Annex 1

17.11.2025

Register number FIMEA/2025/006104

1 (29)

Annex 1

17.11.2025

Register number FIMEA/2025/006104

Assessment form as an Annex to the draft measure

Narcotics Act (373/2008), section 3a

SUBSTANCE

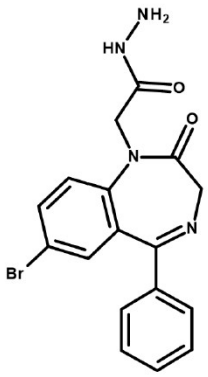
Gidazepam (2-(7-bromo-2-oxo-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-1-yl)acetohydrazide) / **Gidazepam (**2-(7-bromo-2-oxo-5-phenyl-2,3-dihydro-1*H*-1,4-bensodiazepin-1- yl)acetohydrazide)

1. Name, synonyms, street names, CAS number

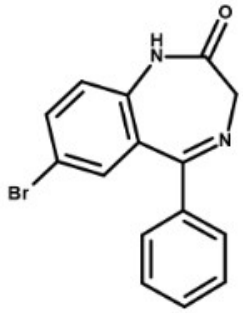
IUPAC name: 2-(7-bromo-2-oxo-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-1- yl)acetohydrazide
Used name: Gidazepam
Other names: hidazepam, hydazepam, gidazepam
CAS number: 129186-29-4

InChIKey: XLGCMZLSEXRBSG-UHFFFAOYSA-N

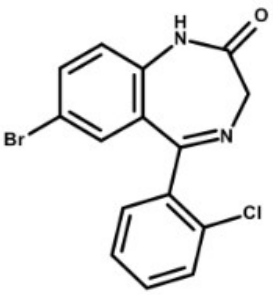
2. Chemical structure



a) gidazepam



b) desalkylgidazepam



c) phenazepam

For comparison, structural diagrams of gidazepam (a), desalkylgidazepam (b), which is banned from the consumer market in Finland, and phenazepam (c), which is controlled internationally under the 1971 Convention on Psychotropic Substances.

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

Molecular formula: $C_{17}H_{15}BrN_4O_2$

Drug class: Benzodiazepines

3. Physical properties

Physical state: Gidazepam has been seized as white round tablets in a blister pack.

Molecular weight: 387.23 g/mol

4. Mechanism of action

Gidazepam is structurally a 1,4-benzodiazepine. Its active metabolite, desalkylgidazepam, is classified in Finland as a psychoactive substance prohibited on the consumer market (Government decree 1130/2014). Structurally, this active metabolite of gidazepam closely resembles phenazepam, which is internationally classified as a narcotic.

Gidazepam was developed in the 1990s and has been used as a prescription medicine in Russia and Ukraine since 1997.

The pharmacological effect of benzodiazepine is based on the molecule binding to the gamma-aminobutyric acid receptor (GABA) in the central nervous system. As a result of the binding, the inhibitory effect of GABA is enhanced. This will result in a nonspecific slowing down of the nerve paths, causing sedative, hypnotic, anxiolytic and anticonvulsant effects.

In *in vitro* tests, gidazepam has been shown to be a partial antagonist to the GABA-A receptor. Gidazepam binds to the GABA-A receptor less strongly (Ki = 2200 nM) than desalkylgidazepam (Ki = 3.5 nM).

The effect of gidazepam differs from the general effect of benzodiazepines in that the substance has anxiety-relieving (anxiolytic) properties, but lacks the sedative and muscle-relaxing effects typical of other benzodiazepines. The binding of gidazepam to peripheral benzodiazepine receptors has also been considered as an explanation for this different effect from other benzodiazepines.

Gidazepam is effectively absorbed from the gastrointestinal tract and very rapidly metabolised into an active desalkylgidazepam. The bioavailability of gidazepam is 70–99%, peak concentration is reached in 4 hours and the effect begins in 30–60 minutes. The half-life of desalkylgidazepam as gidazepam is on average 87 hours after administration, so gidazepam can be considered as a long-acting benzodiazepine.

5. Manufacture

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

Published information is available on the manufacture of benzodiazepines.

6. Effective doses, abusive doses

For medical use, gidazepam is available as 20 mg and 50 mg tablets and as formulations to be administered under the tongue. The recommended daily dose for up to four months is 40 to 60 mg for the treatment of migraine, 60 to 200 mg for anxiety and 50 to 600 mg for the treatment of alcohol withdrawal symptoms. According to the product summary, the dosage to be administered sublingually is as follows: 20–50 mg three times daily. If necessary, the dose may be increased by 50–200 mg/day to achieve the therapeutic effect. Optimal daily dose: approximately 100 mg. Higher doses (150–200 mg/day) may cause increased daytime drowsiness and muscle weakness. For alcohol withdrawal symptoms, an initial dose of 50 mg, an average of 150 mg/day, a maximum dose of 500 mg/day. Treatment period: from a few days to one to four months, at the physician's discretion.

At higher doses (100–150 mg/day), the effects resemble the sedative effects of classic benzodiazepines.

No information is available on the misuse of standard doses, but in online discussions, one writer reported having been addicted to the lowest medicinal dose (20 mg) for years. The doses of the active metabolite in misuse are described as 3–9 mg and traded online as 1–3 mg pellets or tablets.

7. Polysubstance use

The use of benzodiazepines in combination with other central nervous system depressants, such as alcohol, increases the risk of adverse health effects.

8. Health risks

Health risks to the individual

Common adverse effects of benzodiazepines include muscle weakness, motor coordination impairment, nausea, memory impairment and drowsiness. The paralysing effect on the nervous system will increase if benzodiazepines are used together with alcohol or other psychoactive drugs, such as sleep aids, sedatives or anti-psychotic drugs.

Tolerance to benzodiazepines develops rapidly, and long-term use may result in physical and psychological addiction to the substance. The addiction risk grows with the dose and duration of use and is increased if several benzodiazepines are used simultaneously.

fimea

Annex 1

17.11.2025
Register number FIMEA/2025/006104

Side effects reported with the therapeutic use of gidazepam include drowsiness, weakness, myasthenia gravis, dependence, dysmenorrhoea (menstrual pain), allergic reactions, impaired coordination, ataxia and severe muscle weakness.

