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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-415F]

Schedules of Controlled Substances: Removal of [¹²³I]Ioflupane from Schedule II of the Controlled Substances Act

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final rule.

SUMMARY: With the issuance of this final rule, the Administrator of the Drug Enforcement Administration removes [¹²³I]ioflupane from the schedules of the Controlled Substances Act. This action is pursuant to the Controlled Substances Act which requires that such actions be made on the record after an opportunity for a hearing through formal rulemaking. Prior to the effective date of this rule, [¹²³I]ioflupane was, by definition, a schedule II controlled substance because it is derived from cocaine via ecgonine, both of which are schedule II controlled substances. This action removes the regulatory controls and administrative, civil, and criminal sanctions applicable to controlled substances, including those specific to schedule II controlled substances, on persons who handle (manufacture, distribute, reverse distribute, dispense, conduct research, import, export, or conduct chemical analysis) or propose to handle

[¹²³I]ioflupane.

DATES: *Effective Date:* [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

FOR FURTHER INFORMATION CONTACT: John R. Scherbenske, 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, each 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 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 scheduled substances is published at 21 CFR part 1308.

Pursuant to 21 U.S.C. 811(a)(2), the Attorney General may, by rule, “remove any drug or other substance from the schedules if he finds that the drug or other substance does not meet the requirements for inclusion in any schedule.” The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA, 28 CFR 0.100.

The CSA provides that proceedings for the issuance, amendment, or repeal of the 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 the Department of Health and Human Services (HHS),¹ or (3) on the petition of any interested party. 21 U.S.C. 811(a). This action was initiated at the request of the Assistant Secretary for Health of the HHS, and is supported by, inter alia, a recommendation from the Assistant Secretary of the HHS and an evaluation of all relevant data by the DEA. This action removes the regulatory controls and administrative, civil, and criminal sanctions applicable to controlled substances, including those specific to schedule II controlled substances, on persons who handle or propose to handle [¹²³I]ioflupane.

Background

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.

[¹²³I]Ioflupane is, by definition, a schedule II controlled substance because it is derived from cocaine, a schedule II substance, via ecgonine (a schedule II substance). See 21 U.S.C. 812(c), Schedule II, (a)(4). [¹²³I]Ioflupane is the active pharmaceutical ingredient (API) in the drug product DaTscan and it is a new molecular entity. The Food and Drug Administration (FDA) approved the New Drug Application (NDA) for DaTscan on January 14, 2011, for the indication of visualizing striatal DATs in the brains of adult patients with suspected Parkinsonian syndromes (PS).

DEA and HHS Eight Factor Analyses

Pursuant to 21 U.S.C. 811(b), (c), and (f), the HHS recommended to the DEA on November 2, 2010, that FDA-approved products containing [¹²³I]ioflupane be removed from schedule II of the CSA. The HHS provided to DEA a scientific and medical evaluation document entitled “Basis for the Recommendation to Remove FDA Approved Products Containing [¹²³I]Ioflupane from Schedule II of the Controlled Substances Act (CSA).” Pursuant to 21 U.S.C. 811(b), this document contained an eight-factor analysis of FDA-approved products containing [¹²³I]ioflupane, along with the HHS’s recommendation to remove FDA-approved products containing [¹²³I]ioflupane from the schedules of the CSA. The HHS later clarified to DEA that its November 2, 2010, recommendation also supports the decontrol of the substance [¹²³I]ioflupane.²

In response, the DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by the HHS, and all other relevant data. The DEA and HHS collaborated further regarding the available information. In a letter dated February 2, 2015, the HHS provided detailed responses to specific inquiries from the DEA (submitted

² Letter from Karen B. DeSalvo, Acting Assistant Secretary for Health, HHS to John J. Riley, Acting Deputy Administrator, DEA (Aug. 19, 2015).

by letter dated September 16, 2014). Upon further review of all of the available information, the DEA completed its own eight-factor review document on FDA-approved diagnostic products containing [¹²³I]ioflupane (currently, only DaTscan) pursuant to 21 U.S.C. 811(c).

