APPROVED 6/4/2024

A RESOLUTION

Section 1: Summary

The Ohio Board of Pharmacy (BOP), pursuant to section 3719.45 of the Ohio Revised Code, proposes the emergency placement of the following nine compounds into Schedule I:

1. *N*-Pyrrolidino metonitazene (2-(4-methoxybenzyl)-5-nitro-1-(2-(pyrrolidin-1-yl)ethyl)-1H-benzo[d]imidazole, 2-hydroxy-1,2,3-propanetricarboxylate);
2. *N*-Pyrrolidino protonitazene (5-nitro-2-(4-propoxybenzyl)-1-(2-(pyrrolidin-1-yl)ethyl)-1H-benzo[d]imidazole);
3. Ethyleneoxynitazene (2-(2-((2,3-dihydrobenzofuran-5-yl)methyl)-5-nitro-1H-benzo[d]imidazol-1-yl)-N,N-diethylethan-1-amine, 2-hydroxypropane-1,2,3-tricarboxylic acid);
4. *N*-Desethyl isotonitazene (N-(2-(3-ethyl-2-oxoimidazolidin-1-yl)-5-nitrophenyl)-2-(4-isopropoxyphenyl)acetamide);
5. 5-Methyl etodesnitazene (2-[(4-ethoxyphenyl)methyl]-N,N-diethyl-5-methyl-1H-benzimidazole-1-ethanamine, 2-hydroxypropane-1,2,3-tricarboxylic acid);
6. 3', 4'-Methylenedioxynitazene (2-(2-(benzo[d][1,3]dioxol-5-ylmethyl)-5-nitro-1H-benzo[d]imidazol-1-yl)-N,N-diethylethan-1-amine);
7. *N*-Pyrrolidino Isotonitazene (2-(4-isopropoxybenzyl)-5-nitro-1-(2-(pyrrolidin-1-yl)ethyl)-1H-benzo[d]imidazole, 2-hydroxy-1,2,3-propanetricarboxylate);
8. Ethylene etonitazene (2-(2-(4-ethoxyphenethyl)-5-nitro-1H-benzo[d]imidazol-1-yl)-N,N-diethylethan-1-amine, 2-hydroxypropane-1,2,3-tricarboxylic acid); and
9. N-Desethyl etonitazene (2-[(4-ethoxyphenyl)methyl]-N-ethyl-5-nitro-1H-benzimidazole-1-ethanamine).

Section 2: Background

Pursuant to section 3719.45 of the Ohio Revised Code, the Board may, "by emergency rule adopted in accordance with division (G) of section 119.03 of the Revised Code . . . add a previously unscheduled compound . . . to schedule I if the board determines that the

compound . . . has no accepted medical use in treatment in this state and poses an imminent hazard to the public health, safety, or welfare."

In making a determination to add an unscheduled compound, the Board is required to consider the following 3 criteria:

(1) The actual or relative potential for abuse;
(2) The scope, duration, and significance of abuse; and
(3) The risk to the public health.

Section 3: Evaluation of the Compounds Pursuant to ORC 3719.45

(1) The actual or relative potential for abuse.

As previously recognized by the Board, the growing availability and abuse of novel psychoactive substances[1] (NPSs) over the past decade is unparalleled. A subset of NPSs are new synthetic opioids (NSOs). Attributed by some to a 2018 control measures in China aimed at reducing the availability of fentanyl-related compounds, new non-fentanyl NSOs, such as "nitazene" compounds, continue to appear in the illicit market.

Many of the NSOs illicitly available today were synthesized by pharmaceutical companies in the second half of the twentieth century. These syntheses were designed in an effort to identify compounds that are safer and more effective alternatives to morphine. Published literature related to these efforts—including patents—serve as a database for underground chemists to manufacture gray market NSOs.

Nitazenes have a high potential for abuse. As early as 1975, Alexander Shulgin suggested that nitazenes were "a fertile field for the search for heroin substitutes that can be domestically synthesized and are potent at levels that would encourage illicit investigation." Moreover, Blanckaert and others (2019) warn that, "[s]ince multiple substances in the [nitazene] class trump morphine's potency by at least an order of magnitude, the number of future possible [nitazene] opioids cannot be underestimated." This is reinforced by the fact that the number of new nitazene compounds identified has grown each year since 2021.

[1] NPSs are defined by the United Nations Office on Drugs and Crime (UNODC) as, "substance of abuse, either in pure form or a preparation, that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, but which may pose a public health threat."

Actual abuse of nitazene compounds has grown in both the United States and abroad. The presence of unscheduled nitazenes has been relayed by several forensic lab systems in Ohio. This includes the confirmed presence of *N*-Pyrrolidino metonitazene; *N*-Pyrrolidino protonitazene; Ethyleneoxynitazene; *N*-Desethyl Isotonitazene; 5-Methyl etodesnitazene; 3', 4'-Methylenedioxynitazene; *N*-Pyrrolidino isotonitazene; Ethylene etonitaze; and N-Desethyl etonitazene.

Although these nine nitazene compounds may be found to be controlled substance analogs, inconsistent reporting across lab systems renders quantifying actual abuse elusive. For instance, case law in certain court jurisdictions may create barriers to prosecution for trafficking analogs or labs may not target their analysis for the identification of the non-controlled substance when a more common controlled substance is present. Further compounding this issue for the subject compounds is that many nitazenes are highly potent and the concentration of some may fall below standard laboratory detection levels.

