NDA 212102/S-014

SUPPLEMENT APPROVAL

UCB, Inc.
Attention: Courtney Bone, PhD
US Regulatory Lead, Global Regulatory Affairs
1950 Lake Park Drive
Building 2100
Smyrna, GA 30080

Dear Dr. Bone:

Please refer to your supplemental new drug application (sNDA) dated and received October 5, 2023, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Fintepla (fenfluramine) oral solution.

This Prior Approval sNDA provides for proposed modifications to the approved Fintepla risk evaluation and mitigation strategy (REMS). This supplement is in response to our August 10, 2023 REMS Assessment Acknowledgment/REMS Modification Notification letter.

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

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Fintepla was originally approved on June 25, 2020, and the most recent REMS modification was approved on May 30, 2023. The REMS consists of a communication plan, elements to assure safe use (ETASU), an implementation system, and a timetable for submission of assessments of the REMS.

In order to ensure the benefits of Fintepla outweigh its risks and to minimize the burden on the healthcare delivery system of complying with the REMS, we determined that you were required to make the REMS modifications outlined in our REMS Assessment Acknowledgement/REMS Modification Notification letter dated August 10, 2023. In addition, your proposed modifications to the REMS include the following:

- REMS Document—changes to the Timetable for Submission of Assessments
- Cardiovascular Adverse Event (CVAE) Reporting Form—questions added regarding previous fenfluramine exposure in a clinical trial and treatment start and stop dates, as well as editorial changes.

- Patient Status Form—questions added regarding pulmonary arterial systolic pressure value, previous submission of CVAE Reporting Form and changes in reported abnormalities, as well as editorial changes.

- Website Screenshots—changes to align with the amended CVAE Reporting Form and Patient Status Form

Your proposed modified REMS, submitted on October 5, 2023, amended and appended to this letter, is approved. The modified REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

The timetable for submission of assessments of the REMS must be revised to submit REMS Assessments on August 23, 2024, and annually thereafter.

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

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

Implementation and Operations

1. REMS Certification and Enrollment Statistics

   a. Healthcare provider certification

      i. The number of newly certified healthcare providers and the number of active (i.e., who have prescribed Fintepla at least once during the reporting period) healthcare providers stratified by provider type (e.g., Doctor of Medicine, Doctor of Osteopathic Medicine, Advanced Nurse Practitioner, Physician Assistant, Other), specialty, and geographic region (as defined by US Census).

      ii. A summary of the methods of healthcare provider certification (e.g., fax, online).

      iii. The number of healthcare providers who were unable to become certified, accompanied by a summary of the reasons they were unable to be certified.

      iv. The number of healthcare providers who became decertified, accompanied by a summary of reasons for decertification.

   b. Pharmacy certification

      i. The number of newly certified pharmacies, the number of active (i.e., have dispensed Fintepla at least once during the reporting period) pharmacies,

and the number of recertified pharmacies stratified by pharmacy setting (i.e., inpatient, outpatient) and geographic region (as defined by US Census).

ii. A summary of the methods of pharmacy certification and recertification (e.g., fax, online).

iii. The number of pharmacies that were unable to become certified, accompanied by a summary of the reasons they were unable to become certified.

iv. The number of pharmacies that became decertified, accompanied by a summary of reasons for decertification.

c. Patient enrollment

i. The number of newly enrolled patients and the number of active (i.e., have received Fintepla at least once during the reporting period) patients stratified by age, gender, race, ethnicity, and geographic region (as defined by US Census).

ii. A summary of the methods of patient enrollment (e.g., fax, mail)

d. Wholesalers/Distributor enrollment

i. The number of newly enrolled wholesalers/distributors and the number of active (i.e., have shipped Fintepla at least once during the reporting period) wholesalers/distributors

2. Fintepla Utilization Data

a. The number of pharmacies sent Fintepla shipments, stratified by setting (i.e., outpatient or inpatient) and geographic region (as defined by US Census).

b. The number of Fintepla prescriptions that were dispensed, overall and stratified by quantity dispensed per prescription and whether the prescription was new or a refill.

