SUMMARY SHEET
SOUTH CAROLINA BOARD OF HEALTH AND ENVIRONMENTAL CONTROL

April 9, 2020

(X) ACTION/DECISION
( ) INFORMATION

I. **TITLE:** Request for Placement of Cenobamate into Schedule V for Controlled Substances in South Carolina.

II. **SUBJECT:** Placement of Cenobamate into Schedule V of the South Carolina Controlled Substances Act.

III. **FACTS:** Controlled substances are governed by the Controlled Substances Act ("CSA"), Title 44, Chapter 53 of the S.C. Code of Laws. Schedule V substances are listed in Section 44-53-270. Section 44-53-160 is titled, "Manner in which changes in schedule of controlled substances shall be made." Pursuant to Section 44-53-160, controlled substances are generally designated by the General Assembly upon recommendation by the Department of Health and Environmental Control ("Department"). Section 44-53-160(C) provides a process by which the Department can expeditiously designate a substance as a controlled substance if the federal government has designated the substance as such.

South Carolina Code Section 44-53-160(C) states:

> If a substance is added, deleted, or rescheduled as a controlled substance pursuant to federal law or regulation, the department shall, at the first regular or special meeting of the South Carolina Board of Health and Environmental Control within thirty days after publication in the federal register of the final order designating the substance as a controlled substance or rescheduling or deleting the substance, add, delete, or reschedule the substance in the appropriate schedule. The addition, deletion, or rescheduling of a substance by the department pursuant to this subsection has the full force of law unless overturned by the General Assembly. The addition, deletion, or rescheduling of a substance by the department pursuant to this subsection must be in substance identical with the order published in the federal register effecting the change in federal status of the substance. Upon the addition, deletion, or rescheduling of a substance, the department shall forward copies of the change to the Chairman of the Medical Affairs Committee and the Judiciary Committee of the Senate, the Medical, Military, Public and Municipal Affairs Committee and the Judiciary Committee of the House of Representatives, and to the Clerks of the Senate and House, and shall post the schedules on the department's website indicating the change and specifying the effective date of the change.

On November 21, 2019, the U.S. Food and Drug Administration ("FDA") approved a new drug application for XCOPRI (cenobamate) tablets. Cenobamate is chemically known as [(1R)-1-(2-chlorophenyl)-2-(tetrazol-2- yl)ethyl] carbamate. The U.S. Department of Health and Human Services ("DHHS") provided the federal Drug Enforcement Administration ("DEA") with a recommendation that cenobamate be placed in schedule V of the Federal Controlled Substances Act ("Federal CSA"). In accordance with the Federal CSA, as revised by the Improving Regulatory Transparency for New Medical Therapies Act, the DEA issued an interim final rule placing cenobamate and its salts in schedule

V of the Federal CSA, effective March 10, 2020, in the *Federal Register*, Volume 85, Number 47, pages 13741-13746; https:// govinfo.gov/content/pkg/FR-2020-03-10/pdf/2020-04963.pdf.

IV. ANALYSIS: Cenobamate is a new molecular entity with central nervous system ("CNS") depressant properties. Cenobamate is a voltagegated sodium channel ("NaV") blocker that also has gamma-aminobutyric acid (GABA)-A channel positive allosteric modulator ("PAM") activity. On November 21, 2018, SK Life Science ("Sponsor") submitted a new drug application ("NDA") to the FDA for cenobamate 12.5, 25, 50, 100, 150, and 200 mg oral tablets. On November 22, 2019, the DEA received notification that the FDA approved the NDA on November 21, 2019 for the treatment of partial-onset seizures in adult patients.

The DEA received a letter on December 10, 2019 from the DHHS, dated December 3, 2019, that contained a scientific and medical evaluation document prepared by the FDA related to cenobamate. This document contained an eight-factor analysis of the abuse potential of cenobamate, along with the DHHS' recommendation to control cenobamate under schedule V of the CSA. In response, the DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by the DHHS, along with all other relevant data, and completed its own eight-factor review document pursuant to 21 U.S.C. 811(c). The DEA concluded that cenobamate met the 21 U.S.C. 812(b)(5) criteria for placement in schedule V of the CSA.

21 U.S.C. 812(b) requires the evaluation of a substance's abuse potential, accepted medical use, and safety for use under medical supervision for scheduling under the CSA as a controlled substance. After consideration of the above eight-factor determination of control of a substance found in 21 U.S.C. 811(c), and a review of the scientific and medical evaluation, and scheduling recommendation provided by DHHS, the DEA finds that cenobamate meets the following criteria for placement in schedule V of the CSA pursuant to 21 U.S.C. 812(b)(5):

1) Cenobamate has a low potential for abuse relative to the drugs or other substances in Schedule IV. Cenobamate, similar to the schedule IV substance lacosamide, which is a voltagegated sodium channel blocker that also has GABA-A channel PAM activity, similar to schedule IV benzodiazepines. In drug discrimination studies, cenobamate partially generalized to the discriminative stimulus effects of midazolam (schedule IV) but fully generalized to the discriminative stimulus effects of chlordiazepoxide (schedule IV) in rats. In self-administration studies, cenobamate was self-administered by rodents, but the self-administration (i.e., number of infusions) of cenobamate was lower than that of midazolam. In the HAP studies, cenobamate produced drug-liking scores higher than placebo but less than that of alprazolam, a schedule IV substance. Based on all of these studies, the DHHS concluded that cenobamate has an abuse potential similar to that of substances in schedule V of the CSA. Thus, the DEA finds that the potential for abuse of cenobamate is less than that of schedule IV benzodiazepines but similar to that of substances in schedule V of the CSA.

2) Cenobamate has a currently accepted medical use in the United States. The FDA recently approved the NDA for cenobamate for partial-onset seizures in adult patients. Therefore, cenobamate has a currently accepted medical use in treatment in the United States.

3) Abuse of cenobamate may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule IV. Cenobamate may lead to physical or psychological dependence that is low relative to substances in schedule IV, and similar to that of substances in schedule V.

IV. RECOMMENDATION: The Acting Administrator of the DEA concludes that cenobamate, including its salts, warrants control in schedule V of the CSA.

Pursuant to South Carolina Code Section 44-53-160(C), the Department recommends the placement of cenobamate in Schedule V for controlled substances in South Carolina and the amendment of Section 44-53-270 of the South Carolina Code of Laws to include:

> ( ) Cenobamate ([(1R)-1-(2-chlorophenyl)-2-(tetrazol-2-yl)ethyl] carbamate; 2H-tetrazole-2-ethanol, alpha-(2-chlorophenyl)-, carbamate (ester), (alphaR)-; carbamic acid (R)-(+)-1-(2-chlorophenyl)-2-(2H-tetrazol-2-yl)ethyl ester).

The Department recommends the Board place cenobamate in Schedule V of the South Carolina Controlled Substances Act.

Submitted by:

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Director
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Gwendolyn C. Thompson
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Healthcare Quality

Attachment:
Federal Register, Volume 85, Number 47, March 10, 2020, Pages 13741-13746

4a, 80b–6(4), 80b–6a, and 80b–11, unless otherwise noted.

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■ 2. Amend § 275.203(l)–1 by revising the introductory text to paragraph (a) to read as follows:

§ 275.203(l)–1 Venture capital fund defined.

(a) *Venture capital fund defined.* For purposes of section 203(*l*) of the Act (15 U.S.C. 80b–3(*l*)), a venture capital fund is any entity described in subparagraph (A), (B), or (C) of section 203(b)(7) of the Act (15 U.S.C. 80b–3(b)(7)) (other than an entity that has elected to be regulated or is regulated as a business development company pursuant to section 54 of the Investment Company Act of 1940 (15 U.S.C. 80a–53)) or any entity described in subparagraph (A) or (B) of section 203(b)(8) of the Act (15 U.S.C. 80b–3(b)(8)) (other than an entity that has elected to be regulated or is regulated as a business development company pursuant to section 54 of the Investment Company Act of 1940 (15 U.S.C. 80a–53)) or any private fund that:

* * * * *

■ 3. Amend § 275.203(m)–1 by revising paragraph (d)(1) to read as follows:

§ 275.203(m)–1 Private fund adviser exemption.

* * * * *

(d) * * *

(1) *Assets under management* means the regulatory assets under management as determined under Item 5.F of Form ADV (§ 279.1 of this chapter), except the following shall be excluded from the definition of assets under management for purposes of this section:

(i) The regulatory assets under management attributable to a private fund that is an entity described in subparagraph (A), (B), or (C) of section 203(b)(7) of the Act (15 U.S.C. 80b–3(b)(7)) (other than an entity that has elected to be regulated or is regulated as a business development company pursuant to section 54 of the Investment Company Act of 1940 (15 U.S.C. 80a–53)); and

(ii) The regulatory assets under management attributable to a private fund that is an entity described in subparagraph (A) or (B) of section 203(b)(8) of the Act (15 U.S.C. 80b–3(b)(8)) (other than an entity that has elected to be regulated or is regulated as a business development company pursuant to section 54 of the Investment Company Act of 1940 (15 U.S.C. 80a–53).