Dependence occurs in user reports, although due to the substance's effects, which differ slightly from other benzodiazepines (mainly anxiolytic), and its long half-life, gidazepam is considered to be well tolerated and to have a low potential for dependence.

Public health and social risks

The public health and social risks associated with gidazepam are partly comparable to those associated with other benzodiazepines.

9. Connection with other forms of crime

No data available

10. Documented observations on use of the substance

Medical and industrial use

Gidazepam has no known medicinal or industrial use in Finland. In Russia and Ukraine, the substance is used as a medicinal product.

Reported occurrences in Finland

The Customs Laboratory's statistics contain entries on gidazepam findings in samples examined in 2017 (30 samples), 2020 (5 samples) and 2021 (30 samples). In recent years, this has not been reflected in customs statistics. There is no record of gidazepam findings in police forensic laboratory statistics. Post-mortem examinations by the Finnish Institute for Health and Welfare THL have found gidazepam's metabolite desalkylgidazepam in one case in 2022.

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

Gidazepam was reported to the EWS system of the European Union Drugs Agency by Denmark in 2024. Danish customs seized tablets containing gidazepam in April 2024.

11. Availability

Gidazepam is available in 20 mg and 50 mg tablets under the brand name Gidazepam IC® in Russia and Ukraine. Both gidazepam and desalkylgidazepam are available as reference substances.

fimea

Annex 1

17.11.2025
Register number FIMEA/2025/006104

12. Use profile

Based on EUDA, UNODC and national monitoring and scientific literature, the misuse of benzodiazepine derivatives and the resulting serious harm, in particular in the context of polydrug use, have been significant and increasing worldwide for more than ten years. The abuse of these substances may be an attractive alternative to benzodiazepines, which are subject to prescription. Benzodiazepines are often used as a recreational substance together with other sedatives or alcohol. They are also used to alleviate the adverse effects of stimulants. Based on reports from internet forums, users of designer benzodiazepine are often familiar with benzodiazepines. However, some users also appear to be new users.

13. Current status

Gidazepam is not controlled under the Narcotics Act in Finland. Its active metabolite, desalkylgidazepam, is controlled as a psychoactive substance prohibited on the consumer market.

14. Other information

The abuse of gidazepam is most often comparable to the abuse of benzodiazepines that are used as medicine in Finland. As a selective anxiolytic agent, gidazepam may be an attractive option for users who want a calming effect without causing fatigue and drowsiness.

15. References

1. Gidazepam, Compound Summary. Pubchem database. National Library of Medicine. https://pubchem.ncbi.nlm.nih.gov/compound/Gidazepam (Information retrieved on 29 September 2025)
2. Gidazepam, Substance Profile. EUDA-EDND. Password-protected database. (Information retrieved on 29 September 2025)
3. Maskell PD, Wilson G, Manchester KR. Designer benzodiazepines gidazepam and desalkylgidazepam (bromonordiazepam): what do we know? *J. Anal. Toxicol*. 2023; **47**: 324-331.
4. Advisory Council on the Misuse of Drugs, Recently encountered uncontrolled novel benzodiazepines and related compounds (2024 update), https://www.gov.uk/ (Information retrieved 17 October 2025)
5. Syvälahti E., Hietala J. Ahdistuneisuus- ja unihäiriöiden lääkeaineet. In Koulu, Mervaala, Tuomisto (eds.) Farmakologia ja toksikologia, Medicina, 2012.
6. Korkhov VM, Tkachkuk NA et al. Affinities of gidazepam and its analogs for mitochondrial benzodiazepine receptors. *J. Recept. Signal Transduct. Res*. 2002; **22**:411-20.
7. Golovenko NY, Larionov VB. Pharmacodynamical and neuroreceptor analysis of the permeability of the blood-brain barrier for derivatives of 1,4-benzodiazepine. *Neurophysiol.* 2014; **46**:199-205.
8. Litvin AA, Kolyvanov GB et al. Relationship between physicochemical characteristics and pharmacokinetic parameters of 1,4-benzodiazepine derivatives. *Pharm Chem.* 2004; 38:583–586
9. Azimova Y.E., Petelin D.S. Gidazepam – daytime tranquilizer for the treatment of anxiety. Nevrologiya, neiropsikhiatriya, Psikhosomatika / Neurology, Neuropsychiatry, Psychosomatics. 2024;**16(5)**:91–98. (Translated to Finnish from Ukrainian, abstract in English.)
10. Synthesis of benzodiazepines. Patent WO1996005178. https://patentimages.storage.googleapis.com/c1/37/d9/702a520b9e3ae9/WO1996005178A1.pdf
11. Interchem. Gidazepam sublingual, summary of product characteristics (Translated to Finnish from Ukrainian.) http://178.20.155.134/uploads/drugs/g%D1%96dazepam_%D0%86s_R_sublingv_.pdf (Information retrieved on 17 October 2025)
12. Internet chatrooms (Information retrieved 29 September 2025) https://www.flashback.org/t2176913

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

https://benzobuddies.org/topic/274988-hi-i-am-addicted-to-the-benzodiazepine-gidazepam-diazepam-i-want-to-quit/
https://www.bluelight.org/community/threads/gidazepam.925009/
https://drugs-forum.com/wiki/Gidazepam

