

DEPARTMENT OF JUSTICE**Drug Enforcement Administration****21 CFR Part 1308**

[Docket No. DEA-325P]

Schedules of Controlled Substances: Placement of Lacosamide into Schedule V

AGENCY: Drug Enforcement Administration, Department of Justice.
ACTION: Notice of proposed rulemaking.

SUMMARY: This proposed rule is issued by the Deputy Administrator of the Drug Enforcement Administration (DEA) to place the substance lacosamide [(R)-2-acetoamido-N-benzyl-3-methoxypropionamide] and all products containing lacosamide into Schedule V of the Controlled Substances Act (CSA). This proposed action is based on a recommendation from the Acting Assistant Secretary for Health of the Department of Health and Human Services (DHHS) and on an evaluation of the relevant data by DEA. If finalized as proposed, this action will impose the regulatory controls and criminal sanctions applicable to Schedule V non-narcotics on those who handle lacosamide and products containing lacosamide.

DATES: Written comments must be postmarked, and electronic comments must be sent, on or before April 9, 2009. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after midnight Eastern time on the last day of the comment period.

ADDRESSES: To ensure proper handling of comments, please reference "Docket No. DEA-325" on all written and electronic correspondence. Written comments being sent via regular or express mail should be sent to the Drug Enforcement Administration, Attention: DEA Federal Register Representative/ODL, 8701 Morrisette Drive, Springfield, VA 22152. Comments may be sent to DEA by sending an electronic message to dea.diversion.policy@usdoj.gov. Comments may also be sent electronically through <http://www.regulations.gov> using the electronic comment form provided on that site. An electronic copy of this document is also available at the <http://www.regulations.gov> Web site. DEA will accept electronic comments containing MS Word, WordPerfect, Adobe PDF, or Excel file formats only. DEA will not accept any file format other than those specifically listed here.

Please note that DEA is requesting that electronic comments be submitted before midnight Eastern time on the day the comment period closes because <http://www.regulations.gov> terminates the public's ability to submit comments at midnight Eastern time on the day the comment period closes. Commenters in time zones other than Eastern time may want to consider this so that their electronic comments are received. All comments sent via regular or express mail will be considered timely if postmarked on the day the comment period closes.

FOR FURTHER INFORMATION CONTACT: Christine A. Sannerud, Ph.D., Chief, Drug and Chemical Evaluation Section, Office of Diversion Control, Drug Enforcement Administration, 8701 Morrisette Drive, Springfield, VA 22152 or by phone at (202) 307-7183.

SUPPLEMENTARY INFORMATION: *Posting of Public Comments:* Please note that all comments received are considered part of the public record and made available for public inspection online at <http://www.regulations.gov> and in the Drug Enforcement Administration's public docket. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter.

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 posted online or made available in the public docket, you must include the phrase "PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all the personal identifying information you do not want posted online or made available in the public docket 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 posted online or made available in the public docket, you must include the phrase "CONFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify confidential business information to be redacted within the comment. If a comment has so much confidential business information that it cannot be effectively redacted, all or part of that comment may not be posted online or made available in the public docket.

Personal identifying information and confidential business information identified and located as set forth above will be redacted and the comment, in redacted form, will be posted online and

placed in the DEA's public docket file. Please note that the Freedom of Information Act applies to all comments received. If you wish to inspect the agency's public docket file in person by appointment, please see the **FOR FURTHER INFORMATION CONTACT** paragraph.

Note Regarding This Scheduling Action

In accordance with the provisions of the CSA (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 (5 U.S.C. 556 and 557). Interested persons are invited to submit their comments, objections or requests for a hearing with regard to this proposal. Requests for a hearing should be made in accordance with 21 CFR 1308.44 and should state, with particularity, the issues concerning which the person desires to be heard. All correspondence regarding this matter should be submitted to the DEA using the address information provided above.

Background

Lacosamide, known chemically as (R)-2-acetoamido-N-benzyl-3-methoxypropionamide, is a central nervous system depressant drug with a mechanism of action different from those of other central nervous system depressants (e.g. benzodiazepines, barbiturates etc.) that are controlled under the CSA. Unlike other depressant drugs (benzodiazepines, barbiturates etc.), lacosamide does not act on the gamma amino butyric acid (GABA) system and does not have biologically significant affinity at numerous receptors, channels and transporters that are associated with known drugs of abuse. Although the precise mechanism of action of lacosamide remains undetermined, in vitro studies suggest that it causes selective enhancement of slow inactivation of voltage-gated sodium channels and binds to the collapsing response mediator protein 2 (CRMP-2).

On October 28, 2008, the Food and Drug Administration (FDA) approved lacosamide [(R)-2-acetoamido-N-benzyl-3-methoxypropionamide] for marketing under the trade name Vimpat® for use as an adjunctive therapy in treatment of partial-onset seizures in patients with epilepsy aged 17 years and older.

Animal studies have demonstrated that lacosamide protects against seizures in various anticonvulsant models and produces antinociceptive effects in preclinical neuropathic pain models. Animal studies also indicate that

lacosamide has abuse potential. Lacosamide produces dose dependent sedative-type behaviors in rats. In drug discrimination tests, Schedule IV drugs, alprazolam and phenobarbital, partially generalizes to lacosamide in rats trained to recognize lacosamide.

Clinical studies also indicate that lacosamide has abuse potential. In a clinical study with recreational abusers of sedative hypnotic drugs, lacosamide, similar to alprazolam, produced subjective responses of "sedation," "high," "euphoria," "drug liking," and "good drug effects" similar to alprazolam. These effects of lacosamide were shorter in duration as compared to those of alprazolam. In clinical pharmacokinetic and electrocardiographic studies, healthy subjects reported a high rate of euphoria-type responses following lacosamide administration, suggesting its ability to produce psychological dependence. The data from animal and human studies indicate that chronic administration of lacosamide does not produce physical dependence, as there were no withdrawal symptoms upon its discontinuation.

Adverse events from clinical studies included cognitive disorder, disturbance in attention, mood alteration, depressed mood, irritability, feeling drunk, memory impairment, somnolence, and dizziness. These and other data indicate that public health risks of lacosamide are similar, but in a lower intensity and shorter duration, to those of other sedative hypnotics and central nervous system depressants, such as benzodiazepines.

Lacosamide is a new molecular entity and has not been marketed in the United States. As such, there has been no evidence of diversion, abuse, and law enforcement encounters involving lacosamide.

On December 2, 2008, the Assistant Secretary for Health of the DHHS sent the Administrator of the DEA a scientific and medical evaluation and a letter recommending that lacosamide be placed into Schedule V of the CSA. Enclosed with the December 2, 2008 letter was a document prepared by the FDA entitled, "Basis for the Recommendation for Control of Lacosamide in Schedule V of the Controlled Substances Act (CSA)." The document contained a review of the factors which the CSA requires the Secretary to consider (21 U.S.C. 811(b)).

The factors considered by the Acting Assistant Secretary of Health and DEA with respect to lacosamide were:

1. Its actual or relative potential for abuse;

2. Scientific evidence of its pharmacological effects;

3. The state of current scientific knowledge regarding the drug;

4. Its history and current pattern of abuse;

5. The scope, duration, and significance of abuse;

6. What, if any, risk there is to the public health;

7. Its psychic or physiological dependence liability; and

8. Whether the substance is an immediate precursor of a substance already controlled under this subchapter. (21 U.S.C. 811(c))

Based on the recommendation of the Acting Assistant Secretary for Health, DHHS, received in accordance with § 201(b) of the Act (21 U.S.C. 811(b)), and the independent review of the available data by the DEA, the Deputy Administrator of the DEA, pursuant to §§ 201(a) and 201(b) of the Act (21 U.S.C. 811(a) and 811(b)), finds that:

1. Lacosamide has a low potential for abuse relative to the drugs or other substances in Schedule IV;

2. Lacosamide has a currently accepted medical use in treatment in the United States; and

3. Abuse of lacosamide may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in Schedule IV.

Based on these findings, the Deputy Administrator of the DEA concludes that lacosamide and all products containing lacosamide, warrant control in Schedule V of the CSA.