* * * * *

By the Commission.

Dated: March 2, 2020.

Vanessa A. Countryman,

Secretary.

[FR Doc. 2020–04571 Filed 3–9–20; 8:45 am]

BILLING CODE 8011–01–P

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA–581]

Schedules of Controlled Substances: Placement of Cenobamate in Schedule V

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Interim final rule, with request for comments.

SUMMARY: On November 21, 2019, the U.S. Food and Drug Administration (FDA) approved a new drug application for XCOPRI (cenobamate) tablets. Cenobamate is chemically known as [(1R)-1-(2-chlorophenyl)-2-(tetrazol-2-yl)ethyl] carbamate. Thereafter, the Department of Health and Human Services provided the Drug Enforcement Administration (DEA) with a scheduling recommendation to place cenobamate in schedule V of the Controlled Substances Act (CSA). In accordance with the CSA, as revised by the Improving Regulatory Transparency for New Medical Therapies Act, DEA is hereby issuing an interim final rule placing cenobamate, including its salts, in schedule V of the CSA.

DATES: The effective date of this rulemaking is March 10, 2020. Interested persons may file written comments on this rulemaking in accordance with 21 U.S.C. 811(j)(3) and 21 CFR 1308.43(g). Electronic comments must be submitted, and written comments must be postmarked, on or before April 9, 2020. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Interested persons may file a request for hearing or waiver of hearing pursuant to 21 U.S.C. 811(j)(3) and 21 CFR 1308.44. Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before April 9, 2020.

ADDRESSES: To ensure proper handling of comments, please reference "Docket No. DEA–581" on all correspondence, including any attachments.

• *Electronic comments:* The Drug Enforcement Administration encourages that all comments be submitted electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the web page or attach a file for lengthier comments. Please go to *http://www.regulations.gov* and follow the online instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on *Regulations.gov*. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.

• *Paper comments:* Paper comments that duplicate the electronic submission are not necessary and are discouraged. Should you wish to mail a paper comment *in lieu of* an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA **Federal Register** Representative/DPW, 8701 Morrissette Drive, Springfield, VA 22152.

• *Hearing requests:* All requests for hearing and waivers of participation must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/LJ, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA **Federal Register** Representative/DPW, 8701 Morrissette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Scott Brinks, Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (571) 362–3261.

SUPPLEMENTARY INFORMATION:

Posting of Public Comments

Please note that all comments received are considered part of the public record. They will, unless reasonable cause is given, be made available by the Drug Enforcement Administration (DEA) for public inspection online at *http://www.regulations.gov*. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act (FOIA) applies to all comments received. If you want to

submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be made publicly available, you must include the phrase "PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase "CONFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify the confidential business information to be redacted within the comment.

Comments containing personal identifying information and confidential business information identified as directed above will generally be made publicly available in redacted form. If a comment has so much confidential business information or personal identifying information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments posted to *http://www.regulations.gov* may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this document and supplemental information, including the complete Department of Health and Human Services (HHS) and DEA eight-factor analyses, to this interim final rule are available at *http://www.regulations.gov* for easy reference.

Request for Hearing, Notice of Appearance at Hearing, or Waiver of Participation in Hearing

Pursuant to 21 U.S.C. 811(a), this action is a formal rulemaking "on the record after opportunity for a hearing." Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551–559. 21 CFR 1308.41–1308.45; 21 CFR part 1316, subpart D. Interested persons may file requests for a hearing, or notices of intent to participate in a hearing, in conformity with the requirements of 21 CFR 1308.44(a) or (b), and include a statement of interest in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any interested person may file a waiver of an opportunity for a hearing or to participate in a hearing together with a written statement regarding the interested person's position on the matters of fact and law involved in any hearing as set forth in 21 CFR 1308.44(c).

All requests for a hearing and waivers of participation must be sent to DEA using the address information provided above.

Background and Legal Authority

Under the Improving Regulatory Transparency for New Medical Therapies Act (Pub. L. 114–89), which was signed into law on November 25, 2015, DEA is required to commence an expedited scheduling action with respect to certain new drugs approved by the United States Food and Drug Administration (FDA). As provided in 21 U.S.C. 811(j), this expedited scheduling is required where both of the following conditions apply: (1) The Secretary of the Department of Health and Human Services (Secretary of HHS or the Secretary) has advised DEA that a New Drug Application (NDA) has been approved for a drug that has a stimulant, depressant, or hallucinogenic effect on the central nervous system (CNS), and that it appears that such drug has an abuse potential; and, (2) the Secretary recommends that DEA control the drug in schedule II, III, IV, or V pursuant to 21 U.S.C. 811(a) and (b). In these circumstances, DEA is required to issue an interim final rule controlling the drug within 90 days.

The law further states that the 90-day timeframe starts the later of: (1) The date DEA receives HHS' scientific and medical evaluation/scheduling recommendation or (2) the date DEA receives notice of the NDA approval by HHS. In addition, the law specifies that the rulemaking shall become immediately effective as an interim final rule without requiring DEA to demonstrate good cause therefor. Thus, the purpose of subsection (j) is to speed the process by which DEA schedules newly approved drugs that are currently either in schedule I or not controlled (but which have sufficient abuse potential to warrant control) so that such drugs may be marketed without undue delay following FDA approval.[1]

Subsection (j) further provides that the interim final rule shall give interested persons the opportunity to comment and to request a hearing. After the conclusion of such proceedings, DEA must issue a final rule in accordance with the scheduling criteria of subsections 21 U.S.C. 811(b), (c), and (d) and 21 U.S.C. 812(b).

Cenobamate is a new molecular entity with CNS depressant properties, and is chemically known as [(1R)-1-(2-chlorophenyl)-2-(tetrazol-2-yl)ethyl] carbamate. Cenobamate is a voltage-gated sodium channel (Na_V) blocker that also has gamma-aminobutyric acid (GABA)-A channel positive allosteric modulator (PAM) activity. On November 21, 2018, SK Life Science (Sponsor) submitted an NDA to FDA for XCOPRI (cenobamate) 12.5, 25, 50, 100, 150, and 200 mg oral tablets. On November 22, 2019, DEA received notification from HHS that FDA, on November 21, 2019, approved the NDA for XCOPRI (cenobamate) under section 505(c) of the Federal Food, Drug, and Cosmetic Act (FDCA), for the treatment of partial-onset seizures in adult patients.

Determination to Schedule Cenobamate

Pursuant to 21 U.S.C. 811(a)(1), proceedings to add a drug or substance to those controlled under the CSA may be initiated by request of the Secretary of HHS.[2] On December 10, 2019, DEA received from HHS a scientific and medical evaluation document (dated December 3, 2019) prepared by FDA, titled "Basis for the Recommendation to Control Cenobamate and Its Salts in Schedule V of the Controlled Substances Act." Pursuant to 21 U.S.C. 811(b) and (c), this document contained an eight-factor analysis of the abuse potential of cenobamate, along with HHS' recommendation to control cenobamate under schedule V of the CSA.

On January 15, 2020, DEA received from HHS a supplemental letter (dated January 15, 2020) clarifying factors 6 and 7 listed in 21 U.S.C. 811(c), as well as the third finding under 21 U.S.C. 812(b)(5), to control cenobamate in schedule V. This letter did not change HHS' overall recommendation to place cenobamate in schedule V.

In response, DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by HHS, along with all other relevant data, and completed its own eight-factor review document pursuant to 21 U.S.C. 811(c). DEA concluded that cenobamate

[1] Given the parameters of subsection (j), in DEA's view, it would not apply to a reformulation of a drug containing a substance currently in schedules II through V for which an NDA has recently been approved.

[2] As set forth in a memorandum of understanding entered into by HHS, FDA, and the National Institute on Drug Abuse (NIDA), FDA acts as the lead agency within HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of HHS has delegated to the Assistant Secretary for Health of HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

met the 21 U.S.C. 812(b)(5) criteria for placement in schedule V of the CSA.

Pursuant to subsection 811(j), and based on HHS recommendation, NDA approval by HHS/FDA, and DEA's determination, DEA is issuing this interim final rule to schedule cenobamate as a schedule V controlled substance under the CSA.

Included below is a brief summary of each factor as analyzed by HHS and DEA, and as considered by DEA in its scheduling action. Please note that both DEA and HHS analyses are available in their entirety under "Supporting Documents" in the public docket for this interim final rule at *http://www.regulations.gov,* under Docket Number "DEA–581." Full analysis of, and citations to, the information referenced in the summary may also be found in the supporting and related material.

