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2.4.2025
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Assessment form as an Annex to the draft measure

Narcotics Act (373/2008), section 3a

SUBSTANCE

Fluetonitazene

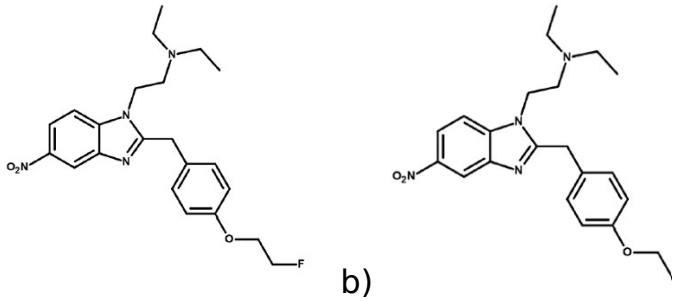
1. Name, synonyms, street names, CAS number

IUPAC name: *N,N*-diethyl-2-[2-[[4-(2-fluoroethoxy)phenyl]methyl]-5-nitro-1*H*-benzimidazole-1-yl]-1-ethanamine

Used name: Fluetonitazene

Other names: *N,N*-diethyl-2-(2-{[4-(2-fluoroethoxy)phenyl]methyl}-5-nitro-1*H*-1,3-benzimidazole-1-yl)-1-ethanamine, F-Etonitazene; F-Eto; 2F-Eto; 2F-Etonitazene; Fluoro-Etonitazene; 4'-(2-fluoroethoxy) nitazene
CAS number: Not known
InChIKey: XCWWXPKOMYPTRP-UHFFFAOYSA-N

2. Chemical structure



a) b)

Molecular formula: $C_{22}H_{27}FN_4O_3$
Drug class: Opioids
The figure shows (a) fluetonitazene and (b) etonitazene controlled under the 1961 Single Convention on Narcotic Drugs.

3. Physical properties

Physical state: Fluetonitazene has been seized in tablet, powder and liquid form.

Molecular weight: 414.47 g/mol

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4. Mechanism of action

Fluetonitazene has a 5-nitro-2-benzylbenzimidazole structure, and it is structurally a fluorinated derivative of of the internationally controlled drug etonitazene. The ethoxy group of etonitazene in the benzyl ring has been replaced in fluetonitazene by the fluoroethoxy group. Etonitazene was one of the first synthesized nitazenes and has been controlled under the 1961 Convention since the 1960s.

The research and development of new opioid painkillers in the 1950s and 60s resulted in the discovery of several 2-benzylbenzimidazole compounds with analgesic properties that are significantly more effective than those of 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.

These so-called nitazene opioids have been detected in the substance abuse market sporadically over the years, but increasingly since 2019. They have also been marketed as an alternative to more well-known opioids used as narcotics, such as heroin and fentanyl. By mid-March 2025, 23 different types of nitazene have been reported to the European monitoring mechanism. There is still limited scientific knowledge on many nitazenes. The World Health Organisation has evaluated the properties of ten of them between 2020 and 2024, all of which have been placed under international control as narcotics. This indicates that nitazenes are dangerous and their misuse has spread.

Based on the structure, the mechanism of action of fluetonitazene is similar to that of other opioids, i.e. the effect is mainly delivered in the central nervous system as a full μ-opioid receptor agonist. The subsequent 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. Based on unpublished *in vitro* studies, fluetonitazepyne is similar in potency to etonitazene and would therefore also be significantly more potent than fentanyl.

5. Manufacture

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

6. Effective doses, abusive doses

No information is available on the effective or abusive doses of fluetonitazene. Seized samples indicate that the substance may have been used orally, by snorting or intravenously.

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7. Polysubstance use

The polysubstance use of opioids with other central nervous system depressants significantly increases the occurrence of adverse effects; in particular, the risk of respiratory depression increases. 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 fluetonitazene. Based on the structure, it is expected that the health risks associated with the misuse of fluetonitazene are comparable to the known health risks of strong opioids such as 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 and the consequent health risks 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 nitazene 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. Naloxone helps in cases of overdose. 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 fluetonitazene, as with other nitazenes, are comparable to those of heroin and fentanyl.