References:

Vandeputte MM, Cannaert A, Stove CP. In vitro functional characterization of a panel of non-fentanyl opioid new psychoactive substances. Arch Toxicol. 94(11):3819-3830. (2020).

Vandeputte MM, Uytfanghe KV, Layle NK, St. Germaine DM, Iula DM, Stove CP. Synthesis, Chemical Characterization, and μ-Opioid Receptor Activity Assessment of the Emerging Group of 'Nitazene' 2-Benzylbenzimidazole Synthetic Opioids. ACS Chem. Neurosci. 2021, 12, 1241–1251.

Lamy FR, Daniulaityte R, Barratt MJ, Lokala U, Sheth A, Carlson RG. Listed for sale: Analyzing data on fenanty, fentanyl analogs and other novel synthetic opioids on one cryptomarket. Drug and Alcohol Dependence. 213 (2020) 108115.

Blanckaert P, Cannaert A, Van Uytfanghe K, Hulpia F, Deconick E, Van Calenbergh S, Stove C. Report on a Novel Emerging Class of Highly Potent Benzimidazole NPS Opioids: Chemical and In Vitro Functional Characterization of Isotonitazene. Drug Test Anal. 2020; 12:422–430.

Schedules of Controlled Substances: Temporary Placement of Butonitozene, Etodesnitazene, Flunitazene, Metodesnitazene, Metonitazene, N-pyrrolidino etonitazene, and Protonitazene in Schedule I; Drug Enforcement Administration; 86 Fed. Reg. 69,182 (Dec. 7, 2021).

UNODC, February 2024 – UNDOC EWA: Nitazenes – a new group of synthetic opioids emerges, 2024, available at https://www.unodc.org/LSS/Announcement/Details/cbec8f4c-73aa-49ee-9e2b-75620af8a910 (last visited May 14, 2024).

EDSWG Quarterly Meetings, Cols. OH, (2021, 2022, 2023, and 2024).

(2) The scope, duration, and significance of abuse.

The scope, duration, and significance of opioid abuse is well-characterized. Illicitly available NSOs deviate from the classical fentanyl and morphinan chemical structures. The vast variety of molecular modifications render the identification of NSOs in both drug seizure and toxicology evidence arduous.

Although these nine nitazene compounds may be found to be controlled substance analogs, inconsistent reporting across lab systems renders quantifying actual abuse elusive. For instance, case law in certain court jurisdictions may create barriers to prosecution for trafficking analogs or labs may not target their analysis for the identification of the non-controlled substance when a more common controlled substance is present. Nonetheless, it is known that as opioid abuse continues to rise, so too do efforts by clandestine chemists to synthesize and distribute NSOs that skirt chemical control policies.

Following the pattern of other NPSs before them, nitazenes are a public health concern that are continuing to grow. This is due in no small part to the efforts of clandestine chemists to undermine prohibitions on the possession and trafficking of nitazenes. These efforts merit additional counter-control measures.

Moreover, data from law enforcement suggest that these nine compounds are being abused recreationally in Ohio. Each has been confirmed by an Ohio crime lab. Although law enforcement data are not direct evidence of abuse, they are used to establish an inference that drugs are being diverted and abused.

Evidence from the dark web compiled by the Ohio Narcotics Intelligence Center (ONIC), demonstrates the availability and interest in nitazene compounds for illicit use. Of note, dark web users and vendors often refer to N-pyrro compounds as “pyne” drugs. Examples of such posts can be found in Appendix I of this document.

References:

Schedules of Controlled Substances: Temporary Placement of N-Desethyl Isotonitazene and N-Piperidinyl Etonitazene in Schedule I; Drug Enforcement Administration; 88 Fed. Reg. No. 205, 73293, 73294 (Oct. 25, 2023).

Ohio Narcotics Intelligence Center. Dark Web Research. Completed May 21, 2024 (documentation on file with ONIC).

EDSWG Quarterly Meetings, Cols. OH, (2022, 2023, and 2024).

(3) The risk to the public health.

Synthetic opioids are the primary cause of deaths related to unintentional drug poisonings in the United States. Nitazene compounds contribute to those poisonings. Indeed, in its October 25, 2023, Notice of Intent to Schedule new nitazene compounds, the DEA stated that, "the continued trafficking and identification of benzimidazole-opioids in toxicology cases pose a significant threat to public health and safety. Adverse health effects associated with the misuse and abuse of synthetic opioids have led to devastating consequences including death."

Nitazenes have a high abuse potential. In 1975, Alexander Shulgin suggested that nitazenes were "a fertile field for the search for heroin substitutes that can be domestically synthesized and are potent at levels that would encourage illicit investigation." Moreover, Blanckaert and others (2019) warn that, "[s]ince multiple substances in the [nitazene] class trump morphine's potency by at least an order of magnitude, the number of future possible [nitazene] opioids cannot be underestimated."

Several nitazene compounds are known to be highly potent and to present an elevated risk of death caused by unintentional drug poisonings. In multiple unintentional drug poisonings, nitazenes have been the only compounds reported and assessed to be causal or contributory to the negative health outcome.