1. *Its Actual or Relative Potential for Abuse:* Cenobamate is a new molecular entity and is not currently available or marketed in any country. Evidence regarding its diversion, illicit manufacturing, or deliberate ingestions is currently lacking. However, as reported by HHS, preclinical studies show that cenobamate shares similar mechanisms of action as substances in schedules IV or V. Cenobamate, like the schedule V substance lacosamide, is a voltage-gated sodium channel (Na_v) blocker. In addition, cenobamate, like the schedule IV substances alprazolam, chlordiazepoxide, and midazolam, has gamma-aminobutyric acid (GABA)-A channel positive allosteric modulator (PAM) activity and increases the effects of the inhibitory neurotransmitter, GABA. Data obtained from general behavioral studies demonstrate that cenobamate produces abuse-related CNS activity. In a preclinical drug discrimination study in rats, cenobamate mimicked the discriminative stimulus effects of the schedule IV substance chlordiazepoxide. However, in a separate drug discrimination study, cenobamate only partially mimicked the discriminative stimulus effects of the schedule IV substance midazolam. In addition, cenobamate, like midazolam, produced reinforcing effects in a rat self-administration assay by significantly increasing the number of infusions compared to saline infusions. In human abuse potential (HAP) studies, cenobamate produced drug-liking visual analog scale scores that were significantly higher compared to placebo but significantly lower than the schedule IV substance alprazolam. Thus, these studies demonstrate that cenobamate produced behavioral effects in rats comparable to that of schedule IV substances (*i.e.,* similar to chlordiazepoxide but less than midazolam); whereas in humans, cenobamate produced drug-liking effects that were significantly less than that of the schedule IV substance alprazolam. Thus, cenobamate likely has abuse potential less than that of schedule IV substances but similar to that of schedule V substances of the CSA. Based on the totality of the available scientific data, HHS concluded that cenobamate has an abuse potential similar to that of substances in schedule V of the CSA.

2. *Scientific Evidence of Its Pharmacological Effects, if Known:* Cenobamate shares similar mechanisms of action to substances in schedule IV or V and has anti-epileptic activity in humans. Cenobamate, like the schedule V substance lacosamide, is a voltage-gated sodium channel blocker. In addition, cenobamate, like the schedule IV benzodiazepines chlordiazepoxide, midazolam, and alprazolam, is a GABA-A channel positive allosteric modulator. Cenobamate and other GABAergic substances interact directly with the GABA-A receptor which is a ligand-gated chloride ion channel consisting of five subunits and a central chloride channel to enhance the opening of the ligand-gated chloride channel and the influx of chloride. Cenobamate's ability to bind to GABA-A receptors and sodium channel sites is consistent with the action of anti-epileptic or sedative drugs, such as chlordiazepoxide, midazolam, alprazolam, and lacosamide (schedule IV or V substances).

As described in HHS' review document, studies evaluating cenobamate's effect in these general behavioral studies showed that cenobamate mimicked or partially mimicked substances such as chlordiazepoxide, alprazolam, or midazolam (schedule IV substances) in producing behaviors that are associated with abuse. In an *in vivo* drug discrimination study in rats, cenobamate produced chlordiazepoxide-like (schedule IV) discriminative stimulus effects. In a separate drug discrimination study, cenobamate produced discriminative stimulus effects that partially mimicked the effects of the schedule IV substance midazolam. In self-administration studies, cenobamate was self-administered by rodents, but the self-administration (*i.e.,* number of infusions) of cenobamate was lower than that of midazolam, a schedule IV substance. In HAP studies, cenobamate produced drug-liking scores higher than placebo but less than that of the schedule IV substance alprazolam. Based on these studies, HHS concluded that cenobamate has mechanisms of actions that are similar to that of substances in schedule IV or V but the abuse potential of cenobamate is less than that of alprazolam, a schedule IV substance.

3. *The State of Current Scientific Knowledge Regarding the Drug or Other Substance:* Cenobamate is a new molecular entity. It is chemically known as [(1R)-1-(2-chlorophenyl)-2-(tetrazol-2-yl)ethyl] carbamate. Other chemical names for cenobamate include: 2H-tetrazole-2-ethanol, alpha-(2-chlorophenyl)-, carbamate (ester), (alphaR)-; and carbamic acid (R)-(+)-1-(2-chlorophenyl)-2-(2H-tetrazol-2-yl)ethyl ester. It has a molecular formula of $C_{10}H_{10}ClN_5O_2$ and a molecular weight of 267.67 g/mol. Cenobamate is a white to off-white crystalline solid that has a melting point between 96.8–98.3 °C. It is partially soluble in water at a pH between 2 and 12. Pharmacokinetic data indicate that cenobamate is rapidly absorbed, has good bioavailability, and has a long half-life. Additional studies in humans show that cenobamate is not extensively metabolized and does not produce any major circulating metabolites. On November 21, 2019, FDA approved an NDA for XCOPRI (cenobamate) for the treatment of partial-onset seizures in adult patients. Thus, cenobamate has an accepted medical use in the United States.

4. *Its History and Current Pattern of Abuse:* There is no information on the history and current pattern of abuse for cenobamate, since it has not been marketed, legally or illegally, in any country.

On December 19, 2019, DEA conducted a search on the National Forensic Laboratory Information System (NFLIS) [3] and the STARLiMS [4] databases for cenobamate's encounters. Consistent with the fact that cenobamate is a new molecular entity, these databases had no records of encounters by law enforcement.

The pharmacological activity of cenobamate, like schedule IV or V GABAergic or anti-epileptic substances, at sodium channels and GABA-A receptors suggests that cenobamate's pattern of abuse would be less than that

[3] NFLIS is a national forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by Federal, State, and local forensic laboratories in the United States.

[4] STARLiMS is a laboratory information management system that systematically collects results from drug chemistry analyses conducted by DEA laboratories. On October 1, 2014, STARLiMS replaced STRIDE as the DEA laboratory drug evidence data system of record.

of schedule IV substances but similar to that of schedule V anti-epileptic drugs.

5. *The Scope, Duration, and Significance of Abuse:* Cenobamate is not marketed, legally or illegally, in any country. However, HHS stated that based on the preclinical and clinical study data of cenobamate, the scope, duration, and significance of cenobamate abuse would likely be similar to that of schedule V substances.

6. *What, if any, Risk There is to the Public Health:* According to HHS, the public health risk associated with cenobamate is due to its abuse potential. Thus, HHS concluded that the data from preclinical and clinical studies (see Factor 2, above) showed that cenobamate has abuse potential and physical or psychological dependence (Factor 7) similar to that of substances in schedule V.

7. *Its Psychic or Physiological Dependence Liability:* The psychic or physiological dependence liability of drugs can be demonstrated by abuse-related animal and human studies (see Factor 2, above). In animal studies, there were no significant alterations in the withdrawal phase of the study in the measured parameters at either of the tested doses. However, in human studies, cenobamate led to a mild withdrawal syndrome characterized by insomnia, decreased appetite, depressed mood, tremor, and amnesia. Based on these studies, HHS concluded that cenobamate has a psychic or physiological dependence liability similar to that of substances in schedule V.

8. *Whether the Substance is an Immediate Precursor of a Substance Already Controlled under the CSA:* Cenobamate is not an immediate precursor of any substance already controlled in the CSA.

Conclusion: After considering the scientific and medical evaluation conducted by HHS, HHS' recommendation, and its own eight-factor analysis, DEA has determined that these facts and all relevant data constitute substantial evidence of a potential for abuse of cenobamate. As such, DEA hereby schedules cenobamate as a controlled substance under the CSA.

Determination of Appropriate Schedule

The CSA lists the findings required to place a drug or other substance in any particular schedule (I, II, III, IV, or V). 21 U.S.C. 812(b). After consideration of the analysis and recommendation of the Assistant Secretary for Health of HHS and review of all available data, the Acting Administrator of DEA, pursuant to 21 U.S.C. 812(b)(5), finds that:

(1) Cenobamate has a low potential for abuse relative to the drugs or other substances in schedule IV.

Cenobamate, similar to the schedule IV substance lacosamide, is a voltage-gated sodium channel blocker that also has GABA-A channel PAM activity similar to schedule IV benzodiazepines. In drug discrimination studies, cenobamate partially generalized to the discriminative stimulus effects of midazolam (schedule IV) but fully generalized to the discriminative stimulus effects of chlordiazepoxide (schedule IV) in rats. In self-administration studies, cenobamate was self-administered by rodents, but the self-administration (*i.e.,* number of infusions) of cenobamate was lower than that of midazolam. In the HAP studies, cenobamate produced drug-liking scores higher than placebo but less than that of alprazolam, a schedule IV substance. Based on all of these studies, HHS concluded that cenobamate has an abuse potential similar to that of substances in schedule V of the CSA. Thus, DEA finds that the potential for abuse of cenobamate is less than that of schedule IV benzodiazepines but similar to that of substances in schedule V of the CSA.