9. Connection with other forms of crime

No information

10. Documented observations on use of the substance

Medical and industrial use

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Fluetonitazene has no known medicinal or industrial use.

Reported occurrences in Finland

At the time of drafting the assessment, the Customs Laboratory is examining two samples suspected to contain fluetonitazene.

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

Fluetonitazene was reported by the European Drug Agency (EUDA) in Germany in April 2024 and placed under special monitoring by EUDA on 13 March 2025.

11. Availability

Fluetonitazene 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. As a result, new substances such as fluetonitazene are marketed as a substitute for fentanyl derivatives 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

Fluetonitazene is controlled in Finland by Government Decree 1130/2024 as a substance banned from the consumer market.

14. Other information

The United Nations Office on Drugs and Crime (UNODC) has recently highlighted the global spread of nitazenes and its potential dangers. Since 2019 and by mid-March 2025, 23 new opioids belonging to the nitazene group have been reported to the European Drugs Agency. Of these, 7 were reported in 2024.

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. Synthetic opioids belonging to the nitazene family have also been seized in Finland, and this year, suspected deaths have been reported due to the misuse of nitazenes.

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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, be added to the Government Decree (543/2008) on substances, plants and products to be classified as narcotics (Annex IV).

Signatures

This summary is an annex to the electronically signed document.

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Narcotics Act (373/2008), section 3a

SUBSTANCE

Fluetonitazepyne

1. Name, synonyms, street names, CAS number

IUPAC name: 2-{[4-(2-fluoroethoxy)phenyl]methyl}-5-nitro-1-[2-(pyrrolidin-1-yl)ethyl]-1*H*-benzimidazole.

Used name: Fluetonitazepyne

Other names: 2-{[4-(2-fluoroethoxy)phenyl]methyl}-5-nitro-1-[2-(pyrrolidin-1-yl)ethyl]-1*H*-1,3- benzimidazole, 2-{[4-(2-fluoroethoxy)phenyl]methyl}-5-nitro-1-[2-(pyrrolidin-1-yl)-ethyl benzimidazole; 2-{[4-(2-fluoroethoxy)benzyl}-5-nitro-1-(2-(pyrrolidin-1-yl)-1*H*-benzo[d]imidazole; *N*-pyrrolidinefluonitazene, 2F-etonitazepyne

CAS number: Not known

InChIKey: TYLHUWCBBIQCEH-UHFFFAOYSA-N

2. Chemical structure

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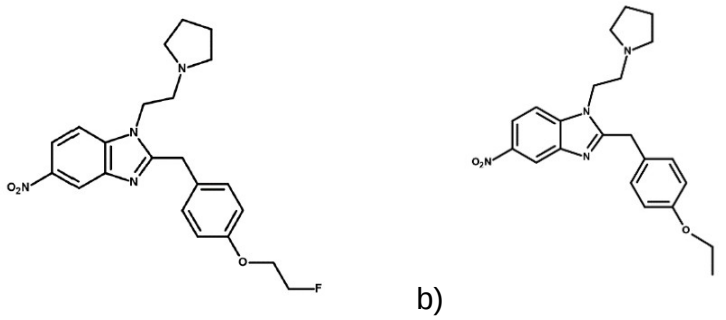

a) b)

Molecular formula: $C_{22}H_{25}FN_4O_3$
Drug class: Opioids
The figure shows (a) fluetonitazepyne and (b) etonitazepyne, which was classified as a narcotic in Finland 2022 and added to the 1961 Single Convention on Narcotic Drugs in 2023.

3. Physical properties

Physical state: The substance has been seized as a yellow powder and in liquid form.

Molecular weight: 412.45 g/mol

4. Mechanism of action

Fluetonitazepyne has a 5-nitro-2-benzylbenzimidazole structure, and it is a fluorinated derivative of of the internationally controlled drug etonitazepyne. The ethoxy group of etonitazepyne in the benzyl group has been replaced in fluetonitazepyne by the fluoroethoxy group.