References:

Schedules of Controlled Substances: Temporary Placement of Butonitozene, Etodesnitazene, Flunitazene, Metodesnitazene, Metonitazene, N-pyrrolidino etonitazene, and Protonitazene in Schedule I; Drug Enforcement Administration; 86 Fed. Reg. No. 232, 69182 (Dec. 7, 2021).

Schedules of Controlled Substances: Temporary Placement of N-Desethyl Isotonitazene and N-Piperidinyl Etonitazene in Schedule I; Drug Enforcement Administration; 88 Fed. Reg. No. 205, 73293, 73294 (Oct. 25, 2023).

Vandeputte MM, Cannaert A, Stove CP. In vitro functional characterization of a panel of non-fentanyl opioid new psychoactive substances. Arch Toxicol. 94(11):3819-3830. (2020).

Blanckaert P, Cannaert A, Van Uytfanghe K, Hulpia F, Deconick E, Van Calenbergh S, Stove C. Report on a Novel Emerging Class of Highly Potent Benzimidazole NPS Opioids: Chemical and In Vitro Functional Characterization of Isotonitazene. Drug Test Anal. 2020; 12:422–430.

UNODC, February 2024 – UNDOC EWA: Nitazenes – a new group of synthetic opioids emerges, 2024, available at https://www.unodc.org/LSS/Announcement/Details/cbec8f4c-73aa-49ee-9e2b-75620af8a910 (last visited May 14, 2024).

Volpe DA, McMahon Tobin GA, Mellon RD, Kadki AG, Parker RJ, Colatsky T, Kropp TJ, Verbois SL (2011). Univorm assessment and ranking of opioid Mu receptor binding constants for selected opioid drugs. Reg. Tox. and Pharm. 59(2011) 385–390.

Blanckaert P, Cannaert A, Van Uytfanghe K, Hulpia F, Deconick E, Van Calenbergh S, Stove C. Report on a Novel Emerging Class of Highly Potent Benzimidazole NPS Opioids: Chemical and In Vitro Functional Characterization of Isotonitazene. Drug Test Anal. 2020; 12:422–430.

Section 4: Finding of the Board

Section 3719.45 of the Revised Code authorizes that the Ohio Board of Pharmacy to add a compound, mixture, preparation, or substance to Schedule I if the Board determines that it has no accepted medical use in treatment in this state and poses an imminent hazard to the public health, safety, or welfare.

After a thorough review of all available data, the Ohio Board of Pharmacy finds that the compounds listed in Section 1 of this Resolution meet the following criteria:

1. Have a high potential for abuse;
2. Have no accepted medical use in treatment in this state;
3. Lack accepted safety for use in treatment under medical supervision; and
4. Pose a risk to the public health of the citizens in this state.

Based on these findings, the Board hereby concludes that these compounds should be controlled as Schedule I narcotic-opiates and hereby issues a resolution requesting the Governor to issue an Executive Order pursuant to division (G) of section 119.03 of the Revised Code to file emergency rule 4729:9-1-01.2 of the Administrative Code as listed in Section 5 of this document.

Section 5: Proposed Rule

4729:9-1-01.2 – Nitazene compounds. (NEW)

Pursuant to section 3719.45 of the Revised Code, the state board of pharmacy hereby classifies as schedule I any of the following opiates, including their salts, isomers, and salts of isomers, unless specifically excepted under federal drug abuse control laws, whenever the existence of these salts, isomers, and salts of isomers is possible within the specific chemical designation:

(A) *N*-Pyrrolidino metonitazene (2-(4-methoxybenzyl)-5-nitro-1-(2-(pyrrolidin-1-yl)ethyl)-1H-benzo[d]imidazole, 2-hydroxy-1,2,3-propanetricarboxylate).

(B) *N*-Pyrrolidino protonitazene (5-nitro-2-(4-propoxybenzyl)-1-(2-(pyrrolidin-1-yl)ethyl)-1H-benzo[d]imidazole).

(C) Ethyleneoxynitazene (2-(2-((2,3-dihydrobenzofuran-5-yl)methyl)-5-nitro-1H-benzo[d]imidazol-1-yl)-N,N-diethylethan-1-amine, 2-hydroxypropane-1,2,3-tricarboxylic acid).

(D) *N*-Desethyl isotonitazene (N-(2-(3-ethyl-2-oxoimidazolidin-1-yl)-5-nitrophenyl)-2-(4-isopropoxyphenyl)acetamide).

(E) 5-Methyl etodesnitazene (2-[(4-ethoxyphenyl)methyl]-N,N-diethyl-5-methyl-1H-benzimidazole-1-ethanamine, 2-hydroxypropane-1,2,3-tricarboxylic acid).