(2) Cenobamate has a currently accepted medical use in the United States.

FDA recently approved an NDA for cenobamate as a treatment for partial-onset seizures in adult patients. Thus, cenobamate has a currently accepted medical use in treatment in the United States.

(3) Abuse of Cenobamate may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule IV.

HHS reported in Factor 7 that cenobamate may lead to mild withdrawal syndromes characterized by insomnia, decreased appetite, and amnesia in humans. Thus, based on clinical study and preclinical data, HHS concluded in Factor 6 that cenobamate has a physical or psychological dependence liability similar to that of substances controlled in schedule V. In a separate letter, dated January 15, 2020, HHS further stated that based on the totality of available scientific data, cenobamate may lead to physical or psychological dependence that is low relative to substances in schedule IV of the CSA and similar to that of substances in schedule V. Based on these data, DEA finds that the abuse of cenobamate may lead to limited physical or psychological dependence relative to the drugs or other substances in schedule IV.

Based on these findings, the Acting Administrator of DEA concludes that cenobamate warrants control in schedule V of the CSA. 21 U.S.C. 812(b)(5).

Requirements for Handling Cenobamate

Cenobamate is subject to the CSA's schedule V regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, dispensing, importing, exporting, research, and conduct of instructional activities and chemical analysis with, and possession involving schedule V substances, including the following:

1. *Registration.* Any person who handles (manufactures, distributes, reverse distributes, dispenses, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses) cenobamate, or who desires to handle cenobamate, must be registered with DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958 and in accordance with 21 CFR parts 1301 and 1312. Any person who currently handles or intends to handle cenobamate, and is not registered with DEA, must submit an application for registration and may not continue to handle cenobamate, unless DEA has approved that application for registration, pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312.

2. *Disposal of stocks.* Any person who does not desire or is not able to maintain a schedule V registration must surrender all quantities of currently held cenobamate or may transfer all quantities of cenobamate to a person registered with DEA in accordance with 21 CFR part 1317, in addition to all other applicable federal, state, local, and tribal laws.

3. *Security.* Cenobamate is subject to schedule III–V security requirements and must be handled and stored in accordance with 21 CFR 1301.71–1301.93.

4. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of cenobamate must comply with 21 U.S.C. 825 and 958(e), and be in accordance with 21 CFR part 1302.

5. *Inventory.* Every DEA registrant who possesses any quantity of cenobamate must take an inventory of cenobamate on hand, pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

Any person who becomes registered with DEA to handle cenobamate must take an initial inventory of all stocks of controlled substances (including

cenobamate) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including cenobamate) on hand every two years, pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

6. *Records and Reports.* DEA registrants must maintain records and submit reports for cenobamate, pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR parts 1304, 1312, and 1317.

7. *Prescriptions.* All prescriptions for cenobamate, or products containing cenobamate, must comply with 21 U.S.C. 829, and be issued in accordance with 21 CFR parts 1306 and 1311, subpart C.

8. *Manufacturing and Distributing.* In addition to the general requirements of the CSA and DEA regulations that are applicable to manufacturers and distributors of schedule V controlled substances, such registrants should be advised that (consistent with the foregoing considerations) any manufacturing or distribution of cenobamate may only be for the legitimate purposes consistent with the drug's labeling, or for research activities authorized by the FDCA and the CSA.

9. *Importation and Exportation.* All importation and exportation of cenobamate must be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

10. *Liability.* Any activity involving cenobamate not authorized by, or in violation of, the CSA or its implementing regulations, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Administrative Procedure Act

Section 553 of the Administrative Procedure Act (APA) (5 U.S.C. 553) generally requires notice and comment for rulemakings. However, 21 U.S.C. 811 provides that in cases where a certain new drug is (1) approved by HHS and (2) HHS recommends control in CSA schedule II–V, DEA shall issue an interim final rule scheduling the drug within 90 days. Additionally, the law specifies that the rulemaking shall become immediately effective as an interim final rule without requiring DEA to demonstrate good cause.

Executive Orders 12866, 13563, and 13771, Regulatory Planning and Review, Improving Regulation and Regulatory Review, and Reducing Regulation and Controlling Regulatory Costs

In accordance with 21 U.S.C. 811(a) and (j), this scheduling action is subject to formal rulemaking procedures performed "on the record after opportunity for a hearing," which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the procedures and criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

This interim final rule is not an Executive Order 13771 regulatory action pursuant to Executive Order 12866 and OMB guidance.[5]

Executive Order 12988, Civil Justice Reform

This regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132, Federalism

This rulemaking does not have federalism implications warranting the application of Executive Order 13132. The rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.

Executive Order 13175, Consultation and Coordination With Indian Tribal Governments

This rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes.

Regulatory Flexibility Act

The Regulatory Flexibility Act (RFA) (5 U.S.C. 601–612) applies to rules that are subject to notice and comment under section 553(b) of the APA. Under 21 U.S.C. 811(j), DEA is not required to publish a general notice of proposed rulemaking. Consequently, the RFA does not apply to this interim final rule.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 *et seq.*, DEA has determined that this action would not result in any Federal mandate that may result "in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any 1 year." Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501–3521. This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Congressional Review Act

This rule is not a major rule as defined by the Congressional Review Act (CRA), 5 U.S.C. 804. This rule will not result in: An annual effect on the economy of $100,000,000 or more; a major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of U.S.-based companies to compete with foreign based companies in domestic and export markets. However, pursuant to the CRA, DEA has submitted a copy of this interim final rule to both Houses of Congress and to the Comptroller General.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, DEA amends 21 CFR part 1308 as follows:

[5] Office of Mgmt. & Budget, Exec. Office of The President, Interim Guidance Implementing Section 2 of the Executive Order of January 30, 2017 Titled "Reducing Regulating and Controlling Regulatory Costs" (Feb. 2, 2017).

PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES

■ 1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

■ 2. Amend § 1308.15 by:

■ a. Redesignating paragraphs (e)(2) through (5) as (e)(3) through (6), respectively;

■ b. Adding new paragraph (e)(2).

The addition reads as follows:

§ 1308.15 Schedule V.

* * * * *

(e) * * *

(2) Cenobamate ([(1R)-1-(2-chlorophenyl)-2-(tetrazol-2-yl)ethyl] carbamate; 2*H*-tetrazole-2-ethanol, alpha-(2-chlorophenyl)-, carbamate (ester), (alpha*R*)-; carbamic acid (*R*)-(+)-1-(2-chlorophenyl)-2-(2*H*-tetrazol-2-yl)ethyl ester)	2720

* * * * *

Dated: March 5, 2020.

Uttam Dhillon,

Acting Administrator.

[FR Doc. 2020–04963 Filed 3–9–20; 8:45 am]

BILLING CODE 4410–09–P

DEPARTMENT OF THE TREASURY

Office of Foreign Assets Control

31 CFR Part 595

Removal of Terrorism Sanctions Regulations

AGENCY: Office of Foreign Assets Control, Treasury.

ACTION: Final rule.

SUMMARY: The Department of the Treasury's Office of Foreign Assets Control (OFAC) is removing from the Code of Federal Regulations the Terrorism Sanctions Regulations as a result of the termination of the national emergency on which the regulations were based.

DATES: *Effective Date:* March 10, 2020.

FOR FURTHER INFORMATION CONTACT: OFAC: Assistant Director for Licensing, 202–622–2480; Assistant Director for Regulatory Affairs, 202–622–4855; or Assistant Director for Sanctions Compliance & Evaluation, 202–622–2490.

SUPPLEMENTARY INFORMATION:

Electronic Availability

This document and additional information concerning OFAC are available on OFAC's website (*www.treasury.gov/ofac*).

Background

On January 23, 1995, the President issued Executive Order 12947, "Prohibiting Transactions With Terrorists Who Threaten To Disrupt the Middle East Peace Process" (E.O. 12947), declaring a national emergency with respect to "grave acts of violence committed by foreign terrorists that disrupt the Middle East peace process," and invoking the authority, *inter alia*, of the International Emergency Economic Powers Act (50 U.S.C. 1701–1706). In E.O. 12947, the President blocked all property and interests in property of (1) persons listed in the Annex to E.O. 12947; (2) foreign persons designated by the Secretary of State, in coordination with the Secretary of the Treasury and the Attorney General, because they are found (a) to have committed, or to pose a significant risk of committing, acts of violence that have the purpose or effect of disrupting the Middle East peace process, or (b) to assist in, sponsor, or provide financial, material, or technological support for, or services in support of, such acts of violence; and (3) persons determined by the Secretary of the Treasury, in coordination with the Secretary of State and the Attorney General, to be owned or controlled by, or to act for or on behalf of, any of the foregoing persons.