The FDA-approved diagnostic product, DaTscan, was used as the basis for the scientific and medical evaluation of FDA-approved products containing [¹²³I]ioflupane for both the HHS and DEA eight-factor analysis. Both the DEA and HHS analyses and other relevant documents are available in their entirety in the public docket of this rule (Docket Number DEA-415F) at <http://www.regulations.gov> under “Supporting and Related Material.”

Determination to Decontrol [¹²³I]ioflupane

After a review of the available data, including the scientific and medical evaluation and recommendation, the Administrator of the DEA published in the *Federal Register* a notice of proposed rulemaking (NPRM) entitled “Schedules of Controlled Substances: Removal of [¹²³I]ioflupane from Schedule II of the Controlled Substances Act” which proposed removal of [¹²³I]ioflupane from the schedules of the CSA. 80 FR 31521, June 3, 2015. The proposed rule provided an opportunity for interested persons to file a request for a hearing in accordance with DEA regulations by July 6, 2015.

No requests for such a hearing were received by the DEA. The NPRM also provided an opportunity for interested persons to submit written comments on the proposal on or before July 6, 2015.

Comments Received

The DEA received nine comments on the proposed rule to decontrol [¹²³I]ioflupane. All commenters supported the decontrol of [¹²³I]ioflupane.

Commenters in support of decontrolling [¹²³I]ioflupane included an international medical society for neurology; an association of industry members that manufacture radiopharmaceuticals; a professional organization representing radiologists, radiation oncologists, interventional radiologists, nuclear medicine physicians, and medical physicists; an advocacy group for the Parkinson's community; a trade association representing medical imaging, radiotherapy and radiopharmaceutical manufacturers; the sponsor of the drug product containing [¹²³I]ioflupane; a physician; a health services company; and a private citizen, all of whom expressed support for the DEA's proposal to decontrol [¹²³I]ioflupane. Some commenters also stated that the proposal would improve patient access to an important diagnostic pharmaceutical and reduce the burden on providers and nuclear pharmacies.

The DEA appreciates the comments in support of this rulemaking.

Effective Date of the Rule

Generally, DEA scheduling actions are effective 30 days from the date of publication of the final rule in the *Federal Register*. 21 CFR 1308.45; *see also* 5 U.S.C. 553(d). In this instance, and in accordance with 21 CFR 1308.45, the DEA finds that the conditions of public health or safety necessitate an earlier effective date, i.e., the date of publication in the *Federal Register*. An earlier effective date would allow specialized members of the healthcare community to readily utilize this substance as a component of an important diagnostic tool, DaTscan. DaTscan, which contains [¹²³I]ioflupane, is used in differentiating essential tremors from tremors due to PS, (idiopathic Parkinson's disease,

multiple system atrophy, and progressive supranuclear palsy), and can help healthcare professionals provide more accurate diagnoses. This earlier effective date will allow patients to receive, without delay, important diagnostic testing that is critical to their health and treatment. These findings, coupled with the fact that this is an action for decontrol, indicate that conditions of public health necessitate an immediate effective date upon publication in the *Federal Register*.

The DEA also notes that its decision to make this rule effective upon publication aligns with the exceptions to the 30-day effective date requirement of the Administrative Procedure Act (APA). One of the APA's exceptions to the 30-day effective date is for a substantive rule granting or recognizing an exemption or which relieves a restriction. 5 U.S.C. 553(d)(3).

Scheduling Conclusion

Based on consideration of all comments, the scientific and medical evaluation and accompanying recommendation and clarification from the HHS, and based on the DEA's consideration of its own eight-factor analysis, the Administrator finds that these facts and all relevant data demonstrate that [¹²³I]ioflupane does not meet the requirements for inclusion in any schedule, and will be removed from control under the CSA.

