NDA 022173/S-040/S-043

SUPPLEMENT APPROVAL

Cheplapharm Registration
Gmbh c/o ITS USA
Attention: Gretchen Pessagno, US Regulatory Agent
139 Wando Reach Rd
Charleston, South Carolina 29492

Dear Gretchen:

Please refer to your supplemental new drug applications (sNDAs) dated and received December 17, 2021 (S-040) and April 3, 2024 (S-043), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zyprexa Relprevv (olanzapine pamoate) for Extended-Release injectable suspension.

NDA 022173 S-040
This Changes Being Effected in 30 Days sNDA provides for proposed modifications to the approved Zyprexa Relprevv (olanzapine pamoate) risk evaluation and mitigation strategy (REMS).

NDA 022173 S-043
This Prior Approval sNDA provides for proposed modifications to the approved Zyprexa Relprevv (olanzapine pamoate) REMS and corresponding changes to the labeling.

We have completed our review of these supplemental applications, as amended. They are approved effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Zyprexa Relprevv (olanzapine pamoate) was originally approved on December 11, 2009, and the most recent REMS modification was approved on April 28, 2021. The REMS consists of a Medication Guide (MG), a communication plan (CP), elements to assure safe use (ETASU), an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modifications to the REMS include the following:

- Updates to remove any mention of "single-use" language in REMS materials.
- Changes to REMS program name to Zyprexa Relprevv REMS.
- Updates to REMS goal and objectives to focus on the safe use behaviors for mitigating the risk of post-injection delirium/sedation syndrome (PDSS).

- Updates to REMS Document with changes that are consistent with the Guidance Document, Format and Content of a REMS Document (January 2023) and the REMS Document Technical Conformance Guide (January 2023).
- Addition of knowledge assessments for prescribers and healthcare settings for initial certification and recertification.
- Addition of requirement for pharmacies to obtain authorization to dispense from the REMS before each dispense.
- Changes to the audit requirements for pharmacies and healthcare settings, and addition of audit requirements for wholesalers-distributors to the REMS Document.
- Streamlined REMS materials to improve messaging of risk and REMS requirements.
- Updates to the REMS website, including changes to layout and addition of the certified pharmacy finder and the certified healthcare setting finder.
- Updates to the Communication Plan to disseminate the Healthcare Professional Letter and Fact Sheet to prescribers, pharmacies, and healthcare settings.

Your proposed modified REMS, submitted on December 17, 2021, and April 3, 2024, amended and appended to this letter, are approved.

The timetable for submission of assessments of the REMS remains the same as that approved on July 8, 2010.

The revised REMS assessment plan must include, but is not limited to, the following:

For each metric, provide data for the two previous, current, and cumulative reporting periods (where applicable), unless otherwise noted.

REMS Outreach and Communication

1. REMS Outreach and Communication (first assessment report post-modification only)
    a. Provide an assessment of whether the REMS Communication Materials were disseminated to the target audience within the stated timeframe as required. Include the following in your assessment:
        i. Stratification of results by communication material type (e.g. Healthcare Professional Letter, Fact Sheet)
        ii. The number and proportion of participants in each target audience (e.g. certified prescribers, authorized representatives for certified pharmacies and healthcare settings, authorized wholesalers-distributors) that had an email with the REMS Communication Material successfully delivered out of those total number of participants in each target audience.
        iii. Provide any additional actions taken to inform the target audience, for example in cases where emails could not be successfully delivered.
    b. Indicate whether the REMS Website Pop-Up Messages were published within

the required timeframe and maintained continuous display for the specified time period as required

c. Provide an assessment of whether the Zyprexa Relprevv REMS System Transition Plan was implemented successfully. Describe any issues identified, affected participants, and affected REMS process, and actions taken to remediate. The assessment should also inform on the following:
   i. Status of REMS participant recertification and reenrollment
   ii. Status of data migration
   iii. Any impact to patient access or unintended burden on the healthcare delivery system