On February 2, 1996, OFAC issued the Terrorism Sanctions Regulations, 31 CFR part 595 (the "Regulations"), as a final rule to implement E.O. 12947. The Regulations were amended on several occasions.

On August 20, 1998, the President issued Executive Order 13099, "Prohibiting Transactions With Terrorists Who Threaten To Disrupt the Middle East Peace Process" (E.O. 13099), amending the Annex to E.O. 12947 in order to take additional steps with respect to the national emergency declared in E.O. 12947. On February 16, 2005, the President issued Executive Order 13372, "Clarification of Certain Executive Orders Blocking Property and Prohibiting Certain Transactions," further amending E.O. 12947 in order to clarify steps taken in E.O. 12947 as amended by E.O. 13099.

On September 9, 2019, the President issued Executive Order 13886, "Modernizing Sanctions To Combat Terrorism" (E.O. 13886). In E.O. 13886, the President found that it was necessary to consolidate and enhance sanctions to combat acts of terrorism and threats of terrorism by foreign terrorists. Accordingly, he terminated the national emergency declared in E.O. 12947, as amended, and revoked that order.

As a result, OFAC is removing the Regulations from the Code of Federal Regulations. Pursuant to section 202 of the National Emergencies Act (50 U.S.C. 1622), termination of the national emergency declared in E.O. 12947, as amended, shall not affect any action taken or proceeding pending and not finally concluded or determined as of 12:01 a.m. eastern daylight time on September 10, 2019 (the effective date of E.O. 13886), any action or proceeding based on any act committed prior to the effective date, or any rights or duties that matured or penalties that were incurred prior to the effective date.

Public Participation

Because the Regulations involve a foreign affairs function, the provisions of Executive Order 12866 and the Administrative Procedure Act (5 U.S.C. 553) requiring notice of proposed rulemaking, opportunity for public participation, and delay in effective date, as well as the provisions of Executive Order 13771, are inapplicable. Because no notice of proposed rulemaking is required for this rule, the Regulatory Flexibility Act (5 U.S.C. 601–612) does not apply.

Paperwork Reduction Act

The Paperwork Reduction Act does not apply because this rule does not impose information collection requirements that would require the approval of the Office of Management and Budget under 44 U.S.C. 3501 *et seq.*

List of Subjects in 31 CFR Part 595

Administrative practice and procedure, Banks, Banking and finance, Blocking of assets, Fines and penalties, Reporting and recordkeeping requirements, Specially designated terrorists, Terrorism, Transfer of assets.

PART 595—[REMOVED]

■ For the reasons set forth in the preamble, and under the authority of 3 U.S.C. 301; 31 U.S.C. 321(b); 50 U.S.C. 1601–1651, 1701–1706; Public Law 101–410, 104 Stat. 890 (28 U.S.C. 2461 note); Public Law 110–96, 121 Stat.1011; E.O. 12947, 60 FR 5079, 3 CFR, 1995 Comp., p. 319; E.O. 13099, 63 FR 45167, 3 CFR, 1998 Comp., p. 208; E.O. 13372, 70 FR 8499, 3 CFR, 2006 Comp., p. 159; and E.O. 13886, 84 FR 48041 (September 12, 2019), OFAC

SUMMARY SHEET
SOUTH CAROLINA BOARD OF HEALTH AND ENVIRONMENTAL CONTROL

April 9, 2020

(X) ACTION/DECISION
( ) INFORMATION

I. **TITLE:** Request for Placement of Lemborexant into Schedule IV for Controlled Substances in South Carolina.

II. **SUBJECT:** Placement of Lemborexant into Schedule IV for Controlled Substances.

II. **FACTS:** Controlled substances are governed by the Controlled Substances Act ("CSA"), Title 44, Chapter 53 of the S.C. Code of Laws. Schedule IV substances are listed in Section 44-53-250. Section 44-53-160 is titled "Manner in which changes in schedule of controlled substances shall be made." Pursuant to Section 44-53-160, controlled substances are generally designated by the General Assembly upon recommendation by DHEC. Section 44-53-160(C) provides a process by which DHEC can expeditiously designate a substance as a controlled substance if the federal government has so designated.

South Carolina Code Section 44-53-160(C) states:

> If a substance is added, deleted, or rescheduled as a controlled substance pursuant to federal law or regulation, the department shall, at the first regular or special meeting of the South Carolina Board of Health and Environmental Control within thirty days after publication in the federal register of the final order designating the substance as a controlled substance or rescheduling or deleting the substance, add, delete, or reschedule the substance in the appropriate schedule. The addition, deletion, or rescheduling of a substance by the department pursuant to this subsection has the full force of law unless overturned by the General Assembly. The addition, deletion, or rescheduling of a substance by the department pursuant to this subsection must be in substance identical with the order published in the federal register effecting the change in federal status of the substance. Upon the addition, deletion, or rescheduling of a substance, the department shall forward copies of the change to the Chairman of the Medical Affairs Committee and the Judiciary Committee of the Senate, the Medical, Military, Public and Municipal Affairs Committee and the Judiciary Committee of the House of Representatives, and to the Clerks of the Senate and House, and shall post the schedules on the department's website indicating the change and specifying the effective date of the change.

On December 20, 2019, the U.S. Food and Drug Administration ("FDA") approved a new drug application for Dayvigo (lemborexant) tablets for oral use. Lemborexant is chemically known as (1R,2S)-2-[(2,4-dimethylpyrimidin-5-yl)oxymethyl]-2-(3-fluorophenyl)-N-(5-fluoropyridin-2-yl)cyclopropane-1-carboxamide. The federal Department of Health and Human Services ("DHHS") provided the federal Drug Enforcement Administration ("DEA") with a recommendation that lemborexant be placed in schedule IV of the federal Controlled Substances Act ("federal CSA"). In accordance with the federal CSA, as revised by the Improving Regulatory Transparency for New Medical Therapies Act, the DEA issued an interim final rule placing lemborexant, including its salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible, in schedule IV of the federal CSA, effective April 7,

2020, in *Federal Register*, Volume 85, Number 67, pages 19387-19391; https://www.govinfo.gov/content/pkg/FR-2020-04-07/pdf/2020-07089.pdf.

III. ANALYSIS:

Lemborexant [(1R,2S)-2-[(2,4-dimethylpyrimidin-5-yl)oxymethyl]-2-(3-fluorophenyl)-N-(5-fluoropyridin-2-yl)cyclopropane-1-carboxamide] is a new molecular entity with central nervous system ("CNS") depressant properties. Lemborexant acts as an antagonist at both orexin-1 and orexin-2 receptors. On December 27, 2018, Eisai, Inc., ("Sponsor") submitted a new drug application ("NDA") to FDA for Dayvigo (lemborexant), 5 and 10 mg oral tablets, with the proposed dosage suggestion of 5 mg, not to exceed a maximum dose of 10 mg once a day. On March 9, 2020, DEA received notification that FDA approved, on December 20. 2019, NDA for Dayvigo (lemborexant) for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance.

On January 9, 2020, the DEA received from the DHHS a scientific and medical evaluation document dated December 19, 2019 prepared by the FDA related to lemborexant. This document contained an eight-factor analysis of the abuse potential of lemborexant, along with DHHS' recommendation to control lemborexant under schedule IV of the South Carolina CSA. In response, the DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by the DHHS, along with all other relevant data, and completed its own eight-factor review document pursuant to 21 U.S.C. 811(c). The DEA concluded that lemborexant met the 21 U.S.C. 812(b)(4) criteria for placement in schedule IV of the South Carolina CSA.

21 U.S.C. 812(b) requires the evaluation of a substance's abuse potential, accepted medical use, and safety for use under medical supervision for scheduling under the South Carolina CSA as a controlled substance. After consideration of the above eight factors determinative of control of a substance (21 U.S.C. 811(c)), and a review of the scientific and medical evaluation and scheduling recommendation provided by DHHS, DEA finds that lemborexant meets the following criteria for placement in schedule IV of the CSA pursuant to 21 U.S.C. 812(b)(4):

1) Lemborexant has a low potential for abuse relative to the drugs or other substances in schedule III. Lemborexant is a dual orexin receptor antagonist, which produces sedation in human behavioral studies. In the HAP study, therapeutic and supratherapeutic doses of lemborexant produced positive subjective responses such as Drug Liking, Overall Drug Liking, Good Drug Effects, High, Stoned, and Take Drug Again that were statistically significantly greater than those produced by placebo. These responses of lemborexant are similar to those produced by schedule IV drugs suvorexant and zolpidem. Because lemborexant is similar to zolpidem and suvorexant in its abuse potential, lemborexant has a low potential for abuse relative to the drugs and other listed substances in schedule III of the CSA.

2) Lemborexant has a currently accepted medical use in the United States. FDA recently approved lemborexant oral tablets for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance. Thus, lemborexant has a currently accepted medical use in treatment in the United States.