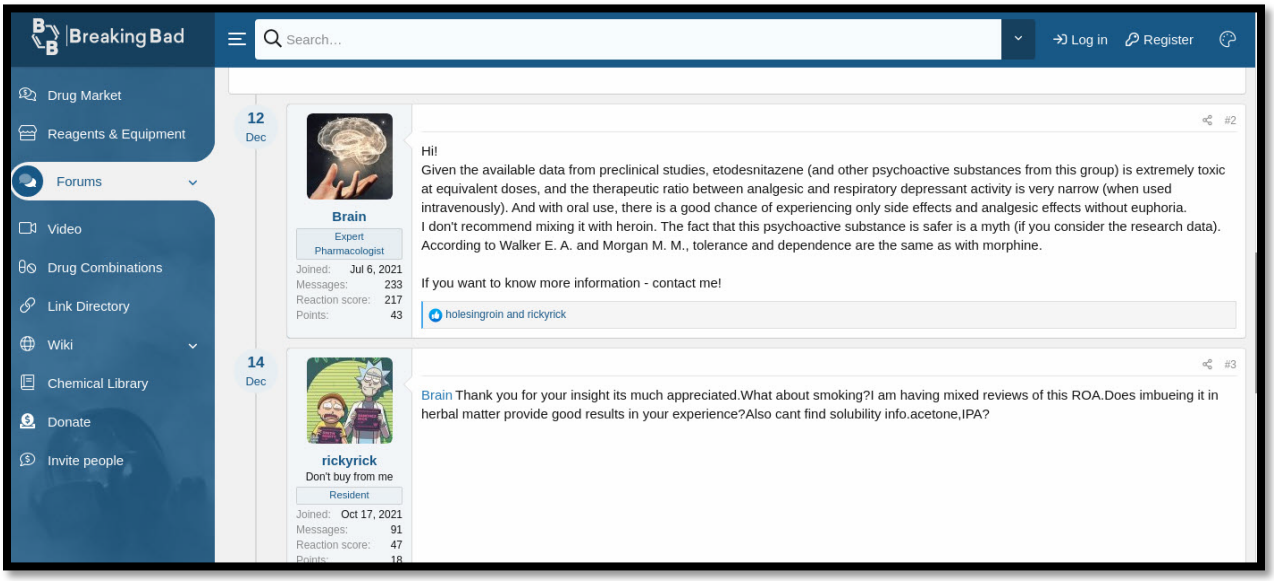
(F) 3', 4'-Methylenedioxynitazene (2-(2-(benzo[d][1,3]dioxol-5-ylmethyl)-5-nitro-1H-benzo[d]imidazol-1-yl)-N,N-diethylethan-1-amine).

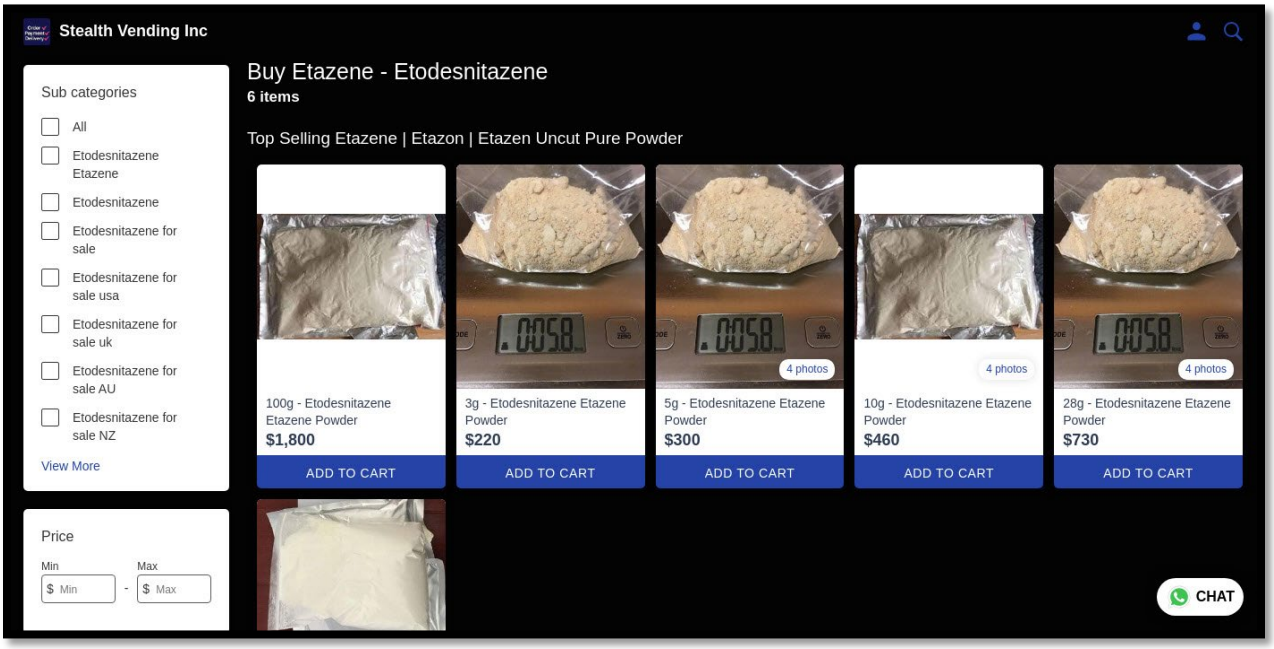
(G) *N*-Pyrrolidino Isotonitazene (2-(4-isopropoxybenzyl)-5-nitro-1-(2-(pyrrolidin-1-yl)ethyl)-1H-benzo[d]imidazole, 2-hydroxy-1,2,3-propanetricarboxylate).