REMS Implementation and Operations

2. REMS Operation and Performance Data
   a. REMS Coordinating Call Center
      i. Number of contacts by participant type (patients, healthcare providers, pharmacies, healthcare settings, wholesalers-distributors, other)
      ii. Summary of reasons for calls (i.e. enrollment question, location of a certified healthcare setting) and by reporter (i.e. authorized representative, healthcare setting, patient/caregiver, other)
      iii. Summary of frequently asked questions (FAQ) by participant type
      iv. Summary report of REMS-related problems identified and resulting corrective actions

3. REMS Certification and Enrollment Statistics
   a. Healthcare provider certification
      i. Number of newly certified healthcare providers,
      ii. Number and percentage of active healthcare providers (have prescribed Zyprexa Relprevv for at least one patient during the reporting period) out of all certified healthcare providers. Stratify by professional degree, medical specialty (Psychiatrist, General Health Practitioner, Other), and geographic regions (as defined by US Census). If “other” accounts for >10% of respondents for professional degree or medical specialty, provide the top 5 most common responses identified.
      iii. Number and percentage of healthcare providers who retrained and recertified during the assessment period out of all healthcare providers who were expected to retrain and recertify during the assessment period.
      iv. Number of healthcare providers who could not complete certification. Include the reason why certification was not completed and any action taken.
   b. Healthcare setting certification
      i. Number of newly certified healthcare settings.
      ii. Number and percentage of active healthcare settings (have administered at least one injection during the reporting period) out of all certified healthcare settings. Stratify by healthcare setting type (prescriber office,

clinic/outpatient setting, hospital, other), and geographic region (as defined by US Census). If “other” accounts for >10% of respondents for type, provide the top 5 most common setting types identified).

iii. Number and percentage of healthcare settings that retrained and recertified during the assessment period out of all healthcare settings that were expected to retrain and recertify during the assessment period
iv. Number of healthcare settings that could not complete certification. Include the reason why certification was not completed and any action taken.

c. Pharmacy certification
   i. Number of newly certified pharmacies.
   ii. Number and percentage of active pharmacies (have filled at least one prescription during the reporting period) out of all certified pharmacies. Stratify by pharmacy type (community/retail, specialty, hospital/institution, healthcare provider office (Buy and Bill) or other), and geographic region (as defined by US Census). If “other” accounts for >10% of respondents for pharmacy type, provide the top 5 most common types identified).
   iii. Number and percentage of pharmacies that retrained and recertified during the assessment period out of all pharmacies that were expected to retrain and recertify during the assessment period.
   iv. Number of pharmacies that could not complete certification. Include the reason why enrollment was not completed and any action taken.

d. Patient Enrollment
   i. Number of newly enrolled patients.
   ii. Number and percentage of active patients (have received at least one injection during the reporting period) out of all enrolled patients. Stratify by age, sex, race and ethnicity.
   iii. Number of patients who could not complete enrollment. Include the reason why enrollment was not completed and any action taken.
   iv. Number of patients inactivated, and reason(s) for inactivation.
   v. Number of patients re-enrolled following inactivation.

e. Wholesalers-distributors
   i. Number of newly authorized wholesalers-distributors.
   ii. Number and percentage of active wholesalers-distributors (have distributed the drug at least once during the reporting period) out of those authorized to distribute.

4. Zyprexa Relprevv Utilization Data
   a. Number of Zyprexa Relprevv shipments distributed to pharmacies, stratified by pharmacy type
   b. Number of Zyprexa Relprevv shipments purchased through buy and bill procedures, stratified by recipient setting type
   c. Number of Zyprexa Relprevv vials distributed by wholesalers-distributors, stratified by recipient setting type and dosage strengths

d. Wholesalers-distributors' "authorization to ship"
   i. Number of approved "authorization to ship" obtained by wholesalers-distributors and the number of shipments associated with an approved "authorization to ship".
   ii. Number of shipments that encountered a rejected "authorization to ship". Include the reasons for the rejection and indicate whether the shipment was ultimately authorized to ship.