13. Chemicals Register, Finnish Safety and Chemicals Agency (Tukes). Written communication, email dated 15 September 2025.
14. Customs Laboratory statistics. Written communication, email dated 11 March 2025 and 15 September 2025
15. National Bureau of Investigation, Forensic Laboratory. Written communication, by email on 16 September 2025.
16. Finnish Institute for Health and Welfare, Forensic Toxicology Unit. Written communication, by email on 10 March 2025 and 16 September 2025.
17. Online shops (Information retrieved on 29 September 2025)
https://www.caymanchem.com/product/36421/gidazepam?srsltid=AfmBOoqN1LojNbJ0F5bx5rEPFBj002FrNMmPV3vqMrDNQz2sBN0U8-Nl
https://www.caymanchem.com/product/36608/desalkylgidazepam?srsltid=AfmBOoqpcwmim1xnvbnYg_MhZ-zBUtnpVcw8c3vdi0A_1rtV87DCQQyD
https://www.medchemexpress.com/Gidazepam.html?srsltid=AfmBOoqmWMEZbzG1VrifXRM7yWuNVF3K5bFi-nscVp--iN2jBtv9Crve
https://www.abcparty.nl/fi/gidazepam
https://www.medchemexpress.com/Gidazepam.html?srsltid=AfmBOor2LNZ1NUhssXRb5EAKdMd7eEjur0Ib7Oi_huXpMASiaKgn4mX3
18. European Monitoring Centre for Drugs and Drug Addiction (2021), New benzodiazepines in Europe – a review, Publications Office of the European Union, Luxembourg.
19. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). European drug report 2024: Trends and developments. Publications Office of the European Union, Luxembourg.
20. United Nations Office of Drugs and Crime. Current NPS Threats Volume VII, July 2024, Vienna, Austria.
21. Van Amsterdam J., van den Brink W. Designer benzodiazepines: Availability, motives, and fatalities. A systematic narrative review of human studies. *Drug Alc. Dep.* 2025; **272**:112708
22. Moosmann B, King LA, Auwärter V. Designer benzodiazepines: a new challenge. *World Psychiatry*. 2015;14:248
23. Orsolini L, Corkery JM et al. 'New/Designer Benzodiazepines': An analysis of the literature and psychonauts' trip reports. *Curr. Neuropharmacol.* 2020;18:809-837.

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 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.

Annex 1

17.11.2025

Register number FIMEA/2025/006104

PO Box 55, FI-00034 FIMEA, FINLAND
Tel. +358 29 522 3341
www.fimea.fi
Business ID FI09215366

Annex 1

17.11.2025
Register number FIMEA/2025/006104

8 (29)

Annex 2

23 October 2025
Register number FIMEA/2025/006104

Assessment form as an Annex to the draft measure

Narcotics Act (373/2008), section 3a

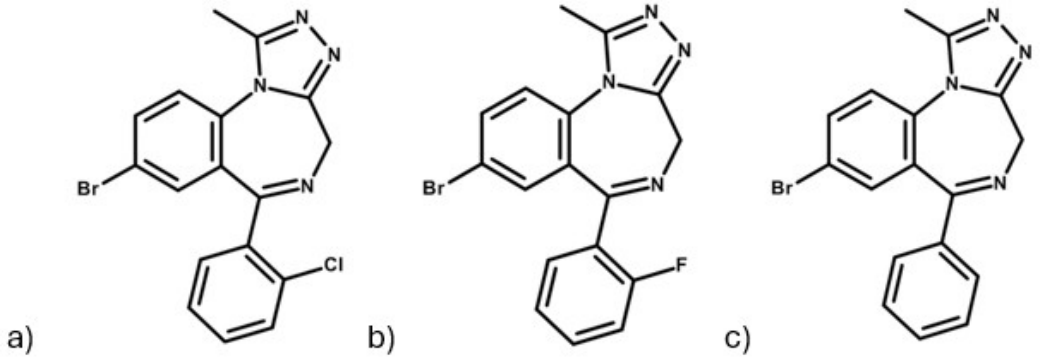
SUBSTANCE

Clobromazolam (8-bromo-6-(2-chlorophenyl)-1-methyl-4*H*-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine) / Clobromazolam ((8-bromo-6-(2-chlorphenyl)-1-methyl-4*H*-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine)

1. Name, synonyms, street names, CAS number

IUPAC name: 8-Bromo-6-(2-chlorophenyl)-1-methyl-4*H*-[1.2.4]triazolo[4.3-a][1,4]benzodiazepine
Other names: phenazolam, BRN 4550445
CAS number: 87213-50-1
InChIKey: BUTCFAZTKZDYCN-UHFFFAOYSA-N

2. Chemical structure



Chemical structure of clobromazolam (a) in relation to the structures of flubromazolam (b) and bromazolam (c), which are controlled substances under the 1971 Convention on Psychotropic Substances.

Annex 1

17.11.2025

Register number FIMEA/2025/006104

Molecular formula: $C_{17}H_{12}BrClN_4$

Drug class: Benzodiazepines[1.,2.]

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

3. Physical properties

Physical state: Clobromazolam has been seized in the form of white powder packed in white capsules.

Molecular weight: 387.67 g/mol

4. Mechanism of action

Based on its structure, clobromazolam is a 1,2,4-triazolobenzodiazepine and a 2-chloro derivative of bromazolam, which is nationally controlled as a narcotic. It is also similar in structure to flubromazolam, which is subject to international control (image in point 2). Clobromazolam is a so-called designer benzodiazepine that was developed in the 1980s but has never been studied in clinical trials or registered for medical use.

The pharmacological effect of benzodiazepine is based on the molecule binding to the gamma-aminobutyric acid receptor (GABA) in the central nervous system. As a result of the binding, the inhibitory effect of GABA is enhanced. This will result in a nonspecific slowing down of the nerve paths, causing sedative, hypnotic, anxiolytic and anticonvulsant effects.

The pharmacological properties of clobromazolam have been evaluated in animal studies by oral administration to mice. The reported results indicate that the substance has very strong anticonvulsant, central nervous system-depressant and motor coordination-impairing effects. At doses of 0.2–1.0 g/kg, pronounced central nervous system depression, ataxia and convulsive reactions were observed, and these symptoms lasted for more than 24 hours. Compared with triazolam, clobromazolam had a similar anticonvulsant effect against pentylenetetrazol; in an electroshock test, its activity was about 25% of that of triazolam, its locomotor-inhibiting effect was 12%, and its coordination-impairing effect was approximately 40%.

5. Manufacture

Published information is available on the manufacture of benzodiazepines, and the synthesis of clobromazolam has been described in the literature.

fimea

Annex 1

17.11.2025
Register number FIMEA/2025/006104

6. Effective doses, abusive doses

No statements can be found on normal user dosages of clobromazolam. However, the triazolobenzodiazepine structure and the affinity for the receptor suggest a small dose range.

