Annex 1

Report
3.11.2025
Dnro FIMEA/2025/006292

Assessment form as an Annex to the draft measure

Narcotics Act (373/2008), section 3a

SUBSTANCE

Protodesnitatseeni (*N*,*N*-dietyyli-2-[(4-propoksifenyyli)metyyli]-1*H*-bentsimidatsoli-1-etaaniamiini)

/ **Protodesnitazene** (*N*,*N*-diethyl-2-[(4-propoxyphenyl)methyl]-1*H*-benzimidazole-1-ethanamine)

1. Name, synonyms, street names, CAS number

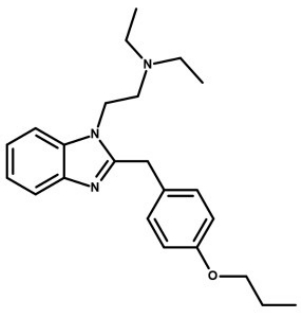
IUPAC name: *N*,*N*-diethyl-2-[2-[(4-propoxyphenyl)methyl]-1*H*-benzimidazol-1-yl]ethanamine or *N*,*N*-diethyl-2-{2-[(4-propoxyphenyl)methyl]-1*H*-1,3-benzimidazol-1-yl}ethan-1-amine

Other names: Protazene, Desnitroprotonitazene

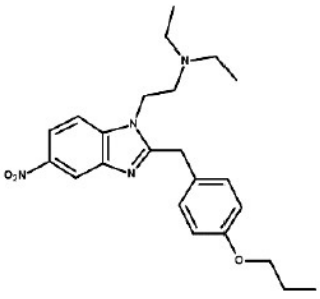
CAS number: 805212-21-9 (base), 1071546-62-7 (HCl)

InChIKey: CEHFMRGBRNNSCM-UHFFFAOYSA-N

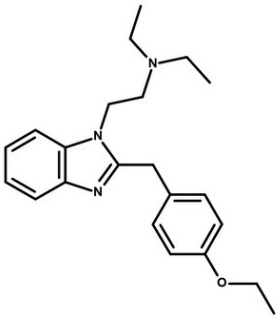
2. Chemical structure



a)



b)



c)

Protodesnitazene (a) and protonitazene (b) and etazene (c), internationally classified as narcotic drugs by the 1961 UN Single Convention on Narcotic Drugs.

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Molecular formula: $C_{23}H_{31}N_3O$

Drug class: Opioids

3. Physical properties

Physical state: Protodesnitazene has been seized in tablet form. Nitazenes are usually sold in powder or liquid form.

Molecular weight: 365.5 g/mol

4. Mechanism of action

Protodesnitazene's structure is that of 5-nitro-2-benzylbenzimidazole. Substances in this group are also called nitazenes. Structurally, protodesnitazene closely resembles protonitazene, which is classified internationally as a narcotic drug. Protodesnitazene differs from protonitazene by the absence of a 5-nitro group in the benzimidazole structure. Protodesnitazene is also structurally similar to etazene, which also lacks a 5-nitro group. Etazene (Point 2, Figure c) was classified nationally as a narcotic in late 2020 and internationally three years later, in 2023.

The research and development of new opioid painkillers in the 1950s and 60s resulted in the discovery of several 2-benzylbenzimidazole compounds with significantly stronger analgesic properties than morphine. Etonitazene was among the first to be synthesised, and in animal experiments, it proved to be an analgesic approximately 1,000 times more effective than morphine. However, these substances have never entered the market as medicinal products.

Based on the structure, the mechanism of action of protodesnitazene is similar to that of other opioids and nitazene opioids in particular, i.e. the effect is mainly delivered in the central nervous system as a full μ-opioid receptor agonist. The effects include pain relief, relaxation, drowsiness, euphoria, slowing heart beat and lower body temperature, and depressed breathing. The latter effect poses a serious health risk at increasing doses.

Protodesnitazene was more than 13 times less potent than protonitazene in the functional characterisation of the μ-opioid receptor (MOR) *in vitro* (MOR–βarr2 EC50= 25.6 nM and GloSensor® cAMP EC50= 2.50 nM for protodesnitazene; MOR–βarr2 EC50= 1.57 nM and GloSensor® cAMP EC50= 0.185 nM for protonitazene), which is consistent with previous data showing that removal of the 5-nitro group leads to a significant decrease in potency in

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benzimidazole opioids.