e. Number of prescriptions dispensed to certified healthcare settings. Stratify by:
   i. Dispensing pharmacy type (community/retail, specialty, hospital/institution, or other)
   ii. Prescriber specialty, provider degree/credentials, geographic region
   iii. Patient demographics (age, sex, race and ethnicity)
   iv. Provide the data source for dispensing data and any limitations associated with the data source.

f. Pharmacies' "authorization to dispense"
   i. Number of approved "authorization to dispense" obtained by pharmacies and the number of dispenses associated with an approved "authorization to dispense", stratified by pharmacy type
   ii. Number of prescription dispenses that encountered a rejected "authorization to dispense". Include the reasons for the rejection and indicate whether the prescription was ultimately authorized to dispense

g. Among the prescriptions dispensed, the number and proportion of prescriptions that came through buy and bill procedures. Provide the data source for dispensing data and any limitations associated with the data source.

5. REMS Compliance

   a. Provide a copy of the audit plan for each audited REMS participant type

   b. The proportion of audits completed out of the total number of audits expected for each audited REMS participant type, stratified by audit type (e.g., initial, annual).
      i. Include how the expected number of audits was calculated for each REMS participant type
      ii. Include reasons that any expected audits were not completed, and follow-up actions taken to complete these outstanding audits
      iii. For audit questionnaires not returned, describe follow-up actions taken (e.g., sites inactivated or decertified)

   c. Report the audit findings for each audited REMS participant type
      i. For each audit type (e.g., initial, annual), provide a tabular summary of all audit findings stratified by REMS participant type, and by finding severity category. For each finding severity category, provide a brief description of the findings.
         1) Report the number and types of deficiencies noted for each group of audited participants.
         2) For those sites with deficiencies noted, report the number that

successfully completed a corrective and preventive action (CAPA) plan within one month of audit.
3) For any that did not complete the CAPA within one month of the audit, describe actions taken.
4) Include a unique ID for each participant that had deviations to track deviations by participant over time.
5) Documentation of completion of training for relevant staff.
6) The existence of documented processes and procedures for complying with the REMS.

d. Provide a copy of the noncompliance plan used, including the criteria for noncompliance for healthcare settings, pharmacies and wholesalers-distributors, actions taken to address noncompliance for each case, and whether any event led to de-certification from the REMS.

e. Healthcare settings (For each noncompliance event, provide the source of the report, a description of the event, the cause of the event, and corrective actions taken)
   i. Number and type of healthcare settings for which noncompliance with the REMS is detected
   ii. Number of times Zyprexa Relprevv was dispensed to a non-certified healthcare setting or other unintended locations (e.g., patient's home, directly to patient, or unauthorized entities)
   iii. Number and type of non-certified healthcare setting that administered Zyprexa Relprevv and the number of incidents for each healthcare setting
   iv. Number of healthcare settings that did not have ready access to emergency response services and that can allow for continuous patient monitoring for at least 3 hours post-injection
   v. Number of patients who were not enrolled prior to receiving Zyprexa Relprevv
   vi. Number of times Zyprexa Relprevv was administered without verifying that the patient is enrolled
   vii. Number of times Zyprexa Relprevv was administered without verifying that the prescriber is certified
   viii. Number of healthcare settings de-certified for noncompliance and reasons for de-certification
   ix. Number of healthcare settings that distributed, transferred, loaned or sold Zyprexa Relprevv
   x. Number of expected annual verifications of Authorized Representatives of healthcare settings and number of completed verifications. Include any follow up that was done (and any corrective actions taken) to address noncompliant participants

f. Healthcare providers (For each noncompliance event, provide the source of the report, a description of the event, the cause of the event, and corrective actions taken)
   i. Number of prescriptions written by a non-certified healthcare provider that

