

EU Early Warning System: Formal Notification

Formal notification of 2-{2-[(4-chlorophenyl)methyl]-1*H*-1,3-benzimidazol-1-yl]-*N,N*-diethylethan-1-amine (desnitroclonitazene) by Belgium as a new psychoactive substance under the terms of Regulation (EU) No 2023/1322 and Council Framework Decision 2004/757/JHA

Date issued

15.11.2024

Issued by

EUDA

RCS ID

EU-EWS-RCS-FN-2024-0036

Transmitted by

Action on New Drugs Sector, EUDA

1. Read me first

This document provides formal notification of the analytical identification of 2-{2-[(4-chlorophenyl)methyl]-1*H*-1,3-benzimidazol-1-yl]-*N,N*-diethylethan-1-amine (desnitroclonitazene) for the first time in Europe.

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

2. Data use restrictions

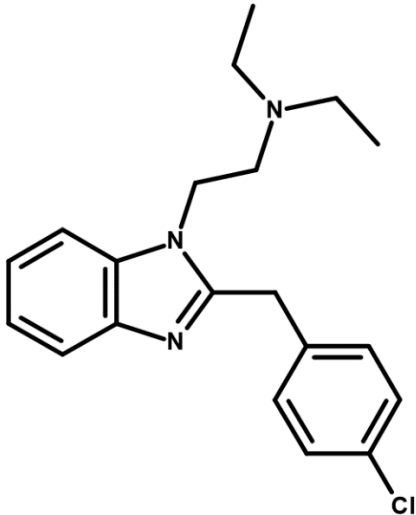
As with all formal notifications issued by the EU Early Warning System (EWS), remember that they may contain information that could be regarded as sensitive. Should you provide some of the information in this notification to other groups we would ask that you exercise your best judgment on what information 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-chlorophenyl)methyl]-1*H*-1,3-benzimidazol-1-yl]-*N,N*-diethylethan-1-amine
- **Chemical names:** 2-[2-[(4-chlorophenyl)methyl]benzimidazol-1-yl]-*N,N*-diethyl-ethanamine; 2-[(4-chlorophenyl)methyl]-*N,N*-diethyl-1*H*-benzimidazole-1-ethanamine; [2-[2-(4-chloro-benzyl)-benzimidazol-1-yl]-ethyl]-diethyl-amine; 2-[2-[(*p*-chlorobenzyl)benzimidazol-1-yl]-*N,N*-diethyl-ethanamine; 2-(*p*-chlorobenzyl)-1-(2-diethylaminoethyl)-benzimidazole
- **Common name:** desnitroclonitazene
- **Other names:** clodesnitazene, clodesnitronitazene
- **Chemical formula:** C₂₀H₂₄ClN₃
- **Molecular weight:** 341.88
- **CAS Registry number:** 100575-54-0 (free base); 114164-12-4 (hydrochloride); 100575-54-0 (methanesulfonate)

- **InChIKey:** BNCZGFWEXSROSK-UHFFFAOYSA-N

Molecular structure:



4. Substance classification

Opioid

5. Detection

Type: Seizure

Case Report identifier: [EDND-CR-2024-1209](#)

Details: Desnitroclonitazene was identified in 13 grams of dark brown powder seized by customs at Brussels Airport.

Desnitroclonitazene was analytically confirmed by GC-MS, FTIR and NMR.





6. Chemistry and Analysis

Chemical classification: azacyclic, azole, benzimidazole

Desnitroclonitazene is a 2-benzylbenzimidazole, structurally related to the internationally controlled [etazene](#) (desnitroetonitazene) and clonitazene (Schedule I of the 1961 United Nations Single Convention on Narcotic Drugs). Desnitroclonitazene differs from etazene by the replacement of the ethoxy group by a chlorine in the *para*-position of the benzyl moiety. It differs from clonitazene by the removal of the nitro group at the 5-position.

Desnitroclonitazene also shares structural similarities with other 2-benzylbenzimidazole opioids under intensive monitoring by the EU EWS, such as [ethometazene](#) (formally notified in January 2023) and [ethyleneoxynitazene](#) (formally notified in February 2023).

The synthesis of desnitroclonitazene has been described by Hunger et al. in 1957 [1].

7. Pharmacology and toxicology

Pharmacological classification: opioid

Currently available information suggests that desnitroclonitazene exhibited a reduced analgesic potency compared to morphine in mice, rats and rabbits. This was also reflected by lower potencies regarding acute toxicity and LD₅₀ values. The reported symptoms of poisoning were consistent with those of opioids [2].

Consistent with the effects shown *in vivo*, a recent *in vitro* study investigating the μ -opioid receptor activation of 2-benylbenzimidazoles confirmed that the removal the nitro group at the 5-position led to a significant reduction in potency, which also applied to the replacement of the alkoxy moiety in the 4-position of the benzyl group with a halogen atom [3].

The cytotoxicity and antiviral activity of a range of 2-benzylbenzimidazoles including desnitroclonitazene have also been evaluated [4,5,6].

8. Further information

Further information on this substance is available on the EDND profile:

<https://ednd2.emcdda.europa.eu/ednd/substanceProfiles/1560>

9. Acknowledgements

The Belgian National Focal Point and the Belgian customs are kindly acknowledged for the information and analytical data provided.

10. Attachments

None.



11. References

- [1] Hunger, A et al. Über Benzimidazolderivate mit starker analgetischer Wirkung. *Experientia* (1957), 13:400-401
- [2] Gross, F and Turrian, H. Über Benzimidazolderivate mit starker analgetischer Wirkung. *Experientia* (1957), 13(10):401-403
- [3] De Vrieze, LM et al. In vitro structure–activity relationships and forensic case series of emerging 2-benzylbenzimidazole ‘nitazene’ opioids. *Archives of Toxicology* (2024) 98:2999–3018
- [4] Tonelli, M et al. Antiviral activity of benzimidazole derivatives. Novel anti-CVB-5, anti-RSV and anti-Sb-1 agents. *Bioorganic & Medicinal Chemistry* (2014), 22(17): 4893-4909
- [5] Wang, J et al. Computational study exploring the interaction mechanism of benzimidazole derivatives as potent cattle bovine viral diarrhoea virus inhibitors. *Journal of Agricultural and Food Chemistry* (2016), 64(29):5941-5950
- [6] Cichero, E. Benzimidazole-based derivatives as privileged scaffold developed for the treatment of the RSV infection: a computational study exploring the potency and cytotoxicity profiles. *Journal of Enzyme Inhibition and Medicinal Chemistry* (2017), 32(1):375-402