The typical doses of flubromazolam, which has a similar structure, are usually very small (0.15-0.40 mg); and for bromazolam, 1-2 mg (see Figure 2b and c), while the typical misuse dose of alprazolam is described as 0.5-1.5 mg.

7. Polysubstance use

The use of benzodiazepines, including clobromazolam, together with other substances is common. In particular, using them with central nervous system depressants, such as alcohol, and especially opioids, is common and carries a significant risk.

8. Health risks

Health risks to the individual

There are no published data on the safety, hazards and risks of clobromazolam. Common adverse effects of benzodiazepines include muscle weakness, motor coordination impairment, nausea, memory impairment and drowsiness. The paralysing effect on the central nervous system will increase if benzodiazepines are used together with alcohol or other psychoactive drugs, such as sedatives, tranquilizers or anti-psychotic drugs.

Tolerance to benzodiazepines develops rapidly, and long-term use may result in physical and psychological addiction to the substance. The addiction risk grows with the dose and duration of use and is increased if several benzodiazepines are used simultaneously.

Public health risks and social risks

The public health risks and social risks of clobromazolam are comparable to the equivalent risks of other benzodiazepines, such as the adverse effects of tiredness or memory problems in working life or traffic. The development of tolerance and dependence and the resulting need to obtain more of the substance may, in the worst case, lead to criminal acts and the neglect of other obligations.

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

9. Connection with other forms of crime

No data available.

10. Documented observations on use of the substance

Medical and industrial use

Clobromazolam has no medicinal or industrial use in Finland.

Reported occurrences in Finland

In the statistics of the police forensic laboratory, there is 1 sample (54 ml) from 2025.

In the customs laboratory statistics, 3 samples (27.97 g) were reported in 2024 and 5 samples (8.9 g) in 2025

In THL statistics, there are 2 cases in post-mortem examinations in 2025

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

Clobromazolam was reported to the EUDA Early Warning System by Sweden in 2018.

11. Availability

Clobromazolam is available as a reference substance. It is also sold in online shops on the open internet for intoxication purposes.

12. Use profile

The abuse of these substances may be an attractive alternative to benzodiazepines, which are subject to prescription. Benzodiazepines are often used for intoxication purposes together with other sedatives or alcohol. Particularly harmful use in combination with opioids has also increased. Benzodiazepine derivates are also used to alleviate the adverse effects of stimulants, among others. Based on reports from internet forums, users of designer benzodiazepine are often familiar with benzodiazepines. However, some users also appear to be new users.

fimea

Annex 1

17.11.2025
Register number FIMEA/2025/006104

13. Current status

Clobromazolam is classified in Finland as a psychoactive substance prohibited on the consumer market (Government decree 1130/2014).

14. Other information

Based on EUDA, UNODC and national monitoring and scientific literature, the misuse of benzodiazepine derivatives and the resulting serious harm, in particular in the context of polydrug use, have been significant and increasing worldwide for more than ten years. In Finland, the first benzodiazepine was brought under national drug control in 2014; since 2016, a total of seven different benzodiazepines have been added to international drug control.

Clobromazolam, like other so-called designer benzodiazepines, is in misuse most commonly compared with the benzodiazepines that are also used as medicines in Finland. Substances excluded from control may be attractive alternatives for those marketing drugs for recreational use as substitutes for controlled narcotics or for psychoactive substances prohibited on the consumer market.

15. References

1. Clobromazolam, Compund Summary. Pubchem database. National Library of Medicine. https://pubchem.ncbi.nlm.nih.gov/compound/1032830 (Information retrieved on 30 September 2025)
2. Clobromazolam, Substance Profile. EUDA-EDND. Password-protected database. (Information retrieved on 30 September 2025)
3. Advisory Council on the Misuse of Drugs, Recently encountered uncontrolled novel benzodiazepines and related compounds (2024 update), https://www.gov.uk/ (Information retrieved on 17 October 2025)
4. Syvälahti E. and Hietala J. Ahdistuneisuus- ja unihäiriöiden lääkeaineet. In Koulu, Mervaala, Tuomisto (eds.) Farmakologia ja toksikologia, Medicina, 2012.
5. Vejdelek Z, Protiva M. Synthesis of two 1-substituted 8-bromo-6-(2-chlorophenyl)-4H-s-triazolo[4,3-a]-1,4-benzodiazepines. *Collection of Czechoslovak Chemical Communications.* 1983; 48(5): 1477-82
6. Synthesis of benzodiazepines. Patent WO1996005178. https://patentimages.storage.googleapis.com/c1/37/d9/702a520b9e3ae9/WO1996005178A1.pdf
7. Manchester KR., Waters L., et al. The blood-to-plasma ratio and predicted GABAA-binding affinity of designer benzodiazepines. *Forensic Toxicol*. 2022;**40**, 349–356.
8. WHO, Critical Review Report: Flubromazolam, Expert Committee on Drug Dependence, Fortythird Meeting, Geneva, 12–20 October 2020.
9. WHO, Critical Review Report: Bromazolam, Expert Committee on Drug Dependence, Fortysixth Meeting, Geneva, 16–20 October 2023.
10. Information on the abuse dose of alprazolam was retrieved e.g. from the Tripsit website: https://tripsit.me/factsheets/alprazolam (Information retrieved on 17 October 2025)
11. Castle JW., Syrjänen R., et al. Identification of clobromazolam in Australian emergency department intoxications using data-independent high-resolution mass spectrometry and the HighResNPS.com database. *J. Anal. Toxicol*. 2024;**48**:273–280.
12. Chemicals Register, Finnish Safety and Chemicals Agency (Tukes). Written communication, email on 15 September 2025
13. Customs Laboratory statistics. Written communication, email on 15 September 2025
14. Police Forensic Laboratory. Written communication, email on 16 September 2025
15. Finnish Institute for Health and Welfare, Forensic Toxicology Unit. Written communication, email, 16 September 2025
16. Online shops (Information retrieved on 30 September 2025) https://www.caymanchem.com/search?q=phenazolam https://absolutechems.com/

