



EU EARLY WARNING SYSTEM FORMAL NOTIFICATION

Date issued	29 May 2024	RCS ID	EU-EWS-RCS-FN-2024-0012
Issued by	EMCDDA	Transmitted by	Action on New Drugs Sector, EMCDDA
Subject	Formal notification of 2-[2-[(4-ethoxyphenyl)methyl]-5-nitro-benzimidazol-1-yl]- <i>N,N</i> -dimethyl-ethanamine (<i>N,N</i> -dimethyl etonitazene) by Latvia as a new psychoactive substance under the terms of Regulation (EC) No 1920/2006 and Council Framework Decision 2004/757/JHA		

1. Read me first

This document provides formal notification of the analytical identification of 2-[2-[(4-ethoxyphenyl)methyl]-5-nitro-benzimidazol-1-yl]-*N,N*-dimethyl-ethanamine (*N,N*-dimethyl etonitazene) for the first time in Europe.

Please report any additional data you have on this substance to: ews@emcdda.europa.eu

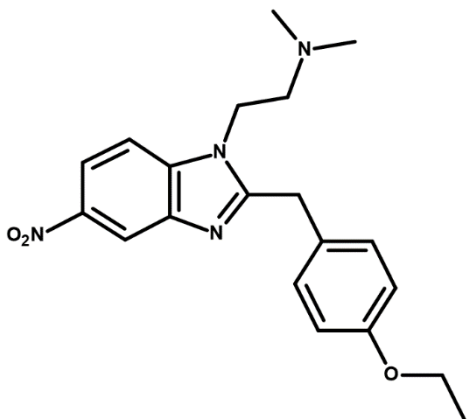
2. Data use restrictions

As with all formal notifications issued by the EU EWS remember that they may contain information that could be regarded as sensitive. Should you provide some of the information in this notification to other groups we would ask that you exercise your best judgment on what information needs to be provided. If you have any questions in this respect, please contact us.

3. Names of substance and other identifiers

- IUPAC name: 2-[2-[(4-ethoxyphenyl)methyl]-5-nitro-benzimidazol-1-yl]-*N,N*-dimethyl-ethanamine
- Chemical names: 2-[2-[(4-ethoxyphenyl)methyl]-5-nitrobenzimidazol-1-yl]-*N,N*-dimethylethanamine; 2-{2-[(4-ethoxyphenyl)methyl]-5-nitro-1*H*-1,3-benzimidazol-1-yl}-*N,N*-dimethylethan-1-amine; (2-(2-(4-ethoxybenzyl)-5-nitrobenzimidazol-1-yl)ethyl)dimethylamine; 2-[(4-ethoxyphenyl)methyl]-*N,N*-dimethyl-5-nitro-1*H*-benzimidazole-1-ethanamine
- Common name: *N,N*-dimethyl etonitazene
- Other names: etonitazene *N,N*-dimethyl analogue; 1-dimethylaminoethyl *N*-desalkyl etonitazene
- Chemical formula: $C_{20}H_{24}N_4O_3$
- Molecular weight: 368.43
- CAS Registry number: 714190-52-0 (base); 112658-05-6 (hydrochloride salt)
- InChIKey: MYLQWWDDZLNZULX-UHFFFAOYSA-N

Molecular structure



4. Substance classification

Opioid

5. Detection

Type: Seizure

Case Report identifier: [EDND-CR-2024-208](#)

Details: *N,N*-dimethyl etonitazene was identified in 2.04 grams of powder seized by Latvian Police in Riga, on 10 November 2023.

The substance was analytically confirmed used NMR and HRMS by the Latvian Institute of Organic Synthesis (OSI).

6. Chemistry and Analysis

Chemical classification: azacyclic; azole; benzimidazole

N,N-dimethyl etonitazene, a 5-nitro-2-benzylbenzimidazole which can also be known as etonitazene *N,N*-dimethyl analogue and 1-dimethylaminoethyl *N*-desalkyl etonitazene, is structurally related to the internationally controlled substance etonitazene (Schedule I of the 1961 United Nations Single Convention on Narcotic Drugs). *N,N*-dimethyl etonitazene differs from etonitazene due to the replacement of the *N,N*-diethyl moiety with an *N,N*-dimethyl moiety.

N,N-dimethyl etonitazene, *N*-desethyl Etonitazene, formally notified in December 2023, and 4'-hydroxy Nitazene (not currently monitored by the EMCDDA) [1] are structural isomers. The identification and discrimination of these isomers can pose analytical challenges due to the fact that these substances have the same molecular weight and similar fragmentation patterns. As a result, in addition to GC-MS, other analytical techniques, such as FTIR or NMR, may be required.

N,N-dimethyl etonitazene (*compound XXXVII*) was originally described by Hunger *et al.*, with a melting point range of 232-233 °C reported for the hydrochloride salt [2].

7. Pharmacology and toxicology

Pharmacological classification: opioid

Information on the pharmacology and toxicology of *N,N*-dimethyl etonitazene is limited. Based on its chemical structure and on its similarity to etonitazene, *N,N*-dimethyl etonitazene is expected to have opioid narcotic analgesic effects.

The antinociceptive potency of *N,N*-dimethyl etonitazene (*compound XXXVII*), relative to 5 mg/kg morphine upon subcutaneous administration in mice, is reported as 20 times that of morphine [2].

During the mid-1950s, attempts to develop better and safer opioid analgesics led to the discovery of a series of 2-benzylbenzimidazole compounds with levels of analgesic potency several orders of magnitude higher than that of morphine.

Similar to other types of opioid analgesics such as morphine and fentanyl, the 2-benzylbenzimidazole compounds activate the μ -opioid receptors in the central nervous system. It is expected that the effects of such compounds are likely to share similarities with fentanyl and other opioid analgesics. The acute effects include: euphoria, relaxation, analgesia (a reduced ability to feel pain), sedation (inducing a state of calm or sleep), bradycardia (slowing of the heart), hypothermia (dangerously low body temperature), and respiratory depression (slowing down of breathing). It is this latter effect that poses the greatest danger to users, as, due to the apparently high potency of some of these compounds, small amounts may cause life-threatening poisoning from respiratory depression. Left untreated, this can lead to respiratory arrest (stopping breathing) and death. This risk can be exacerbated by the use of other central nervous system depressants.

The timely administration of the antidote naloxone has been shown to be effective in reversing respiratory depression caused by potent opioid analgesics. Although the available information is limited, and, similarly to other opioid analgesics, 2-benzylbenzimidazole opioids are likely to have an abuse liability and dependence potential.

8. Further information

Further information on this substance is available on the EDND profile:
<https://ednd2.emcdda.europa.eu/ednd/substanceProfiles/1469>

9. Acknowledgements

The Latvian National Focal Point, Latvian Police and the Latvian Institute of Organic Synthesis (OSI) are kindly acknowledged for the information and analytical data provided.

10. Attachments

None.

11. References

- [1] <https://www.caymanchem.com/product/30218/4'-hydroxy-nitazene>
[2] Hunger VA, et al. Benzimidazol-Derivate und verwandte Heterocyclen III. Synthese von 1-Aminoalkyl-2-nenzyl-nitro-benzimidazolen. Helvetica Chimica Acta. 1960;43(4):1032-46.