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.

These so-called nitazene opioids have increasingly appeared on the substance abuse market since 2019, and they have also been marketed as an alternative to more well-known opioids used as narcotics, such as heroin and fentanyl. By mid-March 2025, 23 different types of nitazene have been reported to the European monitoring mechanism. There is still limited scientific knowledge on many nitazenes. The World Health Organisation has evaluated the properties of ten new nitazenes between 2020 and 2024, all of which have also been placed under international control as narcotics. This indicates that nitazenes are dangerous and their misuse has spread.

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Based on the structure, the mechanism of action of fluetonitazepyne 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.

Etonitazepyne, which is similar to fluetonitazepyne, has been evaluated by the World Health Organisation's Committee of Experts on Drug Abuse Potential (ECDD) in 2022. Etonitazepyne is in the same range of potency as etonitazene, which is considered to be the most potent nitazene. Based on unpublished in vitro studies, fluetonitazepyne is similar in potency to etonitazene and etonitazepyne and would therefore also be significantly more potent than fentanyl.

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 fluetonitazepyne. Seized samples indicate that the substance has been used orally, by snorting or intravenously. In particular, snorting (nasal administration) has been described as a popular route of administration for etonitazepyne, which is structurally similar.

7. Polysubstance use

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

<u>Health risks to the individual</u>
No safety or toxicology studies are known to have been published for fluetonitazepyne. Based on the structure and reported adverse effects, the health risks associated with the misuse of fluetonitazepyne 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

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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 helps in cases of overdose. The required doses may be higher than usual and follow-up should be continued for longer.

Serious poisoning cases and deaths have been reported in Europe and North America as a result of the use of the structurally similar etonitazepyne.

According to information from the police, there are several suspected fatal cases of overdose caused by fluetonitazepyne in the Kymenlaakso and Häme regions in Finland between December 2024 and February 2025.

Public health risks and social risks
The public health and social risks of fluetonitazepyne, as with other nitazenes, are comparable to those of heroin and fentanyl.

9. Connection with other forms of crime

No information.

10. Documented observations on use of the substance

Medical and industrial use
Fluetonitazepyne has no known medicinal or industrial use.

Reported occurrences in Finland
According to police data, several suspected fatal cases of overdose associated with the administration of fluetonitazepyne have been reported in the Kymenlaakso and Häme regions between December 2024 and February 2025. In 2025, fluetonitazepyne has been found in four samples analysed by the forensic laboratory of the National Bureau of Investigation and in four autopsies conducted by the Finnish Institute for Health and Welfare. The Customs Laboratory has also reported that ongoing analyses include a suspected case of fluetonitazepyne.

Fluetonitazepyne has also been discussed in Finnish-language online discussion forums during the first months of 2025.

Reporting in the EU and to the EMCDDA Early Warning System (EWS)
Fluetonitazepyne was reported to the European Union Drugs Agency by Italy in

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September 2024. The sample in question had been seized by the police in July and had come to Italy from Germany. In July 2024, the substance was also identified in a test purchase batch analysed in Germany. In Austria, a suspected death has been reported where fluetonitazepyne has been found at the scene.

11. Availability

Fluetonitazepyne 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 fluetonitazepyne, 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

Fluetonitazepyne is not controlled in Finland under the Narcotics Act or the Medicines Act.

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 mid-March 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.

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 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).

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Signatures

This summary is an annex to the electronically signed document.

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Narcotics Act (373/2008), section 3a

SUBSTANCE

Isobutonitazene

1. Name, synonyms, street names, CAS number

IUPAC name: *N,N*-diethyl-2-[2-[(4-isobutoxyphenyl)methyl]- 5-nitro-benzimidazol-1-yl]-1-ethanamine or *N,N*-diethyl-2-(2-{[4-(2-methylpropoxy)phenyl]methyl}-5-nitro-1*H*-1,3-benzimidazol-1-yl)ethane-1-amine