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

https://www.vulcanchem.com/product/vc3836660

17. Van Amsterdam J., van den Brink W. Designer benzodiazepines: Availability, motives, and fatalities. A systematic narrative review of human studies. *Drug Alc. Dep.* 2025; **272**:112708
18. European Monitoring Centre for Drugs and Drug Addiction (2021), New benzodiazepines in Europe – a review, Publications Office of the European Union, Luxembourg.
19. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). European drug report 2024: Trends and developments. Publications Office of the European Union, Luxembourg.
20. United Nations Office of Drugs and Crime. Current NPS Threats Volume IV, November 2021, Vienna, Austria. (Information retrieved on 17 October 2025)
21. Moosmann B, King LA, Auwärter V. Designer benzodiazepines: a new challenge. *World Psychiatry*. 2015;**14**:248.
22. Orsolini L., Corkery J.M. et al. 'New/Designer Benzodiazepines': An analysis of the literature and psychonauts' trip reports. *Curr. Neuropharmacol.* 2020;**18**:809-837.
23. The Center for Forensic Science and Research (CFSRE), NPS Discovery. NPS Benzodiazepines in the United States—Trend Reports. https://www.cfsre.org/nps-discovery/trend-reports/nps-benzodiazepines/report/49?trend_type_id=1 (Information retrieved on 17 October 2025)

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 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.

Finnish Medicines Agency Fimea
PO Box 55, FI-00034 FIMEA, FINLAND
Tel. +358 29 522 3341
www.fimea.fi
Business ID FI09215366

Annex 1

17.11.2025

Register number FIMEA/2025/006104

15 (29)

Annex 3

23 October 2025

Register number FIMEA/2025/006104

Assessment form as an Annex to the draft measure

Narcotics Act (373/2008), section 3a

SUBSTANCE

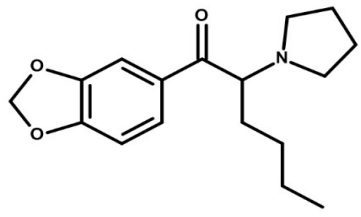
MDPHP (1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)hexan-1-one) /

MDPHP (1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)hexan-1-one)

1. Name, synonyms, street names, CAS number

IUPAC name: 1-(1,3-Benzodioxol-5-yl)-2-(pyrrolidin-1-yl)hexan-1-one
Used name: MDPHP
Other names: 3,4-Methylenedioxy-α-pyrrolidinohexnophenone; 3,4-MDPHP; 3,4-MD-α-PHP
CAS number: 776994-64-0 (alkali), 24622-61-5 (HCl salt)
InChIKey: OBLFRFGUZZRECT-UHFFFAOYSA-N

2. Chemical structure

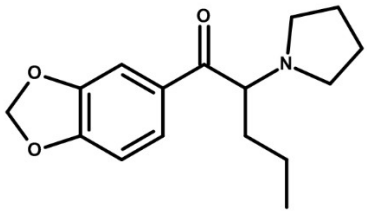


MDPHP
Molecular formula: $C_{17}H_{23}NO_3$
Drug class: Cathinones

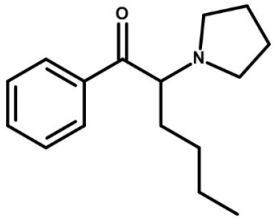
Annex 1

17.11.2025

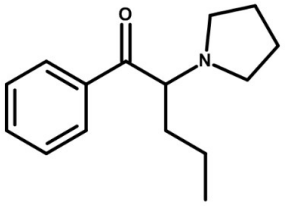
Register number FIMEA/2025/006104



a)



b)



c)

Compared to structurally similar MDPV (a), alpha-PHP (b) and alpha-PVP (c), classified as narcotic drugs under the 1971 UN Convention on Psychotropic Substances.

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

3. Physical properties

Physical state: The substance has been seized in the form of yellow-brown and white powder and as a liquid.

Molecular weight: 289.17 g/mol

4. Mechanism of action

MDPHP is a synthetic pyrovalerone-based cathinone and similar in structure to MDPV, which is classified as a narcotic under the Convention on Psychotropic Substances. It is also similar in structure to alpha-PHP and alpha-PVP, which are classified as narcotics.

Pyrrolidine-structured synthetic cathinones effectively inhibit the reuptake of dopamine and noradrenaline in the central nervous system, but have less effect on serotonin. This increases the misuse potential of these compounds compared with other cathinones, as does the fact that they are highly lipophilic, allowing them to transfer quickly and efficiently to the central nervous system and their site of action. There is some evidence of the particularly harmful effects of these compounds in recreational use compared with other cathinones, but further research is needed.

The intended effects of using synthetic cathinones are feelings of well-being, euphoria and increased energy and concentration. Adverse effects may include palpitations, increased blood pressure, anxiety, nervousness, fever, convulsions, unconsciousness, delusions, hallucinations and psychoses, as well as low mood, irritability, headache, insomnia and nausea. Tolerance can develop to these substances, and they can cause dependence.

In in vitro experiments, MDPHP has been found to be a potent inhibitor of dopamine and noradrenaline reuptake, but considerably less effective as a serotonin reuptake inhibitor (IC50 DAT 50 nM, NET 60 nM, and SERT 9000 nM. For comparison, MDPV IC50 DAT 30 nM, NET 50 nM, and SERT 8400 nM).

In *in vivo* experiments in mice, MDPHP has been observed to affect heart rate and blood pressure similarly to MDPV, as well as increase aggression.

5. Manufacture

Published information is available on the manufacture of synthetic cathinones. MDPHP was synthesised for the first time in the 1960s.

6. Effective doses, abusive doses

Based on online user discussions, the estimated misuse doses are 5–60 mg orally and 1–35 mg when smoked.

7. Polysubstance use

Based on user discussions and chemical analyses following poisoning cases, MDPHP is often used simultaneously with other stimulants.

8. Health risks

Health risks to the individual

The health risks following MDPHP misuse are similar to those of other cathinones, and particularly of pyrrolidinyl-structured cathinones.

Local irritation and ulceration of the oral and nasal mucosa may occur.

Neuropsychiatric health effects can include anxiety, confusion, hallucinations, paranoia and post-use depression. Cardiovascular adverse effects include tachycardia, chest pain, elevated blood pressure, and in severe cases, life-threatening circulatory disturbances of the heart and brain.