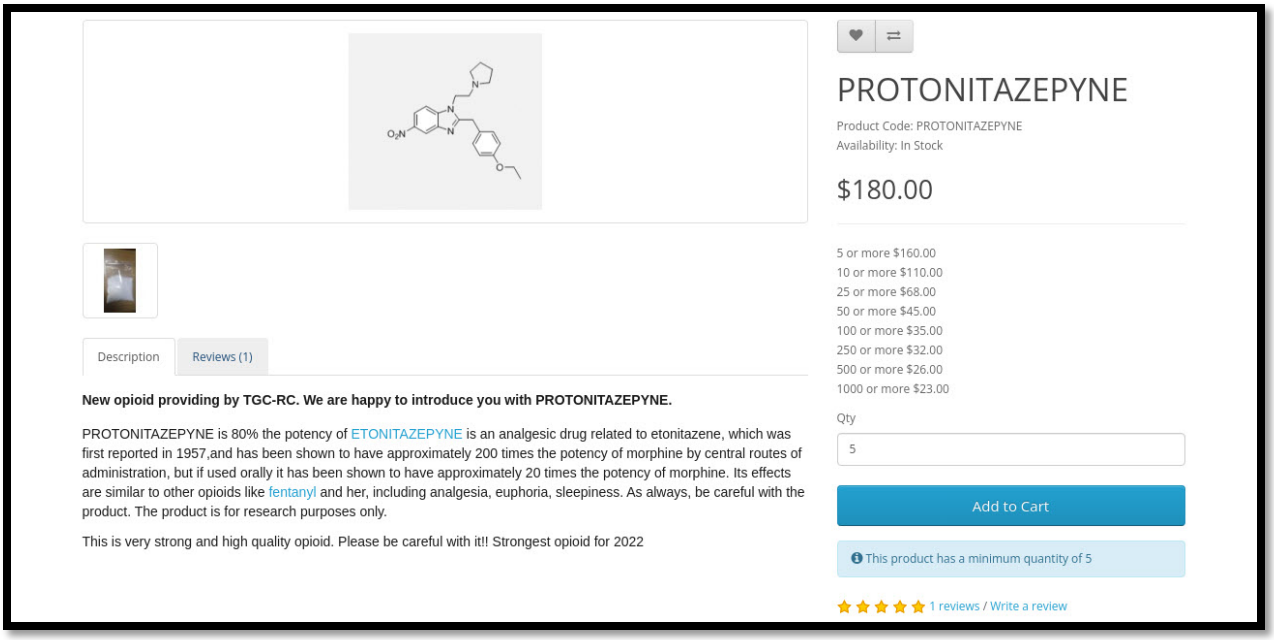
(H) Ethylene etonitazene (2-(2-(4-ethoxyphenethyl)-5-nitro-1H-benzo[d]imidazol-1-yl)-N,N-diethylethan-1-amine, 2-hydroxypropane-1,2,3-tricarboxylic acid).

(I) N-Desethyl etonitazene (2-[(4-ethoxyphenyl)methyl]-N-ethyl-5-nitro-1H-benzimidazole-1-ethanamine).

Appendix I – ONIC Dark Web Research







PROTONITAZEPYNE

Product Code: PROTONITAZEPYNE
Availability: In Stock

$180.00

5 or more $160.00
10 or more $110.00
25 or more $68.00
50 or more $45.00
100 or more $35.00
250 or more $32.00
500 or more $26.00
1000 or more $23.00

