

EU EARLY WARNING SYSTEM ADVISORY

Isotonitazene mis-sold as heroin and linked to severe poisonings — Montpellier, France, February–March 2023

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1. Summary and purpose

Isotonitazene is a potent new synthetic opioid that emerged on the European drug market in early 2019. It is a member of the benzimidazole family of opioids, of which 10 are currently monitored by the EMCDDA. Overdose with isotonitazene can rapidly cause life-threatening poisoning from respiratory depression and arrest. Timely administration of naloxone can reverse this poisoning. Severe, non-fatal poisonings and deaths caused by isotonitazene have been reported in Europe and the United States. During 2023, the substance continues to be available on the drug market in parts of Europe.

The purpose of this advisory is to:

- Inform you that France has reported two collected samples of isotonitazene that were mis-sold as heroin in Montpellier in February and March 2023. Use of the substance was linked to severe nonfatal poisonings.
- Highlight that mis-selling or adulteration of heroin and other established opioids with potent synthetic new opioids continues to occur sporadically and typically without warning in Europe. Such events can cause life-threatening poisoning which can manifest as outbreaks.
- Request that you report similar cases of mis-selling or adulteration to the EMCDDA immediately.

2. Advisory

Details of the event

France has reported two collected samples of isotonitazene that were mis-sold as heroin in Montpellier, France, in February and March 2023. Both samples were collected by the same local harm reduction service. Use of the substance caused severe opioid poisoning, including respiratory depression and loss of consciousness.

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The investigation into the events is ongoing, and the information is provisional and may be subject to change.

In both samples, isotonitazene was analytically confirmed by laboratory analysis. No heroin was identified in the samples. Saccharose was also identified in the first sample collected in February and possibly used as a diluent; saccharose was not identified in the second sample collected in March.

Sample 1: Collected on 26 February 2023. Isotonitazene was mis-sold as 'Chinese heroin' for 40 EUR/gram in a white / off-white powder. The substance was injected intravenously by three people in an abandoned building. The persons subsequently developed respiratory depression and lost consciousness; all recovered.

Sample 2. Collected on 13 March 2023. Isotonitazene was mis-sold as 'heroin' for 120 EUR/gram. It was smoked by four people at home. The substance was reported to have a 'chemical taste' when smoked and had a 'very strong effect' ('too much' according to one person). Three of the persons subsequently overdosed (no further information on the specific symptoms); all recovered.

Relevant health and law enforcement agencies continue to collect additional information to further assess the situation. The local harm reduction service has issued a targeted alert to clients.

This is the first report of the identification of isotonitazene at street-level in France. The event is considered unusual and unexpected because benzimidazole opioids are rarely encountered at street-level.

Additional information

The EMCDDA is not aware of other, recent, similar cases elsewhere in Europe involving the mis-sale of isotonitazene or other benzimidazole opioids as heroin.

Isotonitazene was first identified on the European drug market in April 2019 [1,2]. During 2020, it was risk assessed [1] and controlled across Europe [3]. As of June 2021, it is also under international control [4].

In 2021, 160 seizures of isotonitazene (22% of all new opioids seizures) totalling to 1.9 kg of material (23% of all material containing new opioids) were reported to the EU Early Warning System. Of these, Latvia reported 128 (80%) of the seizures and 1.8 kg (94%) of the amount seized; Estonia reported 25 (16%) of the seizures and 0.085 kg (4%) of the amount seized [5].

During 2022 and 2023, isotonitazene continued to be seized by law enforcement in parts of Europe. Isotonitazene was also identified in four drug-related deaths that occurred in Estonia in 2022 and three deaths that occurred in Latvia in 2023 [5,6].

The mis-selling or adulteration of heroin and other established opioids with potent synthetic opioids (such as the benzimidazoles or fentanils) occurs on a relatively low-frequency in Europe. Nonetheless, such events continue to occur sporadically and typically without warning. They can cause life-threatening poisoning which can manifest as outbreaks [7,8].

In the summer of 2021, an outbreak caused by the adulteration of heroin with isotonitazene was reported in England, United Kingdom [9–12]. The incident was first recognised with a surge in opioid overdoses, with hospitalisations and deaths in early August. In August 2021, a national incident involving isotonitazene was declared [9]. Although there is no information to link these events, prior to the outbreak being recognised, seizures of heroin adulterated with isotonitazene were reported in Northamptonshire, England, between May and July 2021 [13].