Used name: Isobutonitazene

CAS number: Not known

InChI Key: KQZNQVXEZPNJQC-UHFFFAOYSA

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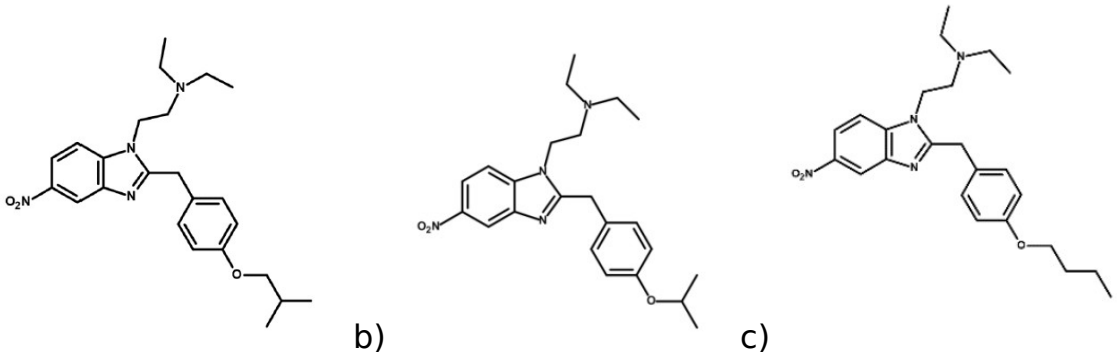
2. Chemical structure



a) b) c)

Molecular formula: $C_{24}H_{32}N_4O_3$
Drug class: Opioids
The figure shows (a) isobutonitazene and the structurally similar (b) isotonitazene and (c) butonitazene, which are included in the 1961 Single Convention on Narcotic Drugs.

3. Physical properties

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

Molecular weight: 424.54 g/mol

4. Mechanism of action

Isobutonitazene has a 5-nitro-2-benzylbenzimidazole structure, and it is structurally most similar to isotonitazene and butonitazene, which are internationally controlled narcotics. The isopropoxy group of isotonitazene in the benzyl group has been replaced in isobutonitazene by the isobutoxy group. The structural isomer of isobutonitazene, butonitazene, was placed under international control by the UN Single Convention on Narcotic Drugs in June 2024.

The research and development of new opioid painkillers in the 1950s and 60s resulted in the synthesis 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.

These so-called nitazene opioids have been detected in the substance abuse market sporadically over the years, but increasingly since 2019. By mid-March 2025, 23 different types of nitazene have been reported to the European monitoring mechanism. There is limited published research data on many of these. The World

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Health Organisation has evaluated the properties of ten new nitazenes between 2020 and 2024, all of which have also been placed under international control as narcotics. This indicates that nitazenes are dangerous and their misuse has spread.

Based on the structure, the mechanism of action of isobutonitazene is similar to that of other opioids, i.e. the effect is mainly delivered in the central nervous system as a full μ-opioid receptor agonist. Effects may include euphoria, relaxation, pain relief, sedation, slowing of heart function, hypothermia and slowing of breathing. The latter effect poses a serious health risk at increasing doses. *In vitro* studies have shown that isobutonitazene is about three times more potent as an opioid receptor agonist (EC50=10.3 nM) than butonitazene (EC50=34.2 nM).

5. Manufacture

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

6. Effective doses, abusive doses

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

7. Polysubstance use

The polysubstance use of opioids with other central nervous system depressants significantly increases the occurrence of adverse effects; in particular, the risk of respiratory depression increases. 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 toxicological studies are known to have been published for isobutonitazene. Based on the structure and conducted studies, it is expected that the health risks associated with the misuse of isobutonitazene are comparable to the known health risks of strong opioids such as 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 and the consequent health risks 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. Naloxone helps in cases of overdose. The required doses may be higher than usual and follow-up should be continued for

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longer.

Particularly in the case of new nitazenes that end up being used as narcotics, the health risk posed is significant, because as strong opioids they can cause life-threatening poisoning even at very small doses.

Public health risks and social risks
The public health and social risks of isobutonitazene, as with other nitazenes, are comparable to those of fentanyl and its derivatives.