3) Lemborexant may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule III. In the HAP study, lemborexant produced positive subjective responses to measures such as Drug Liking, Overall Drug Liking, Good Drug Effects, High, Stoned, and Take Drug Again that were greater than placebo and similar to that of the schedule IV drugs zolpidem and suvorexant. This data suggests that lemborexant can produce psychic dependence to a similar extent as zolpidem and suvorexant. Thus, abuse of lemborexant

may lead to limited psychological dependence relative to the drugs or other substances in schedule III.

IV. RECOMMENDATION: The Acting Administrator of the DEA concludes that lemborexant, including its salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible, warrants control in schedule IV of the South Carolina CSA.

Pursuant to South Carolina Code Section 44-53-160(C), the Department recommends the placement of lemborexant in Schedule IV for controlled substances in South Carolina and the amendment of Section 44-53-250 of the South Carolina Code of Laws to include:

( ) Lemborexant (1R,2S)-2-[(2,4-dimethylpyrimidin-5-yl)oxymethyl]-2-(3-fluorophenyl)-N-(5-fluoropyridin-2-yl)cyclopropane-1-carboxamide.

The Department recommends the Board place lemborexant in Schedule IV of the South Carolina Controlled Substances Act.

Submitted by:

Lisa Thomson

Lisa Thomson
Director
Bureau of Drug Control

Gwendolyn C. Thompson

Gwen Thompson
Director
Healthcare Quality

Attachment:
Federal Register, Volume 85, Number 67, April 7, 2020

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA–600]

Schedules of Controlled Substances: Placement of Lemborexant in Schedule IV

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Interim final rule with request for comments.

SUMMARY: On December 20, 2019, the U.S. Food and Drug Administration approved a new drug application for Dayvigo (lemborexant) tablets for oral use. Lemborexant is chemically known as (1*R*,2*S*)-2-[(2,4-dimethylpyrimidin-5-yl)oxymethyl]-2-(3-fluorophenyl)-*N*-(5-fluoropyridin-2-yl)cyclopropane-1-carboxamide. The Department of Health and Human Services provided the Drug Enforcement Administration (DEA) with a scheduling recommendation to place lemborexant in schedule IV of the Controlled Substances Act (CSA). In accordance with the CSA, as amended by the Improving Regulatory Transparency for New Medical Therapies Act, DEA is hereby issuing an interim final rule placing lemborexant, including its salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible, in schedule IV of the CSA.

DATES: The effective date of this rulemaking is April 7, 2020. Interested persons may file written comments on this rulemaking in accordance with 21 U.S.C. 811(j)(3) and 21 CFR 1308.43(g). Electronic comments must be submitted, and written comments must be postmarked, on or before May 7, 2020. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Interested persons may file a request for hearing or waiver of hearing in accordance with

21 U.S.C. 811(j)(3) and 21 CFR 1308.44. Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing, together with a written statement of position on the matters of fact and law asserted in the hearing, must be received on or before May 7, 2020.

ADDRESSES: To ensure proper handling of comments, please reference "Docket No. DEA–600" on all correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration (DEA) encourages that all comments be submitted electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the web page or attach a file for lengthier comments. Please go to *http://www.regulations.gov* and follow the online instructions at the site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on *Regulations.gov*. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.
- *Paper comments:* Paper comments that duplicate the electronic submission are not necessary and are discouraged. Should you wish to mail a paper comment *in lieu of* an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrissette Drive, Springfield, VA 22152.
- *Hearing requests:* All requests for hearing and waivers of participation, together with a written statement regarding his position on the matter of fact and law involved in such hearing, must be sent to: Drug Enforcement Administration. Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/LJ. 8701 Morrissette Drive, Springfield, Virginia 22152: and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW. 8701 Morrissette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Scott A. Brinks, Regulatory Drafting and Policy Support Section, Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (571) 362–3261.

SUPPLEMENTARY INFORMATION:

Posting of Public Comments

Please note that all comments received are considered part of the public record. They will, unless reasonable cause is given, be made available by the Drug Enforcement Administration (DEA) for public inspection online at *http://www.regulations.gov*. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be made publicly available, you must include the phrase "PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted. If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase "CONFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify the confidential business information to be redacted within the comment.

Comments containing personal identifying information and confidential business information identified as directed above will generally be made publicly available in redacted form. If a comment has so much confidential business information or personal identifying information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments posted to *http://www.regulations.gov* may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this document and supplemental information, including the complete Department of Health and Human Services (HHS) and DEA eight-factor analyses, to this interim final rule are available at *http://www.regulations.gov* for easy reference.

Request for Hearing or Appearance; Waiver

Pursuant to 21 U.S.C. 811(a), this action is a formal rulemaking "on the record after opportunity for a hearing." Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551–559. 21 CFR 1308.41–1308.45; 21 CFR part 1316, subpart D. Interested persons may file requests for a hearing or notices of intent to participate in a hearing in conformity with the requirements of 21 CFR 1308.44(a) or (b), and include a statement of interest in the proceeding and the objections or issues, if any,

concerning which the person desires to be heard. 21 CFR 1316.47(a). Any interested person may file a waiver of an opportunity for a hearing or to participate in a hearing together with a written statement regarding the interested person's position on the matters of fact and law involved in any hearing as set forth in 21 CFR 1308.44(c).

All requests for a hearing and waivers of participation together with a written statement of position on the matters of fact and law involved in such hearing, must be sent to DEA using the address information provided above.

Background and Legal Authority

Under the Improving Regulatory Transparency for New Medical Therapies Act, Public Law 114–89, 2(b), 129 tat. 700 (2015), DEA is required to commence an expedited scheduling action with respect to certain new drugs approved by the Food and Drug Administration (FDA). As provided in 21 U.S.C. 811(j), this expedited scheduling is required where both of the following conditions apply: (1) The Secretary of HHS has advised DEA that a New Drug Application (NDA) has been submitted for a drug that has a stimulant, depressant, or hallucinogenic effect on the central nervous system (CNS), and that it appears that such drug has an abuse potential; and (2) the Secretary of HHS recommends that DEA control the drug in schedule II, III, IV, or V pursuant to 21 U.S.C. 811(a) and (b). In these circumstances. DEA is required to issue an interim final rule controlling the drug within 90 days.

The law further states that the 90-day timeframe starts the later of: (1) The date DEA receives HHS' scientific and medical evaluation and scheduling recommendation, or (2) the date DEA receives notice of the NDA approval by HHS. In addition, the law specifies that the rulemaking shall become immediately effective as an interim final rule without requiring DEA to demonstrate good cause therefore. Thus, the purpose of subsection (j) is to speed the process by which DEA schedules newly approved drugs that are currently either in schedule I or not controlled (but which have sufficient abuse potential to warrant control) so that such drugs may be marketed without undue delay following FDA approval.[1]

Subsection (j) further provides that the interim final rule shall give interested persons the opportunity to comment and to request a hearing. After the conclusion of such proceedings, DEA must issue a final rule in accordance with the scheduling criteria of subsections 21 U.S.C. 811(b), (c), and (d) and 21 U.S.C. 812(b).

Lemborexant [(1*R*,2*S*)-2-[(2,4-dimethylpyrimidin-5-yl)oxymethyl]-2-(3-fluorophenyl)-*N*-(5-fluoropyridin-2-yl)cyclopropane-1-carboxamide] is a new molecular entity with CNS depressant properties. Lemborexant acts as an antagonist at both orexin-1 and orexin-2 receptors (OX1R and OX2R, respectively). On December 27, 2018, Eisai, Inc., submitted an NDA for Dayvigo (lemborexant), 5 and 10 mg oral tablets, with the proposed dosage suggestion of 5 mg, not to exceed a maximum dose of 10 mg once a day. On March 9, 2020, DEA received a letter from FDA, dated March 5, 2020, notifying DEA that FDA, on December 20, 2019, approved the NDA for Dayvigo (lemborexant), under section 505(c) of the Federal Food, Drug, and Cosmetic Act (FDCA), for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance.[2] Lemborexant has not been marketed in any other country for any medical indication.

Determination To Schedule Lemborexant

On January 9, 2020, DEA received from HHS a scientific and medical evaluation (dated December 19, 2019) entitled "Basis for the Recommendation to Control Lemborexant and its Salts in Schedule IV of the Controlled Substances Act" and a scheduling recommendation. Pursuant to 21 U.S.C. 811(b) and (c), this document contained an eight-factor analysis of the abuse potential, legitimate medical use, and dependence liability of lemborexant, along with HHS's recommendation to control lemborexant and its salts under schedule IV of the CSA.

In response, DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by HHS, along with all other relevant data, and completed its own eight-factor review pursuant to 21 U.S.C. 811(c). DEA concluded that lemborexant meets the 21 U.S.C. 812(b)(4) criteria for placement in schedule IV of the CSA.

