission:	06/2032

4787-6 Conduct a randomized, controlled study evaluating the pharmacokinetics, safety, and efficacy of Journavx in pediatric patients from birth to less than 1 year of age with moderate to severe acute pain.

Draft Protocol Submission:	03/2031
Final Protocol Submission:	09/2031
Study Completion:	09/2033
Final Report Submission:	03/2034

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[3]

Submit the protocols to your IND 146185, with a cross-reference letter to this NDA. Reports of these required pediatric postmarketing studies must be submitted as an NDA or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a signal of a serious risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. We have also determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

identify an unexpected serious risk of infant toxicity due to exposure to suzetrigine that may be present in human milk during lactation.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

4787-7 Collect global data from prospective pregnancy exposure registry/registries, preferably disease-based multiproduct pregnancy registry/registries, using a registry-based cohort study design to compare the maternal, fetal, and infant outcomes of women exposed to Journavx during pregnancy with unexposed comparator population(s). Align the U.S. study protocol with protocol(s) outside the U.S. to reach the target sample size. The registry will identify and record pregnancy complications, spontaneous abortion, stillbirths, neonatal deaths, major and minor congenital malformations, pregnancy terminations, preterm births, small-for-gestational-age births, and any other adverse outcomes, including postnatal growth and development. These outcomes should be assessed throughout pregnancy. Infant outcomes, including effects on postnatal growth and development, will be assessed through at least the first year of life.

The timetable you submitted on January 22, 2025, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission:	07/2025
Final Protocol Submission:	01/2026
Interim Report Submissions:	01/2027, 01/2028, 01/2029, 01/2030, 01/2031, 01/2032, 01/2033, 01/2034, 01/2035
Study Completion:	01/2036
Final Report Submission:	07/2036

4787-8 Conduct a retrospective pregnancy cohort study using claims or electronic health record data with medical chart validation that is adequately powered to assess spontaneous abortions, stillbirths, neonatal deaths, major congenital malformations, preterm births, and small-for-gestational-age births in individuals exposed to Journavx during pregnancy compared to appropriate comparator population(s).

The timetable you submitted on January 22, 2025, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission:	07/2025
Final Protocol Submission:	01/2026
Interim Report Submissions:	01/2028, 01/2030, 01/2032, 01/2034
Study Completion:	01/2036
Final Report Submission:	07/2036

4787-9 Perform a milk-only lactation study in lactating women who have received Journavx to measure concentrations of suzetrigine in breast milk using a validated assay. Assess the effects on the breastfed infant, if available, based on study population.

The timetable you submitted on January 22, 2025, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission:	07/2025
Final Protocol Submission:	01/2026
Study Completion:	01/2028
Final Report Submission:	07/2028

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial. [3]

Submit clinical protocol(s) to your IND 146185 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final reports to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **REQUIRED POSTMARKETING PROTOCOL UNDER 505(o), REQUIRED POSTMARKETING FINAL REPORT UNDER 505(o), REQUIRED POSTMARKETING CORRESPONDENCE UNDER 505(o).**

Submission of the protocol(s) for required postmarketing observational studies to your IND is for purposes of administrative tracking only. These studies do not constitute clinical investigations pursuant to 21 CFR 312.3(b) and therefore are not subject to the IND requirements under 21 CFR part 312.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B(a)(1) of the FDCA, as well as

21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B(a)(1) and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

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.*[4]

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.[5] Information and Instructions for completing the form can be found at FDA.gov.[6]

REPORTING REQUIREMENTS

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

POST APPROVAL FEEDBACK MEETING

New molecular entities qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

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

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standards for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website[7].

If you have any questions, contact Rita Joshi, PharmD, Senior Regulatory Health Project Manager, at rita.joshi@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Mary Thanh Hai, MD
Deputy Director
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

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

[7] https://www.uspnf.com/

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/

MARY T THANH HAI
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