were dispensed to a patient

g. Pharmacies (For each noncompliance event, provide the source of the report, a description of the event, the cause of the event, and corrective actions taken)
   i. The number and type of pharmacies for which noncompliance with the REMS is detected, stratified by pharmacy type and severity
   ii. The number and type of non-certified pharmacies that dispensed Zyprexa Relprevv and the number of incidents for each
   iii. Number of times Zyprexa Relprevv was dispensed without obtaining an authorization to dispense (verifying that the patient is enrolled, the prescriber is certified, and the healthcare setting is certified), stratified by pharmacy type
   iv. Number of pharmacies who were de-certified for noncompliance and reasons for de-certification.
   v. Number of pharmacies that dispensed Zyprexa Relprevv to a non-certified healthcare setting and quantity distributed to the non-certified healthcare setting
   vi. Number of pharmacies that dispensed directly to a patient
   vii. Number of expected annual verifications of Authorized Representatives of pharmacies and number of completed verifications. Include any follow up that was done (and any corrective actions taken) to address noncompliant participants

h. Wholesalers-distributors (For each noncompliance event, provide the source of the report, a description of the event, the cause of the event, and corrective actions taken)
   i. The number of times Zyprexa Relprevv was distributed to non-certified healthcare setting and non-certified dispenser.
   ii. Number and percentage of vials distributed to non-certified pharmacies out of the total number of vials distributed
   iii. Number and percentage of vials distributed to non-certified healthcare settings out of the total number of vials distributed

Safe Use Behaviors

6. Report on Forms

   a. Patient Injection Forms
      i. Number of Patient Injection Forms expected, received, and outstanding as of the report cut-off date
      ii. Number and percentage of Patient Injection Forms not received within 3 days out of the total number of Patient Injection Forms expected. Include outreach activities performed to collect the forms
      iii. Number of patient injections administered stratified by dosage strength
      iv. Provide an assessment of how complete the submitted Patient Injection Forms are (i.e., do they contain all the required data) and any steps taken to resolve those forms with incomplete information

   b. Post Injection Delirium Sedation Syndrome (PDSS) Form

i. Number of PDSS forms expected, received, and outstanding as of the report cut-off date
ii. Number of PDSS forms not received within 24 hours. Include outreach activities performed to collect the forms.
iii. Provide an assessment of how complete the submitted PDSS forms are (i.e., do they contain all the required data) and any steps taken to resolve those PDSS forms with incomplete information

7. Safe Use Behaviors – Monitoring Patients after Injections, Patients Being Accompanied
   a. Assessment of the number of patients who were not observed for at least 3 hours after an injection. Include the number of healthcare settings, proportion of events per patient and per injection, and cumulative number of events and patients and proportion of events per patient and per injection. Also include in the assessment:
      i. Numerator and denominator for all calculations, and the data source(s).
      ii. The number and percentage of injections administrated where the patient was monitored for at least 3 hours post injection out of the total number of injections administered. If <100%, provide an analysis of reasons monitoring was not completed, and corrective and preventive actions taken.
      iii. Time deviation from the required time period to monitor for at least three hours post-injection
      iv. Reasons provided for why the patient was not monitored for the required time.
      v. Include any additional reported noncompliance that would inform on this assessment (e.g. missing injection forms, incomplete injection forms, injections administered at noncertified healthcare settings, additional audit data related to the monitoring) and the impact on the results.
   b. Assessment of the number of patients who left the healthcare setting unaccompanied after injection. Include the number of healthcare settings, proportion of events per patient and per injection, and cumulative number of events and patients and proportion of events per patient and per injection.