c. The number of healthcare providers who wrote Fintepla prescriptions that were dispensed, stratified by specialty, the number of dispensed prescriptions written by each healthcare provider, and the number of patients for whom dispensed prescriptions were written by each healthcare provider.

d. The number of unique patients who received Fintepla stratified by age, gender, race, ethnicity, and geographic region (as defined by US Census).

e. The number of prescriptions not dispensed, accompanied by a listing and summary of all reasons for not dispensing the prescription (e.g., prescriber not certified, patient not enrolled, dispensing not authorized by REMS). Specific reasons for not authorizing dispensing will be reported and include prescriber does not authorize continuation of treatment, patient has not fulfilled the REMS requirement of obtaining an ECHO every 6 months (plus a 3-month grace period).

f. The number of prescription dispensing delays (i.e., initial prescription not dispensed within 10 business days of receipt or refill prescription not dispensed by the date that the patient's previous supply is exhausted), overall and stratified by whether the prescription was new or a refill; accompanied by a trend analysis of the mean and median time to dispense for all prescriptions (in days), a summary of the number and percentage of prescriptions delayed, length of the delays, and a listing and summary of reasons for delays in prescription dispensing, including whether the reasons were related to the REMS.

    i. The dispensing delay reasons will be categorized as follows:

        1) Patient not enrolled (missing or incomplete patient enrollment form)

        2) Prescription submitted before baseline ECHO completed

        3) Missing or incomplete Patient Status Form

        4) Insurance delay

        5) Patient request

        6) Other

    ii. A new prescription is defined as the first prescription for a patient who is initiating treatment with Fintepla for the first time.

    iii. A refill prescription is defined as a prescription for a patient who has previously received a prescription for Fintepla.

3. REMS Infrastructure and Performance

    a. REMS Website

        i. The number of visits and unique visits to the REMS website.

        ii. The number of downloads and printings of each REMS material.

    b. REMS Coordinating Center

i. The number of calls received by the REMS coordinating center, stratified by stakeholder type and reason for the call.

ii. The number of REMS materials requested through the REMS coordinating center.

iii. The number of issues/complaints reported to the REMS coordinating center, accompanied by a description of the top 5 reasons for calls by each stakeholder or 80% of calls by each stakeholder (which ever accounts for the greater number of calls) and the resolution (if applicable).

iv. A description of each call, including stakeholder type, that may indicate an issue with access, burden, or an adverse event.

v. A summary of corrective actions resulting from issues identified.

4. REMS Compliance

a. The number and percentage of Fintepla shipments sent to noncertified pharmacies among all shipments.

b. The number and percentage of Fintepla prescriptions dispensed that were written by noncertified healthcare providers among all dispensed prescriptions in the outpatient setting.

i. For all prescriptions dispensed in the outpatient setting that were written by a noncertified healthcare provider, a summary including whether ECHO tests were obtained, whether the healthcare provider later became certified, and if so, the time elapsed between dispensing and healthcare provider certification.

c. The number and percentage of Fintepla prescriptions dispensed that were written by noncertified healthcare providers for patients not under the care of a certified healthcare provider among all dispensed prescriptions in the inpatient setting.

i. For all prescriptions dispensed in the inpatient setting that were written by noncertified healthcare providers for patients not under the care of certified healthcare provider, a summary including whether ECHO tests were obtained, whether the prescribers later became certified, and if so, the time elapsed between dispensing and healthcare provider certification.

d. The number and percentage of Fintepla prescriptions dispensed to nonenrolled patients among all dispensed prescriptions, stratified by pharmacy setting (i.e., outpatient or inpatient).

e. For all prescriptions dispensed to nonenrolled patients, a summary of whether ECHO tests were obtained, whether the patients later became enrolled, and if so,

the time elapsed between dispensing and patient enrollment, stratified by pharmacy setting.

f. The number and percentage of Fintepla prescriptions dispensed that were written by noncertified healthcare providers for nonenrolled patients among all dispensed prescriptions, stratified by pharmacy setting (i.e., outpatient or inpatient).

    i. For all prescriptions dispensed that were written by noncertified healthcare providers for non-enrolled patients, a summary of whether ECHO tests were obtained, whether the patients later became enrolled, and if so, the time elapsed between dispensing and patient enrollment, stratified by pharmacy setting.