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3. Action required and possible response options

The EMCDDA requests that you maintain a high level of vigilance for similar types of cases of mis-selling or adulteration, as relevant to your national situation. Please immediately report events such as:

- Cases of mis-selling or adulteration of heroin or other drugs with isotonitazene or other new synthetic opioids.
- Unusual or unexpected reports of opioid poisonings or an increase frequency or severity of poisonings.

Information should be reported to: ews@emcdda.europa.eu

Early recognition of cases of mis-selling or adulteration involving new synthetic opioids and the identification of the specific substance involved is essential to ensure timely public health responses. It requires a high level of vigilance and technical support from analytical and toxicological laboratories. In such cases, and depending on the national relevance, preparedness and response options might include regular and ad hoc contact with:

- Law enforcement agencies and their laboratory networks responsible for the forensic analysis of seizures to determine if seizures or events involving mis-selling (substitution, mislabelling) or adulteration have been reported (either analytically confirmed or suspected).
- Poison centres and related toxicosurveillance systems to determine if there have been any unusual
 or unexpected reports of poisonings, or an increased frequency or severity of poisonings (including
 clusters/outbreaks).
- Relevant health and care systems to determine if there have been any unusual or unexpected reports of poisonings, or an increased frequency or severity of poisonings (including clusters/outbreaks). Given that patients may present to different harm reduction services and hospitals or be seen by different healthcare professionals, recognition of the event may be delayed unless relevant agencies and personnel are alerted in a timely manner [14]. Users may report 'strong' or 'bad' batches of drugs circulating. For example:
 - o Have the users reported that it is 'strong' or 'bad'?
 - o Have users reported that the effects are unusual or unexpected?
 - o Have users reported that the effects are undesirable?

Further information on the types of events that should be reported to the EMCDDA is available in:

- EWS Guidance note 4: Events of potential high impact on public health
- EWS Guidance note 5: Outbreaks

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4. Further information

EDND profile for isotonitazene: https://ednd2.emcdda.europa.eu/ednd/substanceProfiles/1054

5. How to use this advisory

This advisory is addressed to the Early Warning System Network, specifically the national early warning system correspondents in the Reitox National Focal Points, Europol, and the Commission. Guidance on the use of advisories and other risk communications issued by the EMCDDA is provided in section 4.11.2 of the operating guidelines for the European Union Early Warning System.

If you received this advisory as a national early warning system correspondent at the Reitox National Focal Points, please note that it must be restricted to your national early warning system network and other partners (as relevant to your national situation). Do not make it public. If you have any questions in this respect, please contact the EMCDDA.

If this advisory has been sent to you by your national early warning system correspondent at the Reitox National Focal Point please direct any questions that you may have to them (1).

6. Acknowledgements

The EMCDDA would like to thank the members of the EU Early Warning System Network who contributed to the information used in this advisory, in particular the French National Focal Point, Estonian National Focal Point, and Latvian National Focal Point.

7. References

- EMCDDA. Report on the risk assessment of N,N-diethyl-2-[[4-(1-methylethoxy)phenyl]methyl]-5-nitro-1H-benzimidazole-1-ethanamine (isotonitazene) in accordance with Article 5c of Regulation (EC) No 1920/2006 (as amended). 2020. https://www.emcdda.europa.eu/publications/riskassessments/isotonitazene_en
- 2. Ujváry I, Christie R, Evans-Brown M, et al. DARK Classics in chemical neuroscience: etonitazene and related benzimidazoles. ACS Chem Neurosci. 2021;12(7):1072-1092. https://doi.org/10.1021/acschemneuro.1c00037
- 3. Commission Delegated Directive (EU) 2020/1687 of 2 September 2020 amending the Annex to Council Framework Decision 2004/757/JHA as regards the inclusion of the new psychoactive substance N,N-

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¹ http://www.emcdda.europa.eu/about/national-focal-points-contact-information_en



- diethyl-2-[[4-(1-methylethoxy)phenyl]methyl]-5-nitro-1H-benzimidazole-1-ethanamine (isotonitazene) in the definition of 'drug'. https://eur-lex.europa.eu/eli/dir_del/2020/1687/oj
- UNODC. CND decision on international control of isotonitazene enters into force remaining decisions will enter into force in December 2021. June 2021. https://www.unodc.org/LSS/announcement/Details/65247392-26c7-4446-a2b6-270226103036
- 5. EMCDDA. EU EWS Advisory. Overview of the situation with new opioids Europe, 2021–ongoing. EU-EWS-RCS-AD-2023-0001. 2 February 2023.
- 6. Information reported to EMCDDA by Latvian National Focal Point.
- Centers for Disease Control and Prevention (CDC). Nonpharmaceutical fentanyl-related deaths--multiple states, April 2005-March 2007. MMWR Morb Mortal Wