

et seq.; 22 U.S.C. 7210; E.O. 13026, 61 FR 58767, 3 CFR, 1996 Comp., p. 228; E.O. 13222, 66 FR 44025, 3 CFR, 2001 Comp., p. 783; Notice of August 7, 2015, 80 FR 48233 (August 11, 2015).

Supplement No. 1 to Part 774— [Amended]

■ 21. In Supplement No. 1 to Part 774 (the Commerce Control List), ECCN 1C981 is removed.

Dated: May 5, 2016.

Eric L. Hirschhorn,

Under Secretary for Industry and Security.

[FR Doc. 2016-11047 Filed 5-11-16; 8:45 am]

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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-435]

Schedules of Controlled Substances: Placement of Brivaracetam Into Schedule V

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Interim final rule, with request for comments.

SUMMARY: The Drug Enforcement Administration is placing the substance brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (also referred to as BRV; UCB-34714; Briviact) (including its salts) into schedule V of the Controlled Substances Act. This scheduling action is pursuant to the Controlled Substances Act, as revised by the Improving Regulatory Transparency for New Medical Therapies Act which was signed into law on November 25, 2015.

DATES: The effective date of this rulemaking is May 12, 2016. Interested persons may file written comments on this rulemaking in accordance with 21 CFR 1308.43(g). Electronic comments must be submitted, and written comments must be postmarked, on or before June 13, 2016. 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, defined at 21 CFR 1300.01 as those “adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811),” may file a request for hearing or waiver of hearing pursuant to 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 June 13, 2016.

ADDRESSES: To ensure proper handling of comments, please reference “Docket No. DEA-435” 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/ODW, 8701 Morrisette Drive, Springfield, VA 22152.

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

FOR FURTHER INFORMATION CONTACT:

Barbara J. Boockholdt, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrisette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

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 and Drug Enforcement Administration 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. In accordance with 21 CFR 1308.44(a)-

(c), requests for a hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing may be submitted only by interested persons, defined as those “adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811).” 21 CFR 1300.01. Requests for a hearing and notices of participation must conform to the requirements of 21 CFR 1308.44(a) or (b), as applicable, and include a statement of the interest of the person in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any waiver of an opportunity for a hearing must conform to the requirements of 21 CFR 1308.44(c) including a written statement regarding the interested person’s position on the matters of fact and law involved in any hearing.

Please note that pursuant to 21 U.S.C. 811(a), the purpose and subject matter of the hearing are restricted to “(A) find[ing] that such drug or other substance has a potential for abuse, and (B) mak[ing] with respect to such drug or other substance the findings prescribed by subsection (b) of section 812 of this title for the schedule in which such drug is to be placed. * * *” Requests for a hearing and waivers of participation in the hearing should be submitted to DEA using the address information provided above.

Legal Authority

The DEA implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended, 21 U.S.C. 801–971. Titles II and III are referred to as the “Controlled Substances Act” and the “Controlled Substances Import and Export Act,” respectively, and are collectively referred to as the “Controlled Substances Act” or the “CSA” for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, controlled substances are classified into one of five schedules based upon their potential for abuse, their currently accepted medical use in

treatment in the United States, and the degree of dependence the substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at 21 CFR part 1308.

Pursuant to 21 U.S.C. 811(a)(1), the Attorney General may, by rule, “add to such a schedule or transfer between such schedules any drug or other substance if he * * * finds that such drug or other substance has a potential for abuse, and * * * makes with respect to such drug or other substance the findings prescribed by subsection (b) of section 812 of this title for the schedule in which such drug is to be placed * * *” The Attorney General has delegated this scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

The CSA provides that scheduling of any drug or other substance may be initiated by the Attorney General (1) on her own motion; (2) at the request of the Secretary of Health and Human Services (HHS); or (3) on the petition of any interested party. 21 U.S.C. 811(a). This action imposes the regulatory controls and administrative, civil, and criminal sanctions of schedule V controlled substances for any person who handles or proposes to handle BRV.

The Improving Regulatory Transparency for New Medical Therapies Act (Pub. L. 114–89) was signed into law on November 25, 2015. This law amended 21 U.S.C. 811 and states that in cases where a new drug is (1) approved by the Department of Health and Human Services (HHS) and (2) HHS recommends control in CSA schedule II–V, DEA shall issue an interim final rule scheduling the drug, within 90 days.

The law further states that the 90-day timeframe starts the later of (1) the date DEA receives the HHS scientific and medical evaluation/scheduling recommendation or (2) the date DEA receives notice of drug approval by HHS. In addition, the law specifies that the rulemaking shall become immediately effective as an interim final rule without requiring the DEA to demonstrate good cause therefor.

Specifically, Public Law 114–89 revised section 201 of the CSA (21 U.S.C. 811) by inserting after subsection (i) a new paragraph (j), which requires that with respect to a drug referred to in subsection (f), if the Secretary recommends that the Attorney General control the drug in schedule II, III, IV, or V pursuant to subsections (a) and (b), the Attorney General is required to,

within 90 days, issue an interim final rule controlling the drug in accordance with such subsections and 21 U.S.C. 812(b) using the specified procedures. For purposes of calculating the 90 days, Public Law 114–89 states that such date shall be the later of the date on which the Attorney General receives the scientific and medical evaluation and the scheduling recommendation from the Secretary in accordance with subsection (b), or the date on which the Attorney General receives notification from the Secretary that the Secretary has approved an application under section 505(c), 512, or 571 of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act, or indexed a drug under section 572 of the Federal Food, Drug, and Cosmetic Act, with respect to the drug described in paragraph (1). Public Law 114–89 further stipulates that a rule issued by the Attorney General under paragraph (1) becomes immediately effective as an interim final rule without requiring the Attorney General to demonstrate good cause and requires that the interim final rule give interested persons the opportunity to comment and to request a hearing. After the conclusion of such proceedings, the Attorney General must issue a final rule in accordance with the scheduling criteria of subsections 21 U.S.C. 811(b), (c), and (d) of this section and 21 U.S.C. 812(b).

Background

Brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (also referred to as BRV; UCB–34714; Briviact) is a new molecular entity with central nervous system (CNS) depressant properties. BRV is known to be a high affinity ligand for the synaptic vesicle protein, SV2A, which is found on excitatory synapses in the brain. On November 22, 2014, UCB Inc. (Sponsor) submitted three New Drug Applications (NDAs) to the U.S. Food and Drug Administration (FDA) for the tablet, oral, and intravenous formulations of BRV. The FDA accepted the NDA filings for BRV on January 21, 2015.

On March 28, 2016 the DEA received notification that HHS/FDA approved BRV as an add-on treatment to other medications to treat partial onset seizures in patients age 16 years and older with epilepsy.

Determination to Schedule BRV

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 the HHS.¹ On September 8, 2015, the HHS provided the DEA with a scientific and medical evaluation document prepared by the FDA entitled "Basis for the Recommendation to Place Brivaracetam in Schedule V of the Controlled Substances Act." Pursuant to 21 U.S.C. 811(b), this document contained an eight-factor analysis of the abuse potential of BRV as a new drug, along with the HHS' recommendation to control BRV under schedule V of the CSA.

In response, in December 2015, the DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by the HHS, 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 BRV met the 21 U.S.C. 812(b)(5) criteria for placement in schedule V of the CSA. Subsequently, on March 28, 2016, the DEA received notification that HHS/FDA approved three NDAs for BRV (see Background section).

Pursuant to the provisions of the Improving Regulatory Transparency for New Medical Therapies Act (Pub. L. 114–89), and based on the HHS recommendation, NDA approvals by HHS/FDA, and DEA's determination, DEA is issuing this interim final rule to schedule brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (including its salts) as a controlled substance under the CSA.

Included below is a brief summary of each factor as analyzed by the HHS and the DEA, and as considered by the DEA in its scheduling action. Please note that both the 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-435." Full analysis of, and citations to, the information referenced in the summary may also be found in the supporting and related material.

1. The Drug's Actual or Relative Potential for Abuse: BRV is a new chemical entity and has not been marketed in the United States or in any other country; information on actual abuse of BRV is not available. The HHS characterized BRV as related in its

action to lacasamide and ezogabine, which are both schedule V CNS depressant anti-epileptics (AEDs). Based on data submitted by the Sponsor in their NDAs, the HHS indicated that administration of BRV in mice, rats, and dogs resulted in CNS depressant effects, including decreased locomotor activity and reactivity, motor incoordination, and ataxia.

BRV is not self-administered in animals and, unlike schedule IV benzodiazepines and the schedule III AED perampanel, lacks pentobarbital-like (schedule II) discriminative stimulus and reinforcing effects (HHS review, 2015). In humans, BRV is most similar to the schedule V AEDs lacasamide, ezogabine, and pregabalin in producing positive subjective effects without producing sedation and withdrawal following drug discontinuation that is observed with schedule IV benzodiazepines. Based on this collective evidence, the HHS concluded that BRV has an abuse potential that is most similar to AEDs in schedule V.

2. Scientific Evidence of the Drug's Pharmacological Effects, if Known: BRV selectively binds with high affinity to synaptic vesicle protein 2A (SV2A). It produces reverse inhibition caused by negative modulators of gamma aminobutyric acid (GABA) and glycine and inhibits sodium (Na⁺) channels. These sites appear to underlie pharmacological activity of BRV.

In rats, BRV at high doses partially generalizes to the schedule IV benzodiazepine chlordiazepoxide. BRV, across a wide range of doses, neither initiates nor maintains self-administration in rats trained to self-administer cocaine. Human studies have reported that healthy individuals may experience euphoria, sedation, and a drunken-like feeling following BRV administration. When treatment-emergent adverse events (TEAEs)² were pooled across several clinical BRV studies, the most common TEAEs were dizziness and sedative-related events such as fatigue, extreme drowsiness, and extreme weakness. In a human abuse potential study, the oral abuse potential, safety, tolerability, and pharmacokinetics of BRV (50 mg, 200 mg, and 1000 mg) were compared to 1.5 and 3.0 mg of the schedule IV CNS depressant alprazolam (ALP) and placebo. When surveyed, for all doses of

BRV, there was an increase of drug likability, feeling of a high, and taking the drug again in comparison to placebo. The HHS mentioned that individuals who took BRV had fewer sedative, euphoric, stimulant, dizziness, and overall negative subjective effects compared to ALP.

3. The State of Current Scientific Knowledge Regarding Brivaracetam: The chemical name for brivaracetam is (2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide. Other names include BRV and UCB-34714. The Chemical Abstract Services number (CAS #) of BRV is: 357336-20-0. BRV is a racetam derivative.³ As the HHS noted, BRV does not have structural similarities to any other scheduled AED or to any major classes of abused sedative drugs with noted euphoric effects. Chemical synthesis of BRV is considered highly complex and includes several steps, reagents and specialized equipment.

BRV is readily soluble in water at up to 700 mg/mL. In an *in vitro* oral tablet dissolution evaluation, BRV oral tablets were placed in a buffer (pH 6.4) for 16 hours. Approximately 86–96% of BRV was released after 16 hours in the buffer; 14–30% of BRV was released following 1 hour and 40–66% BRV was released after 4 hours.

Following oral ingestion, BRV is rapidly and completely absorbed. In healthy young males, the half-life of BRV was determined to be approximately 9 hours. According to the HHS, the half-life of BRV is decreased to 6 hours when a repeated oral dose of 800 mg/day BRV is administered. The HHS noted that BRV binds weakly to plasma proteins and is extensively metabolized through several pathways. Clearance through the kidneys represents 5–10% of the total clearance and only 3–7% of the parent compound (BRV) was detected in the urine. The three main metabolites of BRV were detected in urine and according to the HHS, these metabolites are relatively inactive. One BRV metabolite was characterized as having a potency that was 20 times less than BRV, and this metabolite was not detected in human plasma and represented less than 3% of the dose in urine.

4. Its History and Current Pattern of Abuse: As noted by the HHS, information on the history and current pattern of abuse of BRV is not available since this drug is currently not marketed in any country. A review of the animal and human data indicates that BRV has an abuse potential similar to other schedule V AEDs. If BRV were to be

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

² Treatment-emergent adverse event (TEAE): An event or unexpected medical occurrence (*e.g.* adverse event) which first appears during treatment with a drug or substance. TEAEs are typically absent prior to the onset of treatment or would have been exacerbated relative to pre-treatment conditions.

³ Racetams are a class of drugs that have a pyrrolidine center.

approved for medical use, the HHS indicated that BRV would be abused for its euphoric properties and other abuse-related TEAEs that were reported in human clinical studies. Based on the available information, the HHS concluded that the history and pattern of abuse of BRV will be similar to other schedule V CNS depressants.

5. *The Scope, Duration, and Significance of Abuse:* As noted by the HHS, information on the scope, duration, and significance of abuse of BRV is not available since this drug is currently not marketed in any country. Results from animal and human studies suggest that there is abuse potential associated with BRV and if marketed in the United States, it is likely that BRV will be abused similar to other AEDs that are CNS depressants. The HHS stated that it is unlikely that epileptic individuals (the population expected to take this drug) will abuse BRV. The HHS concluded that based on abuse potential similarities between BRV and other schedule V AEDs, it is likely that the scope, duration, and significance of abuse of BRV will be similar to these compounds.

6. *What, if any, Risk There is to the Public Health:* The HHS characterized BRV's drug abuse potential to be similar to schedule V AEDs. As such, the public health risk with BRV will also be similar to other schedule V AEDs. The HHS noted that if BRV were approved for medical use, it would be abused for its rewarding properties. In healthy volunteers administered 600 mg or higher of BRV, cognitive and motor impairment and sedation were observed. It is unknown how BRV would interact in combination with other CNS depressants and if the sedative effects would be additive or even a lethal combination. In an interaction study with BRV and intravenous ethanol in healthy individuals, it was determined that BRV enhanced the effects of ethanol.

7. *Its Psychic or Physiological Dependence Liability:* BRV has limited psychological dependence and does not appear to have physical dependence. When rats were administered BRV for 30 days, no signs of physical dependence were noted in comparison to the schedule IV comparator, chlordiazepoxide. Similarly, in human clinical studies with healthy volunteers, there were no reports or adverse events that noted physical dependence or a withdrawal syndrome associated with BRV use. The low potential for physical dependence observed with BRV is consistent with other schedule V AEDs. There is limited evidence for psychological dependence with BRV.

Clinical studies have reported individuals experiencing increasing euphoria with increasing doses of BRV. Tolerance does not appear to develop with respect to BRV treatment on epileptic seizure reduction.

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

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

Determination of Appropriate Schedule

The CSA outlines 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 the HHS and review of all available data, the Acting Administrator of the DEA, pursuant to 21 U.S.C. 812(b)(5), finds that:

1. BRV has a low potential for abuse relative to the drugs or other substances in schedule IV. The overall abuse potential of BRV is comparable to schedule V controlled substances such as ezogabalin, pregabalin, and lacosamide;

2. With FDA's approval of the new drug applications, BRV has a currently accepted medical use in the United States as adjunctive treatment of partial onset seizures in epileptic individuals ages 16 and older; and

3. Human and animal studies demonstrate that BRV has limited psychological dependence and does not appear to have physical dependence. There was no evidence of physical dependence associated with BRV in human and animal studies since there have been no reports of withdrawal syndromes or other physical dependence effects. Based on these data, abuse of BRV may lead to limited psychological dependence similar to schedule V AEDs but less than that of drugs in schedule IV.

Based on these findings, the Acting Administrator of the DEA concludes that brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (also referred to as BRV; UCB-34714; Briviact), including its salts, warrants control in schedule V of the CSA. 21 U.S.C. 812(b)(5).

Requirements for Handling Brivaracetam

BRV 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) BRV, or who desires to handle BRV, must be registered with the 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 BRV, and is not registered with the DEA, must submit an application for registration and may not continue to handle BRV, unless the 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 obtain a schedule V registration must surrender all quantities of currently held BRV, or may transfer all quantities of currently held BRV to a person registered with the DEA in accordance with 21 CFR part 1317, in addition to all other applicable federal, state, local, and tribal laws.

3. *Security.* BRV is subject to schedule III-V security requirements and must be handled and stored pursuant to 21 U.S.C. 821, 823, and 871(b), and in accordance with 21 CFR 1301.71-1301.93.

4. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of BRV 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 BRV must take an inventory of BRV 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 the DEA must take an initial inventory of all stocks of controlled substances (including BRV) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to 21 U.S.C. 827 and 958, 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 BRV) on hand every two years, pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

6. *Records and Reports.* Every DEA registrant must maintain records and submit reports for BRV, or products containing BRV, 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 BRV or products containing BRV must comply with 21 U.S.C. 829, and be issued in accordance with 21 CFR parts 1306 and 1311, subpart C.

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

9. *Liability.* Any activity involving BRV 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

Public Law 114–89 was signed into law, amending 21 U.S.C. 811. This amendment provides that in cases where a new drug is (1) approved by the Department of Health and Human Services (HHS) and (2) HHS recommends control in CSA schedule II–V, the 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 the DEA to demonstrate good cause. Therefore, the DEA has determined that the notice and comment requirements of section 553 of the APA, 5 U.S.C. 553, do not apply to this scheduling action.

Executive Orders 12866, Regulatory Planning and Review, and 13563, Improving Regulation and Regulatory Review

In accordance with Public Law 114–89, 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.

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

In accordance with 5 U.S.C. 603(a), “[w]henver an agency is required by [5 U.S.C. 553], or any other law, to publish general notice of proposed rulemaking for any proposed rule, or publishes a notice of proposed rulemaking for an interpretive rule involving the internal revenue laws of the United States, the agency shall prepare and make available for public comment an initial regulatory flexibility analysis.” As noted in the above discussion regarding applicability of the Administrative Procedure Act, the DEA has determined that the notice and comment requirements of section 553 of the APA, 5 U.S.C. 553, do not apply to this scheduling action. 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.*, the DEA has determined and certifies 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 for inflation) in any one 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 section 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act (CRA)). 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, the 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, the DEA amends 21 CFR part 1308:

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. Amend § 1308.15 by redesignating paragraphs (e)(1) through (e)(3) as paragraphs (e)(2) through (e)(4) and adding new paragraph (e)(1) to read as follows:

§ 1308.15 Schedule V.

* * * * *
(e) * * *

(1) Brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl]butanamide) (also referred to as BRV; UCB-34714; Briviact) (including its salts) 2710
* * * * *

Dated: May 6, 2016.

Chuck Rosenberg,

Acting Administrator.

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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-434F]

Schedules of Controlled Substances: Temporary Placement of Butyryl Fentanyl and Beta-Hydroxythiofentanyl Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final order.

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this final order to temporarily schedule the synthetic opioids, *N*-(1-phenethylpiperidin-4-yl)-*N*-phenylbutanamide, also known as *N*-(1-phenethylpiperidin-4-yl)-*N*-phenylbutanamide, (butyryl fentanyl) and *N*-[1-[2-hydroxy-2-(thiophen-2-yl)ethyl]piperidin-4-yl]-*N*-phenylpropionamide, also known as *N*-[1-[2-hydroxy-2-(2-thienyl)ethyl]-4-piperidinyl]-*N*-phenylpropanamide, (beta-hydroxythiofentanyl), and their isomers, esters, ethers, salts and salts of isomers, esters and ethers, into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of butyryl fentanyl and beta-hydroxythiofentanyl into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. As a result of this order, the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances will be imposed on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis, or possess), or propose to handle, butyryl fentanyl and beta-hydroxythiofentanyl.

DATES: This final order is effective on May 12, 2016.

FOR FURTHER INFORMATION CONTACT: Barbara J. Boockholdt, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrisette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended, 21 U.S.C. 801-971. Titles II and III are referred to as the “Controlled Substances Act” and the “Controlled Substances Import and Export Act,” respectively, and are collectively referred to as the “Controlled Substances Act” or the “CSA” for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while ensuring an adequate supply is available for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, every controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at 21 CFR part 1308.

Section 201 of the CSA, 21 U.S.C. 811, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she finds that such action is necessary to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, 21 U.S.C. 812, or if there is no exemption or approval in effect for the

substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. 21 U.S.C. 811(h)(1). The Attorney General has delegated her scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of his intention to temporarily place a substance into schedule I of the CSA.¹ The Administrator transmitted the notice of intent to place butyryl fentanyl and beta-hydroxythiofentanyl into schedule I on a temporary basis to the Assistant Secretary by letter dated December 21, 2015. The Assistant Secretary responded to this notice by letter dated January 13, 2016, and advised that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for butyryl fentanyl or beta-hydroxythiofentanyl. The Assistant Secretary also stated that the HHS has no objection to the temporary placement of butyryl fentanyl or beta-hydroxythiofentanyl into schedule I of the CSA. The DEA has taken into consideration the Assistant Secretary’s comments as required by 21 U.S.C. 811(h)(4). Neither butyryl fentanyl nor beta-hydroxythiofentanyl is currently listed in any schedule under the CSA, and no exemptions or approvals are in effect for butyryl fentanyl or beta-hydroxythiofentanyl under section 505 of the FDCA, 21 U.S.C. 355. The DEA has found that the control of butyryl fentanyl and beta-hydroxythiofentanyl in schedule I on a temporary basis is necessary to avoid an imminent hazard to public safety, and as required by 21 U.S.C. 811(h)(1)(A), a notice of intent to temporarily schedule butyryl fentanyl and beta-hydroxythiofentanyl was published in the **Federal Register** on March 23, 2016. 81 FR 15485.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the

¹ As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the 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 the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.