



DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-1143]

Schedules of Controlled Substances: Placement of *N*-Desethyl Isotonitazene and *N*-Piperidinyl Etonitazene in Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final amendment; final order.

SUMMARY: With the issuance of this final order, the Administrator of the Drug Enforcement Administration is permanently placing *N*-ethyl-2-(2-(4-isopropoxybenzyl)-5-nitro-1*H*-benzimidazol-1-yl)ethan-1-amine (other name: *N*-desethyl isotonitazene) and 2-(4-ethoxybenzyl)-5-nitro-1-(2-(piperidin-1-yl)ethyl)-1*H*-benzimidazole (other names: *N*-piperidinyl etonitazene; etonitazepipne), including their isomers, esters, ethers, salts, and salts of isomers, esters, and ethers whenever the existence of such isomers, esters, ethers, and salts are possible within the specific chemical designation, in schedule I under the Controlled Substances Act. This scheduling action discharges the United States' obligations under the Single Convention on Narcotic Drugs (1961). This action imposes permanent regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, import, export, engage in research or conduct instructional activities with or possess), or handle *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene.

DATES: Effective [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: 8701 Morrisette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Dr. Terrence L. Boos, Drug and Chemical Evaluation Section, Diversion Control Division, Drug Enforcement Administration; Telephone: (571) 362-3249.

SUPPLEMENTARY INFORMATION:

Legal Authority

The United States is a party to the United Nations Single Convention on Narcotic Drugs, Mar. 30, 1961, 18 U.S.T. 1407, 520 U.N.T.S. 151 (Single Convention), as amended by the 1972 Protocol. Article 3, paragraph 7 of the Single Convention requires that if the Commission on Narcotic Drugs (Commission) adds a substance to one of the schedules of such Convention, and the United States receives notification of such scheduling decision from the Secretary-General of the United Nations (Secretary-General), the United States, as a signatory Member State, is obligated to control the substance under its national drug control legislation. Under 21 U.S.C. 811(d)(1) of the Controlled Substances Act (CSA), if control of a substance is required “by United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970,” the Attorney General must issue an order controlling such drug under the schedule she deems most appropriate to carry out such obligations, without regard to the findings required by 21 U.S.C. 811(a) or 812(b), and without regard to the procedures prescribed by 21 U.S.C. 811(a) and (b). The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the Drug Enforcement Administration (DEA).¹

Background

On July 29, 2024, DEA issued a temporary scheduling order, placing *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene temporarily in schedule I of the CSA.² That order

¹ 28 CFR 0.100.

² *Schedules of Controlled Substances: Temporary Placement of N-desethyl isotonitazene and N-piperidinyl etonitazene in Schedule I*, 89 FR 60817 (July 29, 2024).

for *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene (codified at 21 CFR 1308.11(h)(68) and (69)) was based on findings by the then-Administrator that the temporary scheduling was necessary to avoid an imminent hazard to public safety.³

On November 21, 2024, the Director-General of the World Health Organization recommended to the Secretary-General that *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene be placed in Schedule I of the Single Convention, as these substances have pharmacological effects similar to other opioid drugs that are controlled in Schedule I of the Single Convention. On June 9, 2025, the Secretariat of the United Nations informed the United States Government, by letter, that the Commission voted to place *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene in Schedule I of the Single Convention during its 68th session on March 12, 2025 (CND Mar 68/4 and 68/3).

***N*-Desethyl Isotonitazene and *N*-Piperidinyl Etonitazene**

N-Desethyl isotonitazene and *N*-piperidinyl etonitazene are temporarily controlled in schedule I of the CSA because they pose imminent hazard to the public safety. Both *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene belong to the benzimidazole-opioid drug class, similar to etonitazene and isotonitazene. Substances of the benzimidazole-opioid drug class share similar pharmacological profile with other opioids such as morphine and fentanyl. *N*-Desethyl isotonitazene and *N*-piperidinyl etonitazene, similar to morphine and fentanyl, act as mu-opioid receptor agonists. Adverse health effects have been associated with the abuse of these benzimidazole-opioids. The abuse of *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene has been associated with several toxicology cases in the United States and in Europe. Several substances belonging to the benzimidazole-opioid drug class have been controlled in the United States, and as a class of drug in China, Canada, and the United Kingdom. The appearance of benzimidazole-opioids on the illicit drug market is similar to other synthetic opioids that are trafficked and abused for their psychoactive effects.