There are numerous reports of poisoning cases caused by MDPHP use, as well as laboratory findings from various poisoning incidents. It has also been shown that the substance can cross the placenta from mother to foetus.

There are published reports of deaths associated with MDPHP use. For example, in Italy, a case was reported in which a 48-year-old man died solely from MDPHP poisoning. MDPHP has also been detected in post-mortem examinations in Finland.

Public health risks and social risks

It is necessary to compare the public health and social risks of MDPHP to the risks associated with the abuse of other known pyrovalerone-based cathinones, such as MDPV, alpha-PHP and alpha-PVP.

9. Connection with other forms of crime

No data available.

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

10. Documented observations on use of the substance

Medical and industrial use

The substance has no known medical or industrial use in Finland.

Reported occurrences in Finland

MDPHP has appeared in the Customs Laboratory statistics since 2015. In 2018, nearly 3.4 kilograms of the substance were seized, and in 2022, there were 39 samples, totalling 329.20 g. Otherwise, after 2022, approximately 10–15 samples (under 100 g) of MDPHP have been seized annually.

In the Police Forensic Laboratory statistics, a few MDPHP confiscations appear each year, with quantities below 50 g per year.

In the Finnish Institute for Health and Welfare's post-mortem examinations, MDPHP was detected in one case in 2023, although the cause of death was not poisoning, and in one poisoning case due to recreational use in 2024. In the latter case, the blood sample contained, in addition to MDPHP, other cathinones as well as fentanyl and flualprazolam.

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

MDPHP was reported to the European Union Drugs Agency's Early Warning System by Sweden in November 2014. Since then, the substance has been reported to the system almost annually by several European countries.

11. Availability

MDPHP is available as a reference substance, and it is also marketed on open online marketplaces. There is also marketing in Finnish.

12. Use profile

Synthetic cathinones may be of particular interest to users of amphetamine and other stimulants. The strong dopaminergic effect of pyrovalerone cathinones exacerbates dependence, and replacing one substance with another that has a similar effect carries risks.

MDPHP is a pyrovalerone cathinone, as is, for example, alpha-PVP, which is currently causing harm in Finland. Both substances can be and are used by smoking.

13. Current status

MDPHP is classified in Finland as a psychoactive substance prohibited on the consumer market (Government decree 1130/2014).

14. Other information

As substitutes for traditional stimulants, several synthetic cathinones have entered the market. In Finland, pyrovalerone-group cathinones in particular, such as MDPV, alpha-PVP and alpha-PHP, have attracted the interest of misusers, and their misuse has caused both health and social harms.

For example, local areas of concentrated use have been observed in the United Kingdom and Italy. In particular, in the United Kingdom, the harms caused by MDPHP misuse have been striking, affecting not only users but also their wider social environment.

15. References

24. Pubchem, NCBI, National Library of Medicine. https://pubchem.ncbi.nlm.nih.gov/compound/119057580 (Information retrieved on 26 September 2025).
25. EUDA-EDND. Password-protected database.
26. Synthetic cathinones: an updated harms assessment. Advisory Council of the Misuse of Drugs. https://www.gov.uk/government/publications/synthetic-cathinones-an-updated-harms-assessment/synthetic-cathinones-an-updated-harms-assessment-accessible (Information retrieved on 25 September 2025)
27. Kolaczynska K, Thomann J, Hoener M, Liechti M. The Pharmacological Profile of Second Generation Pyrovalerone Cathinones and Related Cathinone Derivative. *Int. J. Mol. Sci*. 2021; **22**:8277.
28. Bassi M, Bilel S, Tirri M, Corli G, Di Rosa F, Gregori A et al. (2024-07-01). The synthetic cathinones MDPHP and MDPV: Comparison of the acute effects in mice, in silico ADMET profiles and clinical reports. *Neurotoxicol.*. 2024;**103**:230–255.
29. Patent DE1545591. Koeppe H, Zeile K, Ludwig G. Patent DE – Verfahren zur Herstellung von α-Aminoketonen mit hererocyclisher Aminogruppe. 28. Mai 1965
30. Internet discussion groups (Information retrieved on 25 September 2025) https://www.flashback.org/t2573600 https://knowdrugs.app/substances/mdphp https://tripsit.me/factsheets/mdphp https://sidekicks.berlin/en/monkeydust/
31. Beck O, Bäckberg M et al. Intoxications in the STRIDA project involving a panorama of psychostimulant pyrovalerone derivatives, MDPV copycats. *Clin. Toxicol.* 2018;**56**: 256-263.
32. Arillotta D, Totti A et al.Clinical manifestations and analytical reports for MDPHP acute intoxication cases', *J. Pharm. Biomed. Anal.* 2024;**241**:115974.
33. Croce EB, Dimitrova Aet al. Postmortem distribution of MDPHP in a fatal intoxication case. *J. Anal.Toxicol*. 2025; **49**:137–141.
34. Casati S, Ravelli A et al. Polydrug fatal intoxication involving MDPHP: Detection and *in silico* investigation of multiple 3,4-methylenedioxy-derived designer drugs and their metabolites. *J. Anal. Toxicol.* 2025;49:384-393.
35. Adamowicz P, Hydzik P. Fetal death associated with the use of 3,4-MDPHP and α-PHP., *Clin. Toxicol.* 2019;**57**:112-116.
36. Di Candia D, Boracchi M et al. A unique case of death by MDPHP with no other co-ingestion: a forensic toxicology case. *Int. J. Legal Med.* 2022;**136**:1291–1296.
37. Kriikku P, Ojanperä I. Findings of synthetic cathinones in post-mortem toxicology. *Forensic Sci. Int.* 2024;**365**:112297
38. Chemicals Register, Finnish Safety and Chemicals Agency (Tukes). Written communication, email on 15 September 2025
39. Customs Laboratory statistics. Written communication, email on 15 September 2025
40. Police Forensic Laboratory. Written communication, by email on 16 September 2025
41. Finnish Institute for Health and Welfare, Forensic Toxicology Unit. Written communication by email of 16 September 2025 and 14 October 2025.
42. La Maida N., Aquilina V. et al The rising trend of MDPHP consumption: an Italian snapshot. *J. Anal. Toxicol*. 2025;**49**:417–421.
43. Online store example (Information retrieved on 15 October 2025) https://www.abcparty.nl/fi/mdphp-pellets-25-mg

Annex 1

17.11.2025
Register number FIMEA/2025/006104

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 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.