9. Connection with other forms of crime

No information.

10. Documented observations on use of the substance

Medical and industrial use

Isobutonitazene has no known medicinal use.

Reported occurrences in Finland

Customs, the Forensic Laboratory or the Finnish Institute for Health and Welfare have not found occurrences of isobutonitazene in their investigations.

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

Isobutonitazene was reported to the EU Drugs Agency in November 2023 by Norway, where the substance had been seized by customs in May and June 2023.

11. Availability

Isobutonitazene 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 nitazenes such as isobutonitazene are marketed as a substitute for fentanyl derivatives, and may be of particular interest to opioid users. As ‘legal alternatives’, substances that are not subject to drug control may be of particular interest to persons testing new substances.

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13. Current status

Isobutonitazene is not controlled in Finland under the Narcotics Act or the Medicines Act.

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 mid-March 2025, 23 new opioids belonging to the nitazene group have been reported to the European Drugs Agency. Of these, 7 were reported in 2024.

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. Various synthetic opioids belonging to the nitazene family have been seized in Finland, and this year, suspected deaths have been reported due to the misuse of nitazenes.

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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 be added to the Government Decree (543/2008) on substances, plants and products to be classified as narcotics (Annex IV).

Signatures

This summary is an annex to the electronically signed document.

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Assessment form as an Annex to the draft measure

Narcotics Act (373/2008), section 3a

SUBSTANCE

Isotonitazepyne

1. Name, synonyms, street names, CAS number

IUPAC name: 2-[(4-isopropoxyphenyl)methyl]- 5-nitro-1-(2-pyrrolidin-1-ylethyl)-1*H*-benzimidazole

Used name: Isotonitazepyne, *N*-pyrrolidino isotonitazene

Other names: 5-nitro-2-({4-[propan-2-yl)oxy]phenyl}methyl)-1-[2-(pyrrolidin-1-yl)ethyl]-1*H*-1,3-benzimidazole, 2-[(4-isopropoxyphenyl)methyl]-5-nitro-1-(2-pyrrolidin-1-ylethyl)benzimidazole, 2-(4-isopropoxybenzyl)-5-nitro-1-(2-(pyrrolidin-1-yl)ethyl)-*1H*-benzo[*d*]imidazole, 2-(4-isopropoxybenzyl)-5-nitro-1-[2-(1-pyrrolidinyl)ethyl]-1*H*-benzimidazole, 2-[[4-(1-methyleoxy)phenyl]methyl]-5-nitro-1-[2-(1-pyrrolidinyl)ethyl]-1*H*-benzimidazole

CAS number: 3053113-12-2

InChIKey: VRKDSDBBRNHHCR-UHFFFAOYSA-N

2. Chemical structure

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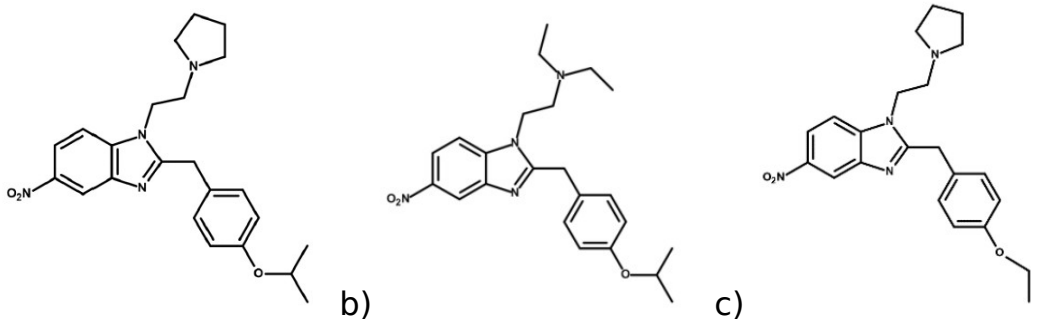

a) b) c)

Molecular formula: $C_{24}H_{32}N_4O_3$

Drug class: Opioids

The figure shows (a) isotonitazepyne as well as isotonitazene (b) and etonitazepyne (c), which are internationally controlled as narcotics.