³ *Id*

Law enforcement reports demonstrate that *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene are being illicitly distributed and abused. According to the National Forensic Laboratory Information System (NFLIS-Drug)⁴ database, which collects drug identification results from drug cases submitted to and analyzed by Federal, State and local forensic laboratories, there have been 151 reports for *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene between January 2022 and July 2025 (query date: July 17, 2025). Benzimidazole-opioids have been identified in counterfeit prescription tablets in the United States and other countries, including Sweden and the United Kingdom. The identification of these substances in counterfeit prescription drug products is of significant concern due to benzimidazole-opioids high potency.

N-Desethyl isotonitazene and *N*-piperidinyl etonitazene have no currently accepted medical use in treatment in the United States. The Department of Health and Human Services (HHS) advised DEA, by letter dated May 11, 2023, that based on a review by the Food and Drug Administration (FDA), there were no investigational new drug applications (IND) or approved new drug applications (NDA) for *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene in the United States. Since this letter, HHS has not advised DEA of any new IND or NDA for these substances. Because *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene are not formulated or available for clinical use as approved medicinal products, all current use of these substances by individuals is based on their own initiative, rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs.

Consistent with 21 U.S.C. 811(d)(1), DEA concludes that *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene have no currently accepted medical use in treatment in the United

⁴ NFLIS-Drug represents an important resource in monitoring illicit drug trafficking, including the diversion of legally manufactured pharmaceuticals into illegal markets. NFLIS-Drug is a comprehensive information system that includes data from forensic laboratories that handle more than 96 percent of an estimated 1 million distinct annual federal, state, and local drug analysis cases. NFLIS-Drug includes drug chemistry results from completed analyses only. While NFLIS-Drug data are not direct evidence of abuse, these can lead to an inference that a drug has been diverted and abused. See *Schedules of Controlled Substances: Placement of Carisoprodol Into Schedule IV*, 76 FR 77330, 77332 (Dec. 12, 2011).

States⁵ and are most appropriately placed permanently in schedule I of the CSA, the same schedule in which they temporarily reside at present. Because control is required under the Single Convention, DEA will not be initiating regular rulemaking proceedings to permanently schedule *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene pursuant to 21 U.S.C.811(a).

Conclusion

In order to meet the United States' obligation under the Single Convention and because *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene have no currently accepted medical use in treatment in the United States, the Administrator has determined that *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene including their isomers, esters, ethers, salts, and salts of isomers, esters, and ethers, whenever the existence of such isomers, esters, and salts are possible within the specific existence of such isomers, esters, ethers, and salts are possible within the specific chemical designation, should be placed permanently in schedule I of the CSA.

Requirements for Handling

As discussed above, *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene have been temporarily controlled in schedule I of the CSA since July 29, 2024. Upon the effective date of