Finnish Medicines Agency Fimea
PO Box 55, FI-00034 FIMEA, FINLAND
Tel. +358 29 522 3341
www.fimea.fi
Business ID FI09215366

Annex 1

17.11.2025
Register number FIMEA/2025/006104

23 (29)

Annex 4

23 October 2025
Register number FIMEA/2025/006104

Assessment form as an Annex to the draft measure

Narcotics Act (373/2008), section 3a

SUBSTANCE

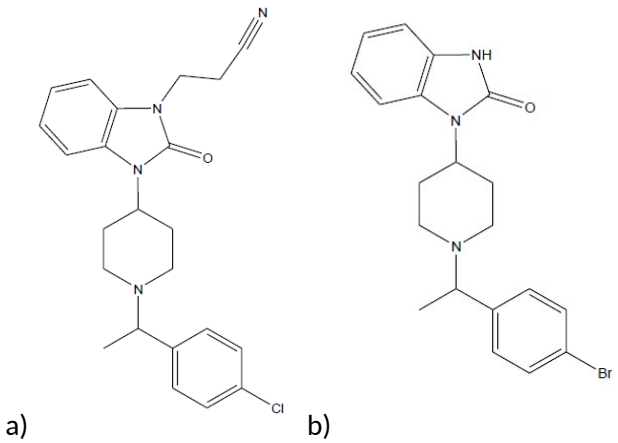
Cychlorphine (3-(3-{1-[1-(4-chlorophenyl)ethyl]piperidine-4-yl}-2-oxo-2,3-dihydro-1*H*-1,3-benzimidazol-1-yl)propanenitrile)

Cychlorphine 3-(3-{1-[1-(4-chlorphenyl)ethyl]piperidine-4-yl}-2-oxo-2,3-dihydro-1*H*-1,3-benzimidazol-1-yl)propannitril

1. Name, synonyms, street names, CAS number

IUPAC name: 3-(3-{1-[1-(4-chlorophenyl)ethyl]piperidine-4-yl}-2-oxo-2,3-dihydro-1*H*-1,3-benzimidazol-1-yl)propanenitrile
Used name: Cychlorphine
Other names: *N*-propionitrile-chlorphine; *N*-propionitrile-chlorophine; cychlorophine
CAS number: 6449-60-1 (alkali); 16145-71-4 (HCl salt)
InChIKey: SWWAVNFEFVMDAG-UHFFFAOYSA-N

2. Chemical structure



a) b)

Cychlorphine (a); and brorphine (b), which is controlled as a narcotic drug by the 1961 UN Single

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

Convention on Narcotic Drugs.
Molecular formula: $C_{23}H_{25}ClN_4O$

Drug class: Opioids

3. Physical properties

Physical state: The substance has been seized as a white powder.

Molecular weight: 408.92 g/mol

4. Mechanism of action

Cychlorphine is a synthetic opioid belonging to the piperidine-benzimidazolone group. Its structure is similar to that of brorphine, which is controlled under the 1961 Single Convention on Narcotic Drugs. Opioids in this chemical group are also called orphines. Orphines differ from opioids in the nitazene group in that they contain a ketone group in their benzimidazole structure, which is referred to as benzimidazolone. Cychlorphine may appear in two mirror-image isomers.

Opioids with an orphine structure have begun to appear on the illicit drug market after fentanyl derivatives and various nitazenes. The typical effects of opioids — analgesia, euphoria, sedation, miosis and respiratory depression — are mediated by their agonistic binding to the μ-opioid receptor in the central nervous system. μ-receptor binding and activation have been shown to be associated with the dependence-producing potential of opioids.

In *in-vitro* studies, brorphine and chlorphine — orphines structurally similar to cychlorphine, with chlorphine containing chlorine instead of bromine — have been found to be μ-opioid receptor agonists comparable to fentanyl and morphine. In mouse studies, they have been shown to be highly effective analgesics.

In *in-vitro* cell studies conducted by the Swedish National Board of Forensic Medicine, cychlorphine was found to be a full μ-opioid receptor agonist, achieving 50% of the receptor's maximal activation (EC50 value) at a concentration of 0.137 nM, which is lower than the corresponding EC50 value of fentanyl (0.829 nM). The results mean that cychlorphine activates the μ-opioid receptor and is about six times more effective than fentanyl.

In vivo experiments with cychlorphine in mice showed that it was 2,300 times more effective than the reference drug pethidine in relieving pain and inducing sedation.

5. Manufacture

The manufacture of so-called orphines is described in patents from the 1960s.

Annex 1

17.11.2025

Register number FIMEA/2025/006104

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

6. Effective doses, abusive doses

In internet discussion forums, users have described cychlorphine as strongly euphoric and sedative (tiring), and similar to protonitazepyne and fentanyl. As an example from the discussions: the duration of the effect of a dose of approximately 3 mg has been described as 8 to 12 hours or even longer. In user reports, the substance has been described as four times stronger than fentanyl, and long-term opioid users warn other potential users about it.

7. Polysubstance use

The polysubstance use of opioids with other central nervous system depressants significantly increases the occurrence of adverse effects; the risk of respiratory depression increases, in particular. 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

Based on the structure and studies carried out, the health risks associated with the misuse of cychlorphine are comparable to the known health risks of fentanyl and other strong opioids, such as other fentanyl derivatives, nitazenes and other orphines.

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.

In the case of new synthetic opioids 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. In overdose cases, the required doses of naloxone may be higher than usual, and monitoring should be continued for longer.

Structurally similar brorphine has been found in several biological samples in connection with post-mortem studies in North America. Other opioids, such as fentanyl, tramadol, isotonitazene and flualprazolam, have also been found in the samples. In the United States, cychlorphine has been reported in seizures and intoxication samples since 2024.

One death from cychlorphine has been reported in Sweden.

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

Public health risks and social risks

The public health and social risks of cychlorphine, like those of other orphines, are comparable to the corresponding risks of strong opioids such as fentanyl and nitazenes.