Knowledge

8. Healthcare Provider Knowledge Assessments (for certification)
   a. Number of completed Prescriber Knowledge Assessments for healthcare providers, including the method of completion
   b. Summary of the most frequently missed Knowledge Assessment questions
   c. Mean, median, and range of attempts to complete the assessment
   d. Summary of potential comprehension or perception issues identified

9. Healthcare Setting Knowledge Assessments (for certification)
   a. Number of completed Knowledge Assessments for healthcare settings,

including the method of completion

b. Summary of the most frequently missed Knowledge Assessment questions
c. Mean, median, and range of attempts to complete the assessment
d. Summary of potential comprehension or perception issues identified

Health Outcomes and/or Surrogates of Health Outcomes

10. Post-injection Delirium/Sedation Syndrome (PDSS) (to be reported for the current reporting period, previous reporting period, and cumulatively)
    a. Analyze U.S. adverse event reports of PDSS. Sources of PDSS reports must include but are not limited to: Patient Injection Forms, PDSS Forms, adverse events reported in the REMS registry, spontaneous adverse event reports, and medical literature. In your analysis, include the following:
        i. Include the search strategy used for each data source and the case definition used. Include search dates and specific Medical Dictionary for Regulatory Activities (MedDRA) terms used.
        ii. After de-duplication, provide a tabular summary of the cases including the following:
            1) Number of PDSS cases from all sources
            2) Number of cases from each source
            3) Seriousness (e.g., number of cases categorized as fatal, life-threatening, requiring initial or prolonged hospitalization, disability or permanent damage, etc.)
            4) Mean/Median/Range of time to onset of PDSS after injection, also report time to onset stratified by $\leq$ 3 hours and >3 hours
            5) Outcome of Event (e.g., recovered/resolved, recovering/resolving, not recovered/not resolved/ongoing, recovered/resolved with sequelae, fatal, unknown)
            6) Assessment of relatedness of drug to event
            7) Root cause analyses of whether the REMS program requirements for patient monitoring were followed
        iii. Include a reference list of case identifiers (e.g., manufacturer control numbers) for all cases included in the analysis above.
    b. Using data from the REMS registry, report the following:
        i. Number and proportion of U.S. PDSS events out of the total number of injections administered
            1) Stratify by time to onset $\leq$ 3 hours and >3 hours,
            2) Stratify by patient sex, and age (in five-year interval)
            3) For the time to onset category specified in 1a, stratify by patient sex, and age (in five-year interval)
        ii. Number and proportion of U.S. patients who experienced at least one episode of PDSS out of the total number of active patients (i.e., patients who received at least one injection)
            1) For each patient who experienced at least one episode of PDSS, indicate the number of injections received prior to the PDSS event,

and the number of PDSS events per person

iii. Overall number and proportion of U.S. PDSS events among U.S. injections that were not observed for three hours and by the category of time to onset ≤ 3 hours and >3 hours
iv. Overall number and proportion of U.S. PDSS events among U.S. injections in which the patients left the healthcare setting (HCF) unaccompanied
v. Include a histogram that depicts the frequency of PDSS events by the number of Zyprexa Relprevv injections

c. Provide new safety findings to inform the incidence, severity, and frequency of PDSS, and an assessment of the effectiveness of the REMS strategy in mitigating the risk

Overall Assessment of the REMS

11. The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified.

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.

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.

Additionally, we recommend that you submit your proposed audit plan and non-compliance plan for FDA review within 60 days of this letter. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters, at the top of your cover letter and at the top of the first page of the main submission document: "**REQUEST FOR REMS ASSESSMENT METHODOLOGY PROTOCOL REVIEW/ AUDIT AND NON-COMPLIANCE PLAN".**

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and 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 assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

> **NDA 022173 REMS ASSESSMENT METHODOLOGY**
> **(**insert concise description of content in bold capital letters, e.g., **ASSESSMENT METHODOLOGY, PROTOCOL, SURVEY METHODOLOGIES, AUDIT 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:

NDA 022173 REMS ASSESSMENT

or

NEW SUPPLEMENT FOR NDA 022173/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 022173/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 022173/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 022173/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 NDA 022173

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, call Ermias Zerislassie, Associate Director for Postmarket Regulatory Science, at 301-796-2770.

Sincerely,

{See appended electronic signature page}

Tiffany R. Farchione, MD
Director
Division of Psychiatry
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- 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/

TIFFANY R FARCHIONE
05/07/2026 06:17:48 PM