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5. Manufacture

The production of nitazenes is described in the literature. Different nitazene structures can be produced by selecting the appropriate reagents.

6. Effective doses, abusive doses

No information is available on the effective or abusive doses of protodesnitazene.

7. Polysubstance use

The polysubstance use of opioids with other central nervous system depressants significantly increases the occurrence of adverse effects, with a particular increase in the risk of respiratory depression. New psychoactive products are available not only in pure form but also often as compound mixtures, which means that the composition is not necessarily known to the seller or the buyer.

8. Health risks

Health risks to the individual

No safety or toxicology studies are known to have been published for protodesnitazene. Based on the structure, the health risks associated with the misuse of protodesnitazene are comparable to the known health risks of fentanyl and other nitazenes.

The most common side effects of opioid use are gastrointestinal disorders, such as constipation and nausea. The most serious adverse effects are based on the action of opioids on the central nervous system, delivered via μ-opioid receptors. The most serious of the acute health risks is respiratory depression, which could be fatal.

Particularly in the case of new nitazenes that end up being used as narcotics, the health risk is significant, because as strong opioids they can cause life-threatening poisoning even at very small doses. Naloxone can be used to treat overdoses, but the required doses may be higher than usual and follow-up should be continued for longer.

Public health risks and social risks

The public health and social risks of protodesnitazene, as with other

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nitazenes, are comparable to those of heroin and fentanyl.

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9. Connection with other forms of crime

No information.

10. Documented observations on use of the substance

Medical and industrial use

There is no known medicinal or industrial use for protodesnitazene.

Reported occurrences in Finland

Customs seized five tablets on 7 October 2025, which were identified as protodesnitazene. The tablets were marketed as a medicinal opioid, oxymorphone.

Reporting in the EU and to the EMCDDA Early Warning System (EWS)

The first report on protodesnitazene in Europe was received from Finland in October 2025.

The first observations of protodesnitazene in 2025 are from Australia, where it was sold in powder form under the name desmetramadol. Observations of protodesnitazene have also been made in Canada and the United States in spring 2025.

11. Availability

Protodesnitazene is available as a reference substance.

12. Use profile

In recent years, numerous new fentanyl derivatives have been classified as narcotics, also under generic classifications in many countries. Partly as a result of this, new opioids belonging to the nitazene group, such as protodesnitazene, are offered on the market as a substitute for fentanyl derivatives and other opioids and may be of particular interest to opioid users. As ‘legal alternatives’, substances that are not controlled may be of particular interest to persons testing new substances.

13. Current status

Protodesnitazene is not controlled in Finland under the Narcotics Act or the

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Medicines Act.

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14.Other information

The United Nations Office on Drugs and Crime (UNODC) has recently highlighted the global spread and dangers posed by nitazenes. Since 2019 and by late October 2025, 23 new synthetic opioids belonging to the nitazene group have been reported to the European Drugs Agency for monitoring. Of these, 7 were reported in 2024 and 3 by late October 2025. The World Health Organisation has evaluated the properties of 12 new nitazenes between 2020 and 2024, which, excluding two nitazenes evaluated this autumn, have also been placed under international control as narcotic drugs. This indicates that nitazenes are dangerous and their misuse has spread worldwide. In the summer of 2025, China banned substances in the nitazene group by means of a general regulation, and they have also been banned in several European countries, such as the United Kingdom.

In recent years, poisoning cases involving a nitazene have been reported around the world, several of them fatal. Falsified medicines containing a strong nitazene in place of a medicinal substance have been detected in several countries, including Finland, in recent years. Marketing as familiar-looking tablets can be considered particularly dangerous for the uninformed user, and compression into tablets can also expand the user base if the tablet form increases the feeling that use is acceptable.

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16.Alternatives to classification as a narcotic and a classification proposal following the assessment

Based on the information gathered about the substance, the Finnish Medicines Agency concludes that the substance should, due to its properties and the

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severe adverse effects caused by them, be added to the Government Decree (543/2008) on substances, plants and products to be classified as narcotics (Annex IV).

Signatures

This document is an annex to the electronically signed document.

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