⁵ There is no evidence suggesting that *N*-desethyl isotonitazene or *N*-piperidinyl etonitazene have a currently accepted medical use in treatment in the United States. To determine whether a drug or other substance has a currently accepted medical use, DEA has traditionally applied a five-part test to a drug or substance that has not been approved by the FDA: i. The drug's chemistry must be known and reproducible; ii. there must be adequate safety studies; iii. there must be adequate and well-controlled studies proving efficacy; iv. the drug must be accepted by qualified experts; and v. the scientific evidence must be widely available. *See Marijuana Scheduling Petition; Denial of Petition; Remand*, 57 FR 10499 (Mar. 26, 1992), pet. for rev. denied, *Alliance for Cannabis Therapeutics v. Drug Enforcement Admin.*, 15 F.3d 1131, 1135 (D.C. Cir. 1994). DEA applied the traditional five-part test and concluded the test was not satisfied. In a recent published letter in a different context, HHS applied an additional two-part test to determine currently accepted medical use for substances that do not satisfy the five-part test: (1) whether there exists widespread, current experience with medical use of the substance by licensed health care providers operating in accordance with implemented jurisdiction-authorized programs, where medical use is recognized by entities that regulate the practice of medicine, and, if so, (2) whether there exists some credible scientific support for at least one of the medical conditions for which part (1) is satisfied. On April 11, 2024, the Department of Justice's Office of Legal Counsel (OLC) issued an opinion, which, among other things, concluded that HHS's two-part test would be sufficient to establish that a drug has a currently accepted medical use. Office of Legal Counsel, Memorandum for Merrick B. Garland Attorney General Re: Questions Related to the Potential Rescheduling of Marijuana at 3 (April 11, 2024). For purposes of this scheduling order, there is no evidence that health care providers have widespread experience with medical use of *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene or that the use of *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene are recognized by entities that regulate the practice of medicine, so the two-part test also is not satisfied. By letter dated May 11, 2023, DEA has been advised by HHS that there are currently no approved new drug applications or investigational new drug applications for *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene. Additionally, HHS communicated no objections to the temporary placement of *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene into schedule I of the CSA.

this final order, *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene will be permanently subject to the CSA's schedule I regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, dispensing, importing, exporting, engagement in research or conduct of instructional activities with, and possession of, schedule I controlled substances, including the following:

1. *Registration.* Any person who handles (manufactures, distributes, reverse distributes, imports, exports, engages in research or conducts instructional activities or chemical analysis with, or possesses), or who desires to handle, *N*-desethyl isotonitazene or *N*-piperidinyl etonitazene 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. Retail sales of schedule I controlled substances to the general public are not allowed under the CSA. Possession of any quantity of these substances in a manner not authorized by the CSA is unlawful and those in possession of any quantity of these substances may be subject to prosecution pursuant to the CSA.

2. *Disposal of stocks.* *N*-Desethyl isotonitazene and *N*-piperidinyl etonitazene must be disposed of in accordance with 21 CFR part 1317, in addition to all other applicable federal, state, local, and tribal laws.

3. *Security.* *N*-Desethyl isotonitazene and *N*-piperidinyl etonitazene are subject to schedule I security requirements and must be handled and stored pursuant to 21 U.S.C. 821, 823, and in accordance with 21 CFR 1301.71 through 1301.76. Non-practitioners handling *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene must comply with the screening requirements of 21 CFR 1301.90 through 1301.93.

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

5. *Quota.* Only registered manufacturers are permitted to manufacture *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene in accordance with a quota assigned pursuant to 21 U.S.C. 826, and in accordance with 21 CFR part 1303.

6. *Inventory.* Any person registered with DEA to handle *N*-desethyl isotonitazene or *N*-piperidinyl etonitazene must have an initial inventory of all stocks of controlled substances (including these substances) 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 *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene) 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.

7. *Records and Reports.* Every DEA registrant must maintain records and submit reports with respect to *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR 1301.74(b) and (c), 1301.76(b), and 1307.11 and parts 1304, 1312, and 1317. Manufacturers and distributors must submit reports regarding *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene to the Automation of Reports and Consolidated Order System pursuant to 21 U.S.C. 827 and in accordance with 21 CFR parts 1304 and 1312.

8. *Order Forms.* Every DEA registrant who distributes *N*-desethyl isotonitazene or *N*-piperidinyl etonitazene must continue to comply with order form requirements pursuant to 21 U.S.C. 828 and in accordance with 21 CFR part 1305.

9. *Importation and Exportation.* All importation and exportation of *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene must continue to comply with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

10. *Liability.* Any activity involving *N*-desethyl isotonitazene or *N*-piperidinyl etonitazene 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

Executive Orders 12866, 13563, 14192, and 14294

This action is not a significant regulatory action as defined by Executive Order (E.O.) 12866 (Regulatory Planning and Review), and the principles reaffirmed in E.O. 13563 (Improving Regulation and Regulatory Review). DEA scheduling actions are not subject to E.O. 14192, Unleashing Prosperity Through Deregulations, or E.O. 14294, Fighting Overcriminalization in Federal Regulations. This action makes no change in the status quo, as *N*-desethyl isotonitazene and *N*-piperidinyl etonitazene are already listed as schedule I controlled substances.