Pursuant to subsection 811(j), and based on HHS's recommendation, the NDA approval by HHS/FDA, and DEA's determination, DEA is issuing this interim final rule to schedule lemborexant as a schedule IV controlled substance under the CSA.

Included below is a brief summary of each factor as analyzed by HHS and DEA, and as considered by DEA in its scheduling action. Please note that both DEA and HHS analyses are available in their entirety under "Supporting Documents" in the public docket for this interim final rule at *http://www.regulations.gov,* under Docket Number "DEA–600." Full analysis of, and citations to, the information referenced in the summary may also be found in the supporting and related material.

1. Its Actual or Relative Potential for Abuse

As noted by HHS, lemborexant is a new molecular entity that has not been marketed in the United States or any other country. Thus, evidence regarding its diversion, illicit manufacture, or deliberate ingestion is currently lacking. DEA notes that there are no reports for lemborexant in the National Forensic Laboratory Information System (NFLIS),[3] which collects drug identification results from drug cases submitted to and analyzed by state and local forensic laboratories. There were also no reports in STARLiMS,[4] DEA's laboratory drug evidence data system of record.

As stated by HHS, lemborexant is a sedative that is highly selective for both the OX1R and OX2R receptors and has little to no affinity to other CNS receptor sites associated with abuse potential. In a clinical study investigating the abuse potential of lemborexant, HHS concluded that lemborexant produced subjective responses that were similar to those for the schedule IV sedative suvorexant.

[1] Given the parameter of subsection (j), in DEA's view, it would not apply to a reformulation of a drug containing a substance currently in schedules II through V for which an NDA has recently been approved.

[2] *https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2019/212028Orig1s000ltr.pdf,* accessed March 11, 2020.

[3] NFLIS represents an important resource in monitoring illicit drug trafficking, including the diversion of legally manufactured pharmaceuticals into illegal markets. NFLIS is a comprehensive information system that includes data from forensic laboratories that handle more than 96% of an estimated 1.0 million distinct annual State and local drug analysis cases. NFLIS includes drug chemistry results from completed analyses only. While NFLIS data is not direct evidence of abuse, it can lead to an inference that a drug has been diverted and abused. *See* 76 FR 77330, 77332, Dec. 12, 2011. NFLIS data were queried January 15, 2020.

[4] On October 1, 2014, DEA implemented STARLiMS (a web-based, commercial laboratory information management system) to replace the System to Retrieve Information from Drug Evidence (STRIDE) as its laboratory drug evidence data system of record. DEA laboratory data submitted after September 30, 2014, are reposited in STARLiMS. STARLiMS data were queried January 15, 2020.

2. Scientific Evidence of Its Pharmacological Effects, if Known

According to HHS, lemborexant primarily acts as a dual orexin receptor antagonist and does not bind with any other CNS receptors that are typically associated with abuse, such as opioid or cannabinoid receptors, GABAergic, and other ion channels. According to HHS, general behavioral studies in animals indicate that acute oral administration of lemborexant using supratherapeutic doses (100, 300, and 1000 mg/kg), produced no overt behavioral changes in hindlimb foot splay, forelimb grip strength, hindlimb grip strength, and rectal temperature in cage-side, hand-held, and open-field using functional observational methods. Additionally, lemborexant, even at supratherapeutic doses, does not significantly impair motor coordination. In drug discrimination studies, which are used to predict subjective effects in humans, lemborexant and suvorexant (a schedule IV substance which is another known dual orexin receptor antagonist) did not fully mimic stimulus effects of zolpidem, a schedule IV sedative. In a self-administration study in rhesus monkeys, the rewarding effects of lemborexant were insufficient to produce reinforcement.

According to HHS, in a human abuse potential (HAP) study conducted by the Sponsor, lemborexant (at therapeutic and supratherapeutic doses) produced statistically significant increases on positive subjective measures in the bipolar visual analog scale (VAS) (*i.e.,* Drug Liking, Overall Drug Liking, Good Effects, High, Stoned, and Take Drug Again) that were greater than placebo and statistically similar to suvorexant and/or zolpidem (schedule IV substances). With respect to two subjective measures, such as drowsiness and sedation, lemborexant, similar to zolpidem and suvorexant, produced statistically significantly greater scores than placebo. HHS concluded that lemborexant produces positive subjective effects and has an abuse potential similar to that of schedule IV sedatives, such as suvorexant and zolpidem, which were used as positive controls in the aforementioned study. According to HHS, in multiple-dose Phase I studies, lemborexant produced dose-dependent "abnormal dreams." There were few incidents of abuse-related adverse events (AEs), such as "euphoric mood," "disturbance in attention," and "memory impairment." Furthermore, in Phase 2 clinical studies, lemborexant produced dose dependent somnolence. This response was considered appropriate given the proposed therapeutic use for lemborexant as a treatment for insomnia. No additional abuse-related AEs were reported by participants at an incidence greater than 1.0 percent. As per the adverse event data obtained from Phase 1 and Phase 2/3 clinical safety and efficacy trials, there were no significant abuse-related signals.

3. The State of Current Scientific Knowledge Regarding the Drug or Other Substance

Lemborexant is a new molecular entity, chemically known as (1*R*,2*S*)-2-[(2,4-dimethylpyrimidin-5-yl)oxymethyl]-2-(3-fluorophenyl)-*N*-(5-fluoropyridin-2-yl)cyclopropane-1-carboxamide. It is nearly insoluble in water and heptane; "sparingly" soluble in 1-octanol; very soluble in dimethyl sulfoxide; and freely soluble in methanol, acetone, ethyl acetate, and benzyl alcohol. Additionally, lemborexant is soluble in acetonitrile and ethanol. On December 20, 2019, FDA approved an NDA for lemborexant for medical use for the treatment of insomnia in adult patients with insomnia characterized by difficulties with sleep onset and/or sleep maintenance. Thus, lemborexant has an accepted medical use in the United States. Lemborexant will be marketed as a once daily tablet taken before bedtime, with at least 7 hours remaining before the planned time of awakening. The recommended dose for lemborexant is 5 mg; however, the dosage may be increased to 10 mg based on clinical response and tolerability.[5]

4. Its History and Current Pattern of Abuse

There is no information available relating to the history and current pattern of abuse of lemborexant because this drug is not currently marketed in any country. As stated in Factor 1, DEA notes that there has been no diversion of lemborexant based on NFLIS and STARLiMS data. HHS notes that lemborexant produces abuse-related signals and abuse potential similar to that of the schedule IV controlled substance suvorexant.

5. The Scope, Duration, and Significance of Abuse

Lemborexant as a single active ingredient in a drug product is currently not marketed in any country. Thus, information on the scope, duration, and significance of abuse for lemborexant is lacking. As described in Factor 4, NFLIS and STARLiMS databases have no evidence of law enforcement encounters of lemborexant. However, as HHS notes, data from preclinical and clinical studies summarized in Factor 2 indicate that the scope, duration, and significance of abuse for lemborexant would be similar to those of suvorexant, a schedule IV substance. As stated by HHS, data from animal and human studies indicate that lemborexant has an abuse potential similar to that of suvorexant.

6. What, if Any, Risk There Is to the Public Health

As stated by HHS, the public health risk associated with lemborexant is largely a risk to the individual due to its abuse potential. The extent of abuse potential of a drug is an indication of its public health risk. Data from the preclinical and clinical studies suggest that the abuse potential of lemborexant is similar to schedule IV substances, such as suvorexant and zolpidem. Lemborexant, similar to schedule IV sedatives, is likely to pose a public health risk of abuse upon marketing in the United States.

7. Its Psychic or Physiological Dependence Liability

Physical dependence for lemborexant was tested in a rat physical dependence study and during Phase 2/3 clinical trials. Based on the data from these studies, HHS concluded that lemborexant lacked physical dependence potential. According to HHS, in the HAP study (presented in Factor 2), lemborexant administration was associated with positive subjective effects as assessed by participant responses to measures of Drug Liking, Overall Drug Liking, Good Drug Effects, High, Stoned, and Take Drug Again. The results indicated that the responses for lemborexant were similar to that of positive control drugs, such as zolpidem and suvorexant. Thus, it is likely that lemborexant can produce psychic dependence similar to that of schedule IV drugs, such as zolpidem and suvorexant.

8. Whether the Substance Is an Immediate Precursor of a Substance Already Controlled Under the CSA

Lemborexant is not an immediate precursor of any controlled substance, as defined in 21 U.S.C. 802(23).

Conclusion

After considering the scientific and medical evaluation conducted by HHS, HHS's recommendation, and its own eight-factor analysis, DEA has determined that these facts and all

[5] *https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212028s000lbl.pdf,* accessed February 6, 2020.

relevant data constitute substantial evidence of a potential for abuse of lemborexant. As such, DEA hereby schedules lemborexant as a controlled substance under the CSA.