9. Connection with other forms of crime

No data available.

10. Documented observations on use of the substance

Medical and industrial use

Cychlorphine has no known medicinal or industrial use.

Reported occurrences in Finland

No findings have been reported for cychlorphine in Finland.

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

Cychlorphine was reported to the European Union Drugs Agency by Sweden in February 2025. This was a sample seized by the police in August 2024.

11. Availability

Cychlorphine is available as a reference substance.

12. Use profile

As ‘legal alternatives’, substances that are not controlled may be of particular interest to persons testing new substances. In recent years, numerous new fentanyl derivatives have been classified as narcotics, also under generic classifications in many countries. As a result of this, new nitazene-group opioids have appeared on the market, and once they came under control, opioids from the orphine group subsequently emerged on the market as substitutes for fentanyl derivatives and other opioids, and they may be of particular interest to opioid users.

13. Current status

Cychlorphine is controlled in Finland as a psychoactive substance prohibited from the consumer market (Government decree 1130/2014). In Sweden, cychlorphine was classified as a narcotic in 2025.

14. Other information

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

Although new synthetic opioids make up a relatively small share of the market for new psychoactive substances, they are often considered the most dangerous subgroup, mainly because of their high risk of overdose (European Union Drugs Agency, 2025). Since 2019, an increase in structurally diverse new synthetic opioids not belonging to the fentanyl group has been observed (United Nations Office on Drugs and Crime, 2020).

15. References

44. Pubchem, NCBI, National Library of Medicine. https://pubchem.ncbi.nlm.nih.gov/compound/201662 (Information retrieved 16 September 2025)
45. EDND, EUDA's password-protected database on new psychoactive substances. (Information retrieved 16 September 2025)
46. Contet, C., Kieffer, B. L., & Befort, K. Mu opioid receptor: A gateway to drug addiction. *Curr.Opin. neurobiol*. 2004:**14**(3); 370-378.
47. Vandeputte M.M., Bilel S. et al. Elucidating the harm potential of brorphine analogues as new synthetic opioids: Synthesis, in vitro, and in vivo characterization. *Neuropharmacol.* 2024;**260**:110
48. Klassificeringsdokument, narkotika. Cyclorfin. Folkhälsomyndigheten, 2025. https://www.aklagare.se/globalassets/dokument/narkotikapreparat/c/cyklorfin.pdf (Information retrieved on 22 September 2025).
49. Janssen, & Eycken, V.d. The chemical anatomy of potent morphine-like analgesics. In A. Burger. (Red.), *Drugs affecting the central nervous system* (Vol. 2, p. 25). Marcel Dekker, Inc., 1968.
50. Ujváry I, Christie, R et al. (2021). Dark classics in chemical neuroscience: Etonitazene and related benzimidazoles. *ACS Chem. Neurosci.* 2021;**12(7)**;1072-1092.
51. Janssen, P.A.J., 1965. Benzimidazolinyl Piperidines. U.S. Patent US3196157.
52. Janssen, P.A.J., 1967. Derivatives of Benzimidazolinyl Piperidine. U.S. Patent US3318900A.
53. Internet discussion groups (accessed 12 September 2025): https://www.bluelight.org/community/threads/cyclorphine-will-it-never-end.939720/ https://www.flashback.org/t3579285
54. NDEWS Alert from the NDEWS Web Monitoring Team: Online mentions of Cyclorphine. September 2024: https://ndews.org/wordpress/files/2024/10/9.27.24_Cyclorphine.pdf (Information retrieved on 9 October 2025)
55. Heroin and other opioids – the current situation in Europe. European Union Drugs Agency, 2025. European Drug Report 2025: Trends and Developments.
56. United Nations Office on Drugs and Crime, 2020. The growing complexity of the opioid crisis. Global SMART Update, Volume 24, Global SMART Update. United Nations publication, Vienna.
57. Critical Review Report: Brorphine. WHO, 2021. https://cdn.who.int/media/docs/default-source/essential-medicines/unedited--advance-copy-44th-ecdd-review-report-brorphine.pdf?sfvrsn=d2f0cc18_3&download=true (Information retrieved on 22 September 2025)
58. *N*-Propionitrile Chlorphine NPS Discovery – New Drug Monograph 17 December 2024, Center for Forensic Science Research and Education, United States. https://www.cfsre.org/images/monographs/N-Propionitrile-Chlorphine-New-Drug-Monograph-NPS-Discovery.pdf (Information retrieved on 09 October 2025)
59. Chemicals Register, Finnish Safety and Chemicals Agency (Tukes). Written communication, email on 15 September 2025

fimea

Annex 1

17.11.2025

Register number FIMEA/2025/006104

60. Customs Laboratory statistics. Written communication, email on 15 September 2025
61. Police Forensic Laboratory. Written communication, by email on 16 September 2025
62. Finnish Institute for Health and Welfare, Forensic Toxicology Unit. Written communication, by email on 16 September 2025
63. Online stores (accessed 12 September 2025): https://www.caymanchem.com/product/40326/n-propionitrile-chlorphine-(hydrochloride)
64. Förordning (1992:1554) om kontroll av narkotika. https://www.riksdagen.se/sv/dokument-och-lagar/dokument/svensk-forfattningssamling/forordning-19921554-om-kontroll-av-narkotika_sfs-1992-1554/ (Accessed 12 September 2025)
65. UNODC Laboratory and Scientific Servide Protals, May 2025. Emerging analogues of brorphine. https://www.unodc.org/LSS/Announcement/Details/55d787ca-cec7-4204-90b0-68236305dcaa (Information retrieved on 22 September 2025)
66. ACMD advice on 2-benzyl benzimidazole and piperidine benzimidazolone opioids", Research and analysis, latest update 29 January 2025. https://www.gov.uk/government/publications/acmd-advice-on-2-benzyl-benzimidazole-and-piperidine-benzimidazolone-opioids (Information retrieved on 22 September 2025)

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 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.

Finnish Medicines Agency Fimea
PO Box 55, FI-00034 FIMEA, FINLAND
Tel. +358 29 522 3341
www.fimea.fi
Business ID FI-09215366