Interested persons are invited to submit their comments, objections or requests for a hearing with regard to this proposal. Requests for a hearing should state, with particularity, the issues concerning which the person desires to be heard. All correspondence regarding this matter should be submitted to the DEA using the address information provided above. In the event that comments, objections, or requests for a hearing raise one or more issues which the Deputy Administrator finds warrant a hearing, the Deputy Administrator shall order a public hearing by notice in the **Federal Register**, summarizing the issues to be heard and setting the time for the hearing.

Requirements for Handling Lacosamide

If this rule is finalized as proposed, lacosamide and all products containing lacosamide would be subject to the CSA and the Controlled Substances Import and Export Act (CSIEA) regulatory controls and administrative, civil and criminal sanctions applicable to the manufacture, distribution, dispensing,

importing, and exporting of a Schedule V controlled substance, including the following:

Registration. Any person who manufactures, distributes, dispenses, imports, exports, engages in research or conducts instructional activities with lacosamide, or who desires to manufacture, distribute, dispense, import, export, engage in instructional activities or conduct research with lacosamide, would need to be registered to conduct such activities in accordance with Part 1301 of Title 21 of the Code of Federal Regulations (CFR).

Security. Lacosamide would be subject to Schedule III–V security requirements and must be manufactured, distributed and stored in accordance with §§ 1301.71, 1301.72(b), (c), and (d), 1301.73, 1301.74, 1301.75(b) and (c), 1301.76, and 1301.77 of Title 21 of the CFR.

Labeling and Packaging. All labels and labeling for commercial containers of lacosamide which are distributed on or after finalization of this rule would need to comply with requirements of §§ 1302.03–1302.07 of Title 21 of the CFR.

Inventory. Every registrant required to keep records and who possesses any quantity of lacosamide would be required to keep an inventory of all stocks of lacosamide on hand pursuant to §§ 1304.03, 1304.04 and 1304.11 of Title 21 of the CFR. Every registrant who desires registration in Schedule V for lacosamide would be required to conduct an inventory of all stocks of the substance on hand at the time of registration.

Records. All registrants would be required to keep records pursuant to §§ 1304.03, 1304.04, 1304.21, 1304.22, and 1304.23 of Title 21 of the CFR.

Prescriptions. All prescriptions for lacosamide or prescriptions for products containing lacosamide would be required to be issued pursuant to 21 CFR 1306.03–1306.06 and 1306.21, 1306.23–1306.27.

Importation and Exportation. All importation and exportation of lacosamide would need to be in compliance with part 1312 of Title 21 of the CFR.

Criminal Liability. Any activity with lacosamide not authorized by, or in violation of, the CSA or the CSIEA occurring on or after finalization of this proposed rule would be unlawful.

Regulatory Certifications

Executive Order 12866

In accordance with the provisions of the CSA (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 5 U.S.C. 556 and 557 and, as such, are exempt from review by the Office of Management and Budget pursuant to Executive Order 12866, § 3(d)(1).

Regulatory Flexibility Act

The Deputy Administrator, in accordance with the Regulatory Flexibility Act (5 U.S.C. 601–612), has reviewed this proposed rule and by approving it certifies that it will not have a significant economic impact on a substantial number of small entities. Lacosamide products will be prescription drugs used for the treatment of partial-onset seizures. Handlers of lacosamide often handle other controlled substances used in the treatment of central nervous system disorders which are already subject to the regulatory requirements of the CSA.

Executive Order 12988

This regulation meets the applicable standards set forth in §§ 3(a) and 3(b)(2) of Executive Order 12988 Civil Justice Reform.

Executive Order 13132

This rulemaking does not preempt or modify any provision of state law; nor does it impose enforcement responsibilities on any state; nor does it diminish the power of any state to enforce its own laws. Accordingly, this rulemaking does not have federalism implications warranting the application of Executive Order 13132.