Qty

5

Add to Cart

This product has a minimum quantity of 5

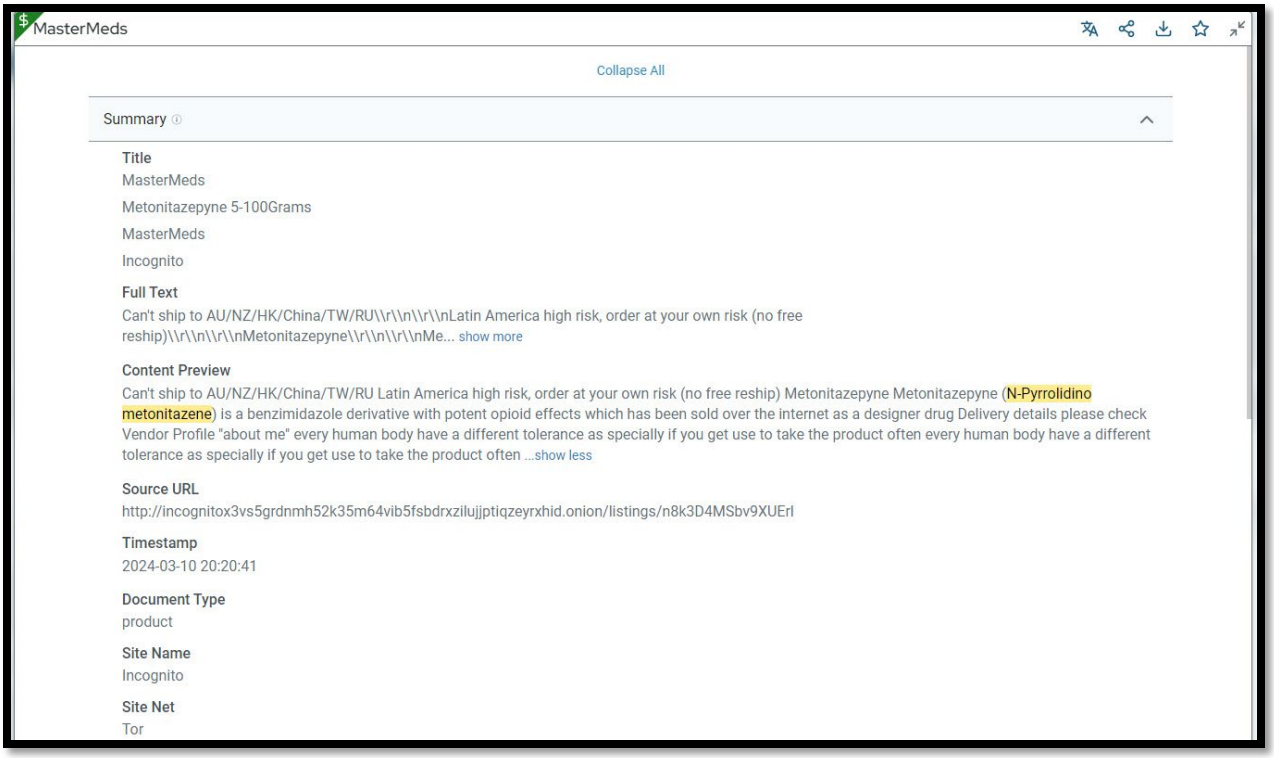
1 reviews / Write a review

Description | Reviews (1)

New opioid providing by TGC-RC. We are happy to introduce you with PROTONITAZEPYNE.

PROTONITAZEPYNE is 80% the potency of ETONITAZEPYNE is an analgesic drug related to etonitazene, which was first reported in 1957,and has been shown to have approximately 200 times the potency of morphine by central routes of administration, but if used orally it has been shown to have approximately 20 times the potency of morphine. Its effects are similar to other opioids like fentanyl and her, including analgesia, euphoria, sleepiness. As always, be careful with the product. The product is for research purposes only.

This is very strong and high quality opioid. Please be careful with it!! Strongest opioid for 2022



MasterMeds

Collapse All

Summary

Title
MasterMeds
Metonitazepyne 5-100Grams
MasterMeds
Incognito

Full Text
Can't ship to AU/NZ/HK/China/TW/RU\\r\\n\\r\\nLatin America high risk, order at your own risk (no free reship)\\r\\n\\r\\nMetonitazepyne\\r\\n\\r\\nMe... show more

Content Preview
Can't ship to AU/NZ/HK/China/TW/RU Latin America high risk, order at your own risk (no free reship) Metonitazepyne Metonitazepyne (N-Pyrrolidino metonitazene) is a benzimidazole derivative with potent opioid effects which has been sold over the internet as a designer drug Delivery details please check Vendor Profile "about me" every human body have a different tolerance as specially if you get use to take the product often every human body have a different tolerance as specially if you get use to take the product often ...show less