    ii. For each prescription dispensed that was written by a noncertified healthcare provider for a non-enrolled patient, a link to the associated pharmacy noncompliance data and root cause analysis (RCA) results.

g. The number and percentage of prescriptions dispensed that bypassed the REMS authorization process among all dispensed prescriptions, stratified by pharmacy setting (i.e., outpatient or inpatient).

    i. For all prescriptions dispensed that bypassed the REMS authorization process, a summary of whether ECHO tests were obtained, healthcare provider certification status, patient enrollment status, whether a current Patient Status Form is on file stratified by pharmacy setting

h. The number and percentage of prescriptions dispensed by noncertified pharmacies.

i. The number and percentage of shipments that were shipped by wholesalers/distributors not enrolled in the REMS.

j. The number of instances of noncompliance accompanied by a description of each instance and the reason for the occurrence (if provided). For each instance of noncompliance provide the following information:

    i. The unique ID(s) of the stakeholder(s) associated with the noncompliance event or deviation to enable tracking over time.

    ii. The source of the noncompliance data.

    iii. The results of RCA.

    iv. The number and percentage of patients who received Fintepla who were not enrolled in the REMS registry among all patients who received

Fintepla and among all patients enrolled in the REMS registry, stratified by pharmacy setting (i.e., outpatient or inpatient).

k. A copy of the current audit plan.

l. A detailed description of deviations and major and minor audit observations, including information about the root cause of the noncompliance and a description of the corrective and preventive actions taken to address noncompliance with distribution and dispensing requirements.

m. Report of audit observations by stakeholder type (i.e., REMS coordinating center, pharmacy, or wholesaler-distributor):

    i. The number of audits expected and performed.

    ii. The number of deficiencies noted, stratified by deficiency type.

    iii. The number of critical events. A critical event is defined as a single occurrence of:

        1) Dispensing to a nonenrolled patient in the inpatient or outpatient setting.

        2) Dispensing a prescription written by a noncertified prescriber in the outpatient setting.

        3) Dispensing after obtaining a “Not Authorized” status.

        4) Dispensing after bypassing the authorization process.

    iv. For stakeholders with observations noted within the audit report, provide the number that successfully completed a corrective and preventative action (CAPA) plan by the due date.

        1) For those with observations noted within the audit report that did not complete the CAPA plan by the due date, a description of the actions taken (e.g., escalation).

    v. The existence of documentation demonstrating the completion of training for all relevant staff.

    vi. The existence of documentation demonstrating the existence of processes and procedures for complying with the REMS.

    vii. The existence of documentation demonstrating the verification of the designated authorized representative at each certified pharmacy.

1) If the authorized representative has changed since initial certification, the number of new authorized representatives and recertifications per pharmacy.

Safe Use Behaviors

5. *Patient Status Forms*

a. The number and percentage of patients who had a *Patient Status Form* submitted prior to initial dispensing among all patients who were dispensed a new prescription for Fintepla, stratified by pharmacy setting (i.e., outpatient or inpatient).

b. The number and percentage of patients who did not have a *Patient Status Form* submitted prior to initial dispensing among all patients who were dispensed a new prescription for Fintepla, stratified by pharmacy setting (i.e., outpatient or inpatient) and whether the patient had an ECHO test.

i. For all patients who did not have a *Patient Status Form* submitted prior to initial dispensing and who did not have an ECHO test performed, a summary of the reasons ECHO tests were not performed and the source of reason information (i.e., healthcare provider or patient). The reasons the ECHO tests were not performed will be provided (e.g., scheduling, transportation, cost, prescriber determination of necessity, patient lost to follow-up, switched healthcare providers, ECHO interrupted, other).

ii. For each patient who did not have a *Patient Status Form* submitted prior to initial dispensing and who did not have an ECHO test performed, the source of noncompliance data and associated CAPA plan.

c. The number and percentages of patients who had a *Patient Status Form* documenting the prescriber not authorizing further prescriptions due to noncompliance with ECHO tests among all patients receiving Fintepla, stratified by the period of time since the last submitted *Patient Status Form* authorizing treatment.