Regulatory Analyses

Executive Orders 12866 and 15363

In accordance with 21 U.S.C. 811(a), this scheduling action is subject to formal rulemaking procedures done "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 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

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

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 Federal Government and the States, or the distribution of power and responsibilities among the various levels of government.

Executive Order 13175

This rule does not have tribal implications warranting the application of Executive Order 13175. This rule 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 Administrator, in accordance with the Regulatory Flexibility Act (5 U.S.C. 601-612) (RFA), has reviewed this rule and by approving it certifies that it will not have a significant economic impact on a substantial number of small entities. The purpose of this rule is to remove [¹²³I]ioflupane from the list of schedules of the CSA. This action

removes regulatory controls and administrative, civil, and criminal sanctions applicable to controlled substances for handlers and proposed handlers of [¹²³I]ioflupane.

Accordingly, it has the potential for some economic impact in the form of cost savings.

This rule will affect all persons who handle, or propose to handle, [¹²³I]ioflupane. Due to the wide variety of unidentifiable and unquantifiable variables that potentially could influence the distribution and administration rates of radiopharmaceutical substances, the DEA is unable to determine the number of entities and small entities which might handle [¹²³I]ioflupane. In other instances where a controlled pharmaceutical drug is removed from the schedules of the CSA, the DEA is able to quantify the estimated number of affected entities and small entities because the handling of the drug is expected to be limited to DEA registrants even after removal from the schedules. In such instances, the DEA's knowledge of its registrant population forms the basis for estimating the number of affected entities and small entities. However, [¹²³I]ioflupane is expected to be handled by persons who hold DEA registrations regardless of whether this rule is promulgated (e.g., hospital radiopharmacies) and by persons who are not currently registered with the DEA to handle controlled substances (e.g., diagnostic clinics and imaging centers that do not routinely handle controlled substances). The DEA does not have a reliable basis to estimate the number of non-registrants who plan to handle [¹²³I]ioflupane.

Although the DEA does not have a reliable basis to estimate the number of affected entities and quantify the economic impact of this final rule, a qualitative analysis indicates that this rule is likely to result in some cost savings for the healthcare industry. The affected entities will continue to meet existing Federal and/or state requirements

applicable to those who handle radiopharmaceutical substances, including licensure, security, recordkeeping, and reporting requirements, which in many cases are more stringent than the DEA's requirements. However, the DEA believes cost savings will be realized from the removal of the administrative, civil, and criminal sanctions for those entities handling or proposing to handle [¹²³I]ioflupane, in the form of saved DEA registration fees, and the elimination of additional physical security, recordkeeping, and reporting requirements.

Because of these facts, this rule will not result in a significant economic impact on a substantial number of small entities.

Unfunded Mandates Reform Act of 1995

The DEA has determined and certifies pursuant to the Unfunded Mandates Reform Act of 1995 (UMRA), 2 U.S.C. 1501 *et seq.*, 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 provisions of UMRA.

Paperwork Reduction Act

This action does not impose a new collection of information requirement under the Paperwork Reduction Act, 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 United States-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 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, 21 CFR part 1308 is amended to read 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. In § 1308.12, revise paragraph (b)(4) to read as follows:

§ 1308.12 Schedule II.

* * * * *

(b) * * *

(4) Coca leaves (9040) and any salt, compound, derivative or preparation of coca

leaves (including cocaine (9041) and ecgonine (9180) and their salts, isomers, derivatives and salts of isomers and derivatives), and any salt, compound, derivative, or preparation thereof which is chemically equivalent or identical with any of these substances, except that the substances shall not include:

- (i) Decocainized coca leaves or extraction of coca leaves, which extractions do not contain cocaine or ecgonine; or
- (ii) [¹²³I]ioflupane.

* * * * *

Dated: September 4, 2015.

Chuck Rosenberg,
Acting Administrator.

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