Determination of Appropriate Schedule

The CSA lists the findings required to place a drug or other substance in any particular schedule (I, II, III, IV, or V). 21 U.S.C. 812(b). After consideration of the analysis and recommendation of the Assistant Secretary for Health of HHS and review of all available data, the Acting Administrator of DEA, pursuant to 21 U.S.C. 812(b)(4), finds that:

1. Lemborexant has a low potential for abuse relative to the drugs or other substances in schedule III.

Lemborexant is a dual orexin receptor antagonist, which produces sedation in human behavioral studies. In the HAP study, therapeutic and supratherapeutic doses of lemborexant produced positive subjective responses such as Drug Liking, Overall Drug Liking, Good Drug Effects, High, Stoned, and Take Drug Again that were statistically significantly greater than those produced by placebo. These responses of lemborexant are similar to those produced by schedule IV drugs suvorexant and zolpidem. Because lemborexant is similar to zolpidem and suvorexant in its abuse potential, lemborexant has a low potential for abuse relative to the drugs and other listed substances in schedule III of the CSA.

2. Lemborexant has a currently accepted medical use in the United States.

FDA recently approved lemborexant oral tablets for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance. Thus, lemborexant has a currently accepted medical use in treatment in the United States.

3. Lemborexant may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in schedule III.

As stated by HHS, data from a rat physical dependence study, as well as a physical dependence assessment at the conclusion of the Phase 2/3 clinical trials, showed that lemborexant did not produce withdrawal symptoms indicative of physical dependence. In the HAP study, lemborexant produced positive subjective responses to measures such as Drug Liking, Overall Drug Liking, Good Drug Effects, High, Stoned, and Take Drug Again that were greater than placebo and similar to that of the schedule IV drugs zolpidem and suvorexant. This data suggests that lemborexant can produce psychic dependence to a similar extent as zolpidem and suvorexant. Thus, abuse of lemborexant may lead to limited psychological dependence relative to the drugs or other substances in schedule III of the CSA.

Based on these findings, the Acting Administrator of DEA concludes that lemborexant warrants control in schedule IV of the CSA. 21 U.S.C. 812(b)(4).

Requirements for Handling Lemborexant

Lemborexant is subject to the CSA's schedule IV regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, dispensing, importing, exporting, research, and conduct of instructional activities and chemical analysis with, and possession involving schedule IV substances, including the following:

1. *Registration.* Any person who handles (manufactures, distributes, reverse distributes, dispenses, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses) lemborexant, or who desires to handle lemborexant, must be registered with DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958 and in accordance with 21 CFR parts 1301 and 1312. Any person who currently handles or intends to handle lemborexant and is not registered with DEA must submit an application for registration and may not continue to handle lemborexant, unless DEA has approved that application for registration, pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312.

2. *Disposal of stocks.* Any person who does not desire or is not able to maintain a schedule IV registration must surrender all quantities of currently held lemborexant or may transfer all quantities of lemborexant to a person registered with DEA in accordance with 21 CFR part 1317, in additional to all other applicable Federal, State, local, and tribal laws.

3. *Security.* Lemborexant is subject to schedule III–V security requirements and must be handled and stored in accordance with 21 CFR 1301.71–1301.77. Non-practitioners handling lemborexant must also comply with the employee screening requirements of 1301.90–1301.93.

4. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of lemborexant must comply with 21 U.S.C. 825 and 958(e), and be in accordance with 21 CFR part 1302.

5. *Inventory.* Every DEA registrant who possesses any quantity of lemborexant must take an inventory of lemborexant on hand, pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

Any person who becomes registered with DEA to handle lemborexant must take an initial inventory of all stocks of controlled substances (including lemborexant) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including lemborexant) on hand at least every two years, pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

6. *Records and Reports.* DEA registrants must maintain records and submit reports for lemborexant, pursuant to 21 U.S.C. 827, 832(a), and 958(e), and in accordance with 21 CFR 1301.74(b) and (c) and parts 1304, 1312, and 1317.

7. *Prescriptions.* All prescriptions for lemborexant, or products containing lemborexant, must comply with 21 U.S.C. 829, and be issued in accordance with 21 CFR parts 1306 and 1311, subpart C.

8. *Manufacturing and Distributing.* In addition to the general requirements of the CSA and DEA regulations that are applicable to manufacturers and distributors of schedule IV controlled substances, such registrants should be advised that (consistent with the foregoing considerations) any manufacturing or distribution of lemborexant may only be for the legitimate purposes consistent with the drug's labeling, or for research activities authorized by the FDCA and the CSA.

9. *Importation and Exportation.* All importation and exportation of lemborexant must be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

10. *Liability.* Any activity involving lemborexant not authorized by, or in violation of, the CSA or its implementing regulations, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Administrative Procedure Act

Section 553 of the APA (5 U.S.C. 553) generally requires notice and comment

for rulemakings. However, 21 U.S.C. 811(j) provides that in cases where a certain new drug is: (1) Approved by HHS, under section 505(c) of the FDCA, and (2) HHS recommends control in CSA schedule II–V, DEA shall issue an interim final rule scheduling the drug within 90 days. As stated in the legal authority section, the 90-day time frame is the later of: (1) The date DEA receives HHS's scientific and medical evaluation/scheduling recommendation, or (2) the date DEA receives notice of the NDA approval by HHS. Additionally, the law specifies that the rulemaking shall become immediately effective as an interim final rule without requiring DEA to demonstrate good cause.

Executive Orders 12866, 13563, and 13771, Regulatory Planning and Review, Improving Regulation and Regulatory Review, and Reducing Regulation and Controlling Regulatory Costs

In accordance with 21 U.S.C. 811(a) and (j), this scheduling action is subject to formal rulemaking procedures performed "on the record after opportunity for a hearing," which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the procedures and criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

This interim final rule is not an Executive Order 13771 regulatory action pursuant to Executive Order 12866 and OMB guidance.[6]

Executive Order 12988, Civil Justice Reform

This regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132, Federalism

This rulemaking does not have federalism implications warranting the application of Executive Order 13132. The rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.

Executive Order 13175, Consultation and Coordination With Indian Tribal Governments

This rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes.

Regulatory Flexibility Act

The Regulatory Flexibility Act (RFA) (5 U.S.C. 601–612) applies to rules that are subject to notice and comment under section 553(b) of the APA. Under 21 U.S.C. 811(j), DEA is not required to publish a general notice of proposed rulemaking. Consequently, the RFA does not apply to this interim final rule.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 *et seq.*, DEA has determined that this action would not result in any Federal mandate that may result "in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any 1 year." Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501–3521. This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Congressional Review Act

This rule is not a major rule as defined by the Congressional Review Act (CRA), 5 U.S.C. 804. This rule will not result in: An annual effect on the economy of $100 million or more; a major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based companies to compete with foreign-based companies in domestic and export markets. However, pursuant to the CRA, DEA has submitted a copy of this interim final rule to both Houses of Congress and to the Comptroller General.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, DEA amends 21 CFR part 1308 as follows:

PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES

■ 1. The authority citation for 21 CFR part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), 956(b), unless otherwise noted.

■ 2. Amend § 1308.14 by:
■ a. Redesignating paragraphs (c)(30) through (c)(56) as (c)(31) through (c)(57); and
■ b. Adding new paragraph (c)(30).

The addition reads as follows:

§ 1308.14 Schedule IV.

* * * * *

(c) * * *

(30) Lemborexant	2245

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Uttam Dhillon,

Acting Administrator.

[FR Doc. 2020–07089 Filed 4–6–20; 8:45 am]

BILLING CODE 4410–09–P

[6] Office of Mgmt. & Budget, Exec. Office of The President, Interim Guidance Implementing Section 2 of the Executive Order of January 30, 2017 Titled "Reducing Regulation and Controlling Regulatory Costs" (Feb. 2, 2017).

DEPARTMENT OF LABOR

Mine Safety and Health Administration

30 CFR Parts 56 and 57

[Docket No. MSHA–2019–0007]

RIN 1219–AB88

Electronic Detonators

AGENCY: Mine Safety and Health Administration, Labor.

ACTION: Direct final rule; confirmation of effective date.

SUMMARY: The Mine Safety and Health Administration (MSHA) confirms the effective date for the direct final rule, Electronic Detonators, which was published on January 14, 2020, to revise certain safety standards for explosives at metal and nonmetal mines.

DATES: The effective date of the final rule published in the **Federal Register**

South Carolina Board of Health and Environmental Control
Final Review Conference
April 9, 2020

Final Review Conference - Docket No. 20-RFR-10, Coastal Timber Co. Dam (D3622) - Hazard Classification Change for Coastal Timber Co. Dam (D3622), Horry County

A Request for Final Review was filed on February 19, 2020.

Counsel of Record –
Nate Haber for SCDHEC

Other Parties –
Wendell Norris, Requestor/Dam Owner