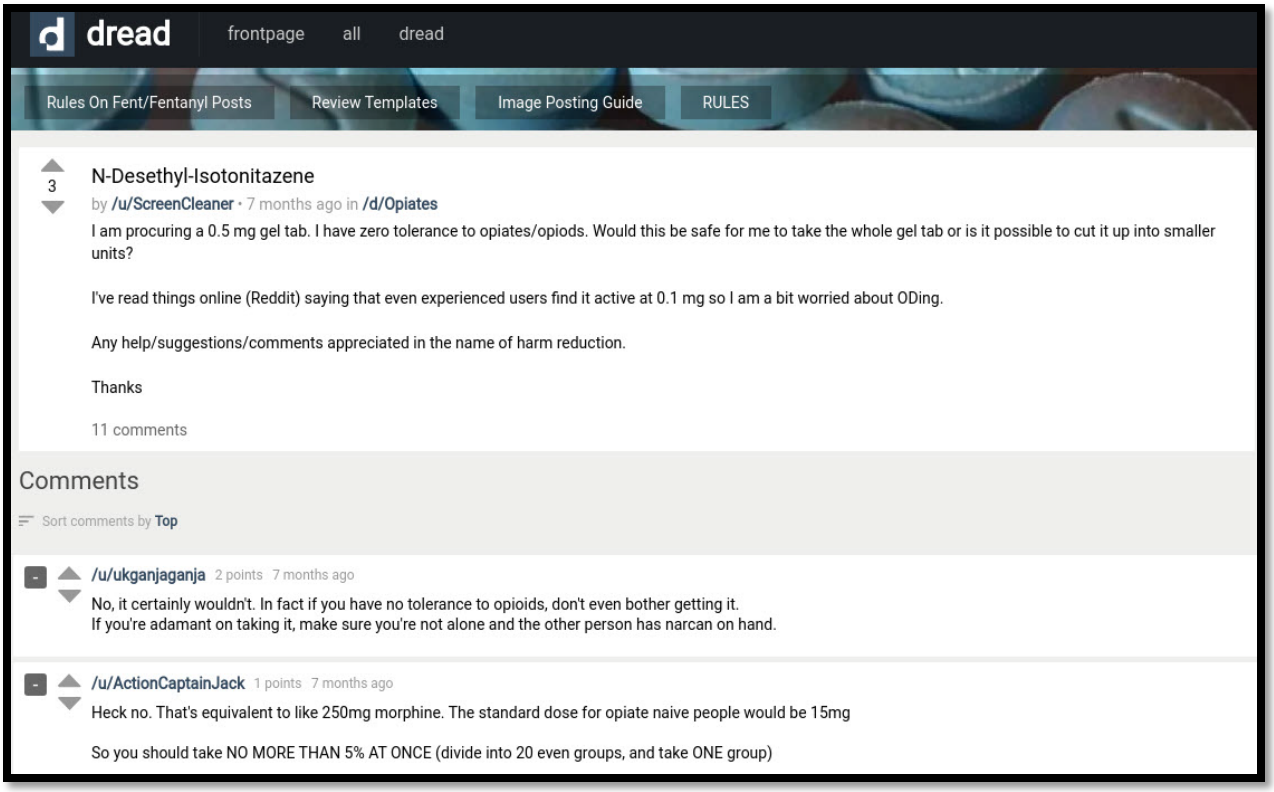
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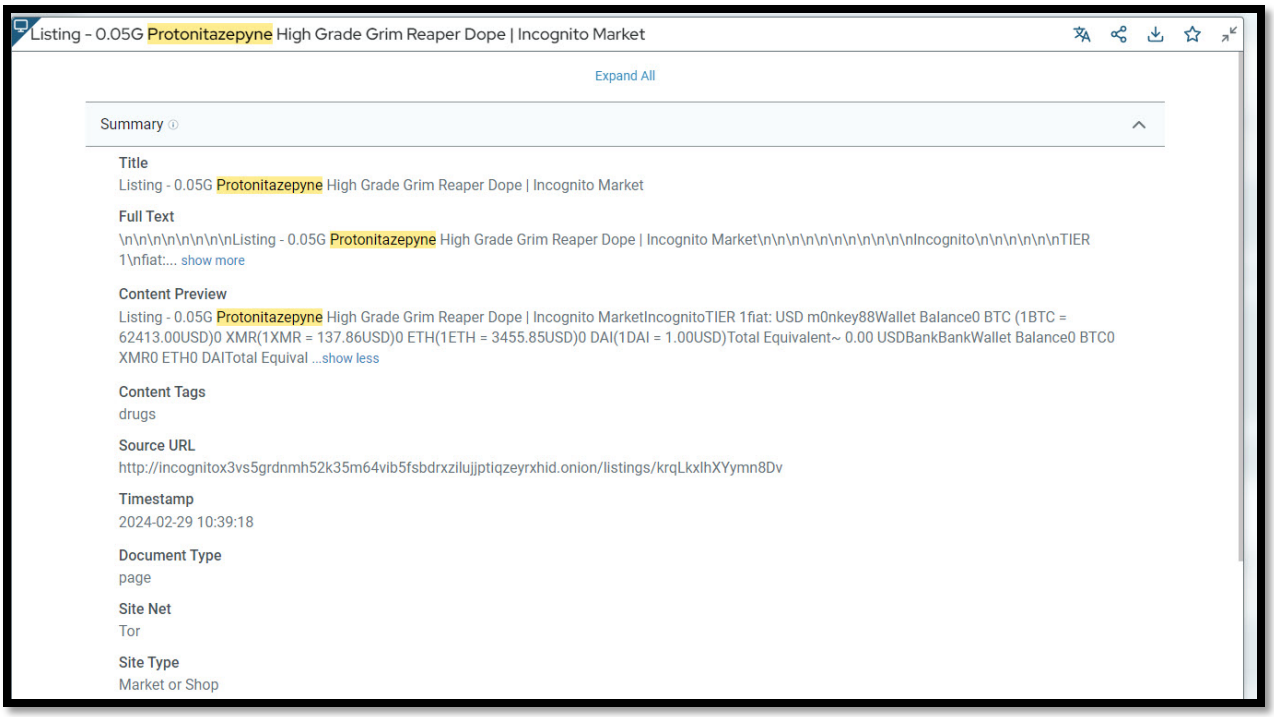
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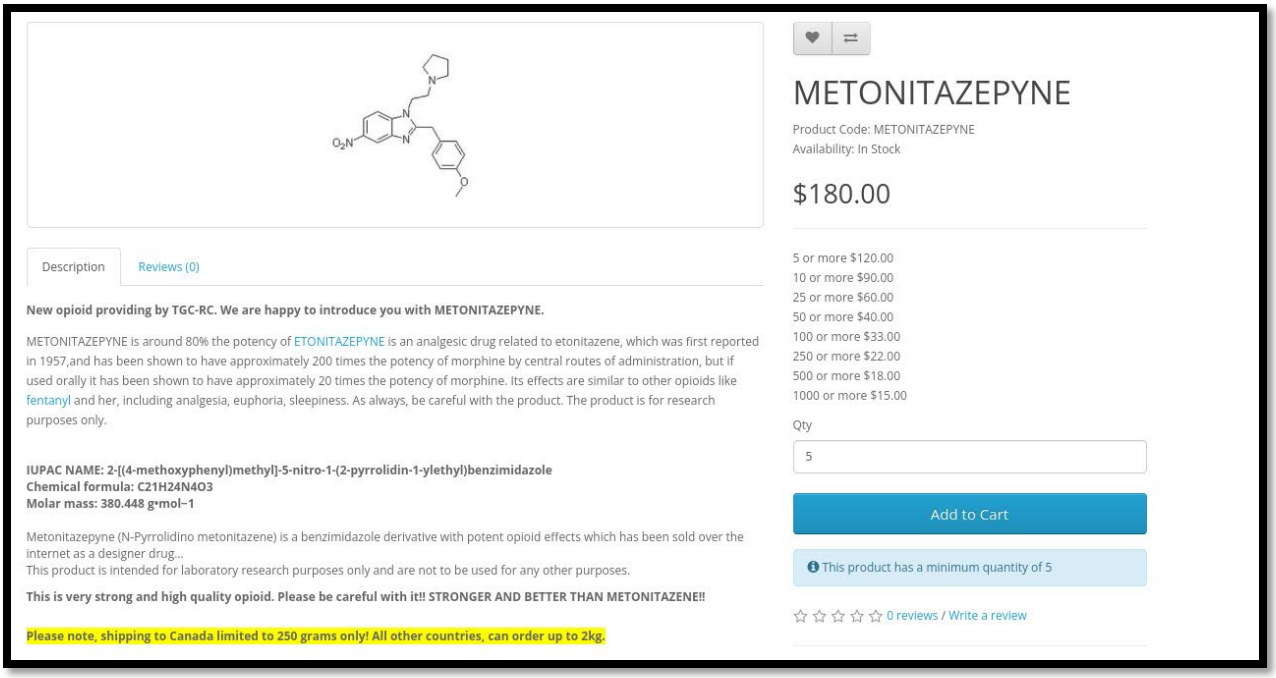
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Site Name
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dread
Rules On Fent/Fentanyl Posts
Review Templates
Image Posting Guide
RULES
3
N-Desethyl-Isotonitazene
by /u/ScreenCleaner • 7 months ago in /d/Opiates
I am procuring a 0.5 mg gel tab. I have zero tolerance to opiates/opiods. Would this be safe for me to take the whole gel tab or is it possible to cut it up into smaller units?
I've read things online (Reddit) saying that even experienced users find it active at 0.1 mg so I am a bit worried about ODing.
Any help/suggestions/comments appreciated in the name of harm reduction.
Thanks
11 comments
Comments
Sort comments by Top
/u/ukganjaganja 2 points 7 months ago
No, it certainly wouldn't. In fact if you have no tolerance to opioids, don't even bother getting it.
If you're adamant on taking it, make sure you're not alone and the other person has narcan on hand.
/u/ActionCaptainJack 1 points 7 months ago
Heck no. That's equivalent to like 250mg morphine. The standard dose for opiate naive people would be 15mg
So you should take NO MORE THAN 5% AT ONCE (divide into 20 even groups, and take ONE group)