Executive Order 12988, Civil Justice Reform

This action meets the applicable standards set forth in sections 3(a) and 3(b)(2) of E.O. 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 action does not have federalism implications warranting the application of E.O. 13132. This action 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 action does not have tribal implications warranting the application of E.O. 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.

Administrative Procedure Act

The CSA provides for an expedited scheduling action where control is required by the United States' obligations under international treaties, conventions, or protocols.⁶ If control is required pursuant to such international treaty, convention, or protocol, the Attorney General, as delegated to the Administrator, must issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations, and "without regard to" the findings and rulemaking procedures otherwise required for scheduling actions in 21 U.S.C. 811(a) and (b).

Id.

In accordance with 21 U.S.C. 811(d)(1), scheduling actions for drugs that are required to be controlled by the United States' obligations under international treaties, conventions, or protocols in effect on October 27, 1970, shall be issued by order, as opposed to scheduling by rule pursuant to 21 U.S.C. 811(a). Therefore, DEA believes that the notice-and-comment requirements of the Administrative Procedure Act (APA), 5 U.S.C. 553, do not apply to this scheduling action.

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 the APA or any other law. As explained above, the CSA exempts this final order from notice and comment. Consequently, the RFA does not apply to this action.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995.⁷ Also, this action does not impose new or modify existing recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. However, this action does require compliance with the following existing OMB collections: 1117-0003, 1117-0004, 1117-0006, 1117-0008, 1117-0009, 1117-0010, 1117-

⁶ 21 U.S.C. 811(d)(1).

⁷ 44 U.S.C. 3501-3521.

0012, 1117-0014, 1117-0021, 1117-0023, 1117-0029, and 1117-0056. 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.

Unfunded Mandates Reform Act of 1995

On the basis of information contained in the “Regulatory Flexibility Act” section above, DEA has determined pursuant to the Unfunded Mandates Reform Act (UMRA) of 1995 (2 U.S.C. 1501 *et seq.*) that this final rule 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.

Congressional Review Act

This order is not a major rule as defined by the Congressional Review Act (CRA), 5 U.S.C. 804. However, DEA is submitting reports under the CRA 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. In § 1308.11:

- a. Redesignate paragraphs (b)(76) through (117) as paragraphs (b)(78) through (119);
- b. Redesignate paragraphs (b)(72) through (75) as paragraphs (b)(73) through (76);
- c. Add new paragraphs (b)(72), (77); and
- h. Remove and reserve paragraphs (h)(68) and (h)(69).

The additions to read as follows:

§ 1308.11 Schedule I.

* * * * *

(b) * * *

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(72) <i>N</i> -Desethyl isotonitazene (<i>N</i> -ethyl-2-(2-(4-isopropoxybenzyl)-5-nitro-1 <i>H</i> -benzimidazol-1-yl)ethan-1-amine)	9760
* * * * *	
(77) <i>N</i> -Piperidinyl etonitazene (2-(4-ethoxybenzyl)-5-nitro-1-(2-(piperidin-1-yl)ethyl)-1 <i>H</i> -benzimidazole (other names: etonitazepipne)	9761
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SIGNING AUTHORITY

This document of the Drug Enforcement Administration was signed on December 17, 2025, by Administrator Terrance Cole. That document with the original signature and date is maintained by DEA. For administrative purposes only, and in compliance with requirements of the Office of the Federal Register, the undersigned DEA Federal Register Liaison Officer has been authorized to sign and submit the document in electronic format for publication, as an

official document of DEA. This administrative process in no way alters the legal effect of this document upon publication in the Federal Register.

Leslie Mayer
Federal Register Liaison Officer
Drug Enforcement Administration

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