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3. Physical properties

Physical state: Isotonitazepyne has been seized in the form of yellow or beige powder. The substance has also been found in yellow tablets, which had been claimed to be oxycodone tablets.

Molecular weight: 408.49 g/mol

4. Mechanism of action

Isotonitazepyne has a 2-benzylbenzimidazole structure. It is structurally similar to isotonitazene and etonitazepyne, which are controlled internationally as narcotics. Isotonitazepyne as well as etonitazepipne and protonitazepyne, which were reported to the European Drugs Agency in 2023 and 2024, are structural isomers, which may pose challenges in distinguishing between these substances through analytical methods.

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.

These so-called nitazene opioids have increasingly appeared on the substance abuse market since 2019, and they have also been marketed as an alternative to more well-known opioids used as narcotics, such as heroin and fentanyl. By mid-March 2025, 23 different types of nitazene have been reported to the European monitoring mechanism. There is still limited scientific knowledge on many nitazenes. The World Health Organisation has evaluated the properties of ten new nitazenes between 2020 and 2024, all of which have also been placed under international control as narcotics. This indicates that nitazenes are dangerous and their misuse has spread.

Based on the structure, the mechanism of action of fluetonitazepyne 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.

Etonitazepyne, which is similar to isotonitazepyne, has been evaluated by the World Health Organisation’s Committee of Experts on Drug Abuse Potential (ECDD) in 2022. Etonitazepyne is in the same range of potency as etonitazene, which is considered to be the most potent nitazene.

Based on the results of an *in vitro* study, isotonitazepyne binds to the μ-opioid

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receptor selectively and almost five times more strongly than fentanyl (EC_{50} 0.260 nM vs. 1.255) and activates the same receptor 40 times more strongly than fentanyl (EC_{50} 0.574 vs 22.7 mM).
In a second *in vitro* study, isotonitazepyne was found to be approximately 1100 times more potent than morphine and 90 times more potent than fentanyl in the μ-opioid receptor activation test (MORβarr2 assay, EC_{50} isotonitazepyne 0.288 nm vs. morphine 327 nm and fentanyl 25.7 nm).

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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 isotonitazepyne. In particular, snorting (nasal administration) has been described as a popular route of administration for etonitazepyne, which is structurally similar.

7. Polysubstance use

The polysubstance use of opioids with other central nervous system depressants significantly increases the occurrence of adverse effects; in particular, the risk of respiratory depression increases. 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 toxicological studies are known to have been published for isotonitazepyne. Based on the structure and reported adverse effects, the health risks associated with the misuse of isotonitazepyne 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. Isotonitazepyne has been reported to be associated with at least one death in the Netherlands.

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 helps in cases of overdose. The required doses may be higher than usual and follow-up should be continued for longer.

Serious poisoning cases and deaths have been reported in Europe and North America as a result of the use of the structurally similar etonitazepyne.

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Public health risks and social risks

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

Isotonitazepyne has no known medicinal or industrial use.

Reported occurrences in Finland

Occurrences of isotonitazepyne have not been observed in Finland.

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

On 14 March 2025, Germany’s submitted an official notification on isotonitazepyne to the European Union Drugs Agency (EUDA). Isotonitazepyne has been found in 2024 and 2025 in three Member States. The EUDA placed isotonitazene under enhanced monitoring on 17 March 2025.

11. Availability

Isotonitazepyne is available as a reference substance, and it is also marketed on open online marketplaces.

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 isotonitazepyne, 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

Isotonitazepyne is not controlled in Finland under the Narcotics Act or the Medicines Act.

14. Other information

The United Nations Office on Drugs and Crime (UNODC) has recently highlighted the

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global spread and dangers posed by nitazenes. Since 2019 and by mid-March 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.

In recent years, poisoning cases involving a nitazene have been reported around the world, including in Finland, 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, be added to the Government Decree (543/2008) on substances, plants and products to be classified as narcotics (Annex IV).

Signatures

This summary is an annex to the electronically signed document.

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