Listing - 0.05G Protonitazepyne High Grade Grim Reaper Dope | Incognito Market
Expand All
Summary
Title
Listing - 0.05G Protonitazepyne High Grade Grim Reaper Dope | Incognito Market
Full Text
\n\n\n\n\n\n\nListing - 0.05G Protonitazepyne High Grade Grim Reaper Dope | Incognito Market\n\n\n\n\n\n\n\n\n\n\nIncognito\n\n\n\n\n\nTIER 1\nfiat:... show more
Content Preview
Listing - 0.05G Protonitazepyne High Grade Grim Reaper Dope | Incognito MarketIncognitoTIER 1fiat: USD m0nkey88Wallet Balance0 BTC (1BTC = 62413.00USD)0 XMR(1XMR = 137.86USD)0 ETH(1ETH = 3455.85USD)0 DAI(1DAI = 1.00USD)Total Equivalent~ 0.00 USDBankBankWallet Balance0 BTC0 XMR0 ETH0 DAITotal Equival ...show less
Content Tags
drugs
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METONITAZEPYNE

Product Code: METONITAZEPYNE
Availability: In Stock

$180.00

5 or more $120.00
10 or more $90.00
25 or more $60.00
50 or more $40.00
100 or more $33.00
250 or more $22.00
500 or more $18.00
1000 or more $15.00

Qty 5

Add to Cart

This product has a minimum quantity of 5

0 reviews / Write a review

Description | Reviews (0)

New opioid providing by TGC-RC. We are happy to introduce you with METONITAZEPYNE.

METONITAZEPYNE is around 80% the potency of ETONITAZEPYNE is an analgesic drug related to etonitazene, which was first reported in 1957,and has been shown to have approximately 200 times the potency of morphine by central routes of administration, but if used orally it has been shown to have approximately 20 times the potency of morphine. Its effects are similar to other opioids like fentanyl and her, including analgesia, euphoria, sleepiness. As always, be careful with the product. The product is for research purposes only.

IUPAC NAME: 2-[(4-methoxyphenyl)methyl]-5-nitro-1-(2-pyrrolidin-1-ylethyl)benzimidazole
Chemical formula: C21H24N4O3
Molar mass: 380.448 g•mol−1

Metonitazepyne (N-Pyrrolidino metonitazene) is a benzimidazole derivative with potent opioid effects which has been sold over the internet as a designer drug...
This product is intended for laboratory research purposes only and are not to be used for any other purposes.

This is very strong and high quality opioid. Please be careful with it!! STRONGER AND BETTER THAN METONITAZENE!!

Please note, shipping to Canada limited to 250 grams only! All other countries, can order up to 2kg.