d. The number and percentage of patients who had a *Patient Status Form* documenting prescriber not authorizing treatment “Other” and the reason for not authorizing.

e. The number and percentage of patients who had a *Patient Status Form* submitted within 180 days (approximately 6 months) of their most recent *Patient Status Form* among all patients who were dispensed Fintepla during the

reporting period and did not have a *Patient Status Form* documenting their discontinuation of Fintepla.

f. The number and percentage of patients who did not have a *Patient Status Form* submitted within 180 days (approximately 6 months) of their most recent *Patient Status Form* among all patients who were dispensed Fintepla and did not have a *Patient Status Form* documenting their discontinuation of Fintepla.

g. The number of "Authorized – Warning" patient statuses sent to pharmacies by the REMS.

h. The type, frequency, and outcome of outreach activities performed to obtain outstanding Patient Status forms for treatment continuation and after treatment discontinuation.

i. The number of healthcare providers who were contacted by the Fintepla REMS documenting the "Authorized Warning" and the results of the outreach.

j. The number and percentage of patients who had a *Patient Status Form* submitted within 270 days (approximately 9 months) of their most recent *Patient Status Form* among all patients who were dispensed Fintepla during the reporting period, did not have a *Patient Status Form* documenting their discontinuation of Fintepla (submitted prior to or within 72 hours of the 6-month due date), and did not have a *Patient Status Form* submitted by the 180-day due date.

k. The number of patients who did not have a *Patient Status Form* submitted within 270 days (approximately 9 months) of their most recent *Patient Status Form*, among all patients who were dispensed Fintepla during the reporting period, did not have a *Patient Status Form* documenting their discontinuation of Fintepla (submitted prior to or within 72 hours of the 6-month due date), and did not have a *Patient Status Form* submitted by the 180-day due date.

    i. For all patients who did not have a *Patient Status Form* submitted within 270 days of their most recent *Patient Status Form* and who did not have an ECHO test performed, a summary of the reasons ECHO tests were not performed and the source of reason information (i.e., healthcare provider or patient). Reasons the ECHO tests were not performed (e.g., scheduling, transportation, cost, prescriber determination of necessity, patient lost to follow up, switched healthcare providers, ECHO interrupted, other).

    ii. For each patient who did not have a *Patient Status Form* submitted within 270 days of their most recent *Patient Status Form* and who did not have an ECHO test performed, the source of noncompliance data and RCA results.

l. The number of patients who were continually dispensed Fintepla for 270 days or more (inpatient dispensing included) who did not have a *Patient Status Form* submitted within 450 days (approximately 15 months) of their most recent *Patient Status Form*.

    i. For all patients who did not have a *Patient Status Form* submitted within 450 days of their most recent *Patient Status Form* and who did not have an ECHO test performed, a summary of the reasons ECHO tests were not performed and the source of reason information (i.e., healthcare provider or patient). Reasons the ECHO tests were not performed (e.g., scheduling, transportation, cost, prescriber determination of necessity, patient lost to follow up, switched healthcare providers, ECHO interrupted, other).

    ii. For each patient who did not have a *Patient Status Form* submitted within 270 days of his/her most recent *Patient Status Form* who was dispensed Fintepla and who did not have an ECHO test performed, the source of noncompliance data and RCA results.

m. The number and percentage of patients who had a *Patient Status Form* submitted within 3 to 6 months after discontinuation of Fintepla among all patients who had a *Patient Status Form* documenting their discontinuation of Fintepla and among all patients who did not receive a dispensed prescription for Fintepla in the past 6 months.

n. The number and percentage of patients who did not have a *Patient Status Form* submitted within 3 to 6 months after discontinuation of Fintepla among all patients who had a *Patient Status Form* documenting their discontinuation of Fintepla and among all patients who did not receive a dispensed prescription for Fintepla in the past 6 months.

o. The number of unique patients who experienced a treatment interruption, including the duration, due to REMS noncompliance, prescriber choice, or a diagnosis of VHD, PAH, or other CVAE.

p. The number and percentage of unique patients who were not authorized to receive Fintepla due to lack of ECHO testing among all patients who received Fintepla in compliance with the REMS requirements.

    i. For all patients who were not authorized to receive Fintepla due to lack of ECHO testing, a summary of the reasons ECHO tests were not performed and the source of reason information (i.e., healthcare provider or patient). Reasons for the ECHO tests were not performed (e.g., scheduling, transportation, cost, prescriber determination of necessity, patient lost to follow-up, change of healthcare providers, ECHO interrupted, travel time, other).

q. The number and proportion of all dispenses that were from appropriately certified prescribers and pharmacies, to enrolled patients, and occurred only when the safe-use condition of an appropriately timed ECHO was obtained.