Unfunded Mandates Reform Act of 1995

This rule will not result in the expenditure by state, local, and tribal governments, in the aggregate, or by the private sector, of \$120,000,000 or more (adjusted for inflation) in any one year, and will not significantly or uniquely affect small governments. Therefore, no actions were deemed necessary under provisions of the Unfunded Mandates Reform Act of 1995.

Congressional Review Act

This rule is not a major rule as defined by § 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act). 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; 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.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Narcotics, Prescription drugs.

Under the authority vested in the Attorney General by § 201(a) of the CSA (21 U.S.C. 811(a)), and delegated to the Administrator of DEA by Department of Justice regulations (28 CFR 0.100), and redelegated to the Deputy Administrator pursuant to 28 CFR 0.104, the Deputy Administrator hereby proposes that 21 CFR part 1308 be amended 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) unless otherwise noted.

2. Section 1308.15 is amended by revising paragraph (e)(1) adding a new paragraph (e)(2) to read as follows:

§ 1308.15 Schedule V.

* * * * *

(e) * * *

- (1) Lacosamide [(R)-2-acetoamido-N-benzyl-3-methoxy-propionamide]—2746
- (2) Pregabalin [(S)-3-(aminomethyl)-5-methylhexanoic acid]—2782

Dated: February 26, 2009.

Michele M. Leonhart,

Deputy Administrator.

[FR Doc. E9–4890 Filed 3–9–09; 8:45 am]

BILLING CODE 4410–09–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

45 CFR Part 88

RIN 0991–AB49

Rescission of the Regulation Entitled “Ensuring That Department of Health and Human Services Funds Do Not Support Coercive or Discriminatory Policies or Practices in Violation of Federal Law”; Proposal

AGENCY: Office of the Secretary, HHS.

ACTION: Proposed rule.

SUMMARY: The Department of Health and Human Services proposes to rescind the December 19, 2008 final rule entitled “Ensuring That Department of Health and Human Services Funds Do Not Support Coercive or Discriminatory Policies or Practices in Violation of Federal Law.” The Department believes it is important to have an opportunity to review this regulation to ensure its consistency with current Administration policy and to reevaluate the necessity for regulations

implementing the Church Amendments, Section 245 of the Public Health Service Act, and the Weldon Amendment.

DATES: Submit written or electronic comment on the regulatory changes proposed by this document by April 9, 2009.

ADDRESSES: In commenting, please refer to “Rescission Proposal.” To better manage the comment process, we will not accept comments by facsimile (FAX) transmission.

You may submit comments in one of four ways (no duplicates, please):

1. *Electronically.* You may submit electronic comments on this regulation to <http://www.Regulations.gov> or via e-mail to proposedrescission@hhs.gov. To submit electronic comments to <http://www.Regulations.gov>, go to the Web site and click on the link “Comment or Submission” and enter the keywords “Rescission Proposal.” [Attachments should be in Microsoft Word, WordPerfect, or Excel; however, we prefer Microsoft Word.]

2. *By regular mail.* You may mail written comments (one original and two copies) to the following address only: Office of Public Health and Science, Department of Health and Human Services, Attention: Rescission Proposal Comments, Hubert H. Humphrey Building, 200 Independence Avenue, SW., Room 716G, Washington, DC 20201.

3. *By express or overnight mail.* You may send written comments (one original and two copies) to the following address only: Office of Public Health and Science, Department of Health and Human Services, Attention: Rescission Proposal Comments, Hubert H. Humphrey Building, 200 Independence Avenue, SW., Room 716G, Washington, DC 20201.

4. *By hand or courier.* If you prefer, you may deliver (by hand or courier) your written comments (one original and two copies) before the close of the comment period to the following address: Room 716G, Hubert H. Humphrey Building, 200 Independence Avenue, SW., Washington, DC 20201. (Because access to the interior of the Hubert H. Humphrey Building is not readily available to persons without federal government identification, commenters are encouraged to leave their comments in the mail drop slots located in the main lobby of the building. A stamp-in clock is available for persons wishing to retain proof of filing by stamping in and retaining an extra copy of the documents being filed.)

Inspection of Public Comments: All comments received before the close of