Knowledge

6. Knowledge Assessments

    a. The number of completed post-training knowledge assessments for prescribers, including the method of completion and the number of attempts to complete.

    b. A summary of the most frequently missed knowledge assessment questions.

    c. A summary of potential comprehension or perception issues identified with the knowledge assessment.

7. Stakeholder Surveys (beginning with the 1-year assessment report and annually thereafter with each assessment report)

    a. Healthcare provider surveys to assess if healthcare providers are educated on the following:

        i. The risk of VHD and PAH associated with Fintepla.

        ii. The need to counsel patients on how to recognize and respond to signs and symptoms of VHD and PAH.

        iii. The need to enroll patients in the REMS.

        iv. The need to submit documentation that baseline and periodic cardiac monitoring of patients is being done to identify VHD and PAH.

    b. Patient (caregiver) surveys to assess if patients (caregivers) are educated on the following:

        i. How to recognize and respond to symptoms of VHD and PAH.

        ii. The need to have baseline and periodic cardiac monitoring.

Health Outcomes and/or Surrogates of Health Outcomes

8. Health Outcomes

    a. Number of cases of patients with changes in the ECHO or abnormal ECHO who were not authorized to receive Fintepla based on *Patient Status Forms* among all patients who were active in the REMS during the reporting period and

cumulatively. Stratify by whether a *Cardiovascular Adverse Event Reporting Form* was received as a result of these ECHO changes or not.

b. Number of patients who had a new diagnosis of VHD or PAH who were not authorized to receive Fintepla based on *Patient Status Forms* among all patients who were active in the REMS during the reporting period and cumulatively. Stratify by whether a *Cardiovascular Adverse Event Reporting Form* was received as a result of these ECHO changes or not.

9. Safety Surveillance

   a. All patients with known adverse events related to VHD, PAH, or other CVAE provided in tabular format to include the following:

      i. N=Number of active patients for the reporting period

      ii. n=Number of patients with ≥1 (new/incident) event in reporting period

      iii. Percentage of patients with ≥1 (new/incident) of the total number of active patients for the reporting period

   b. Provide whether patients identified as having a known adverse event related to VHD, PAH, or other CVAE had received ECHO monitoring as per the Prescribing Information.

   c. Of the unique patients with cardiovascular adverse events (CVAEs), list the following patient outcomes, stratified by type of CVAE (VHD, PAH, Other New Abnormality) as characterized on the Cardiovascular Adverse Event Reporting Form and further pharmacovigilance follow-up. Provide data in tabular format.

      i. Number of patients requiring hospitalization

      ii. Number of patients requiring medication or interventional therapy

      iii. Number of patient deaths

      iv. Number of patients who discontinued treatment due to CV AE

10. 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 1 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.

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 212102 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 212102 REMS ASSESSMENT**
>
> ***or***
>
> **NEW SUPPLEMENT FOR NDA 212102/S-000**
> **CHANGES BEING EFFECTED IN 30 DAYS**
> **PROPOSED MINOR REMS MODIFICATION**
>
> ***or***
>
> **NEW SUPPLEMENT FOR NDA 212102/S-000**
> **PRIOR APPROVAL SUPPLEMENT**
> **PROPOSED MAJOR REMS MODIFICATION**
>
> ***or***

NEW SUPPLEMENT FOR NDA 212102/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 212102/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 212102

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word format is 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, contact Kelly Ross, Regulatory Health Project Manager via email at Kelly.Ross@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Alice T.D. Hughes, MD
Deputy Director for Safety
Division of Neurology 2
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURE(S):
- 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/

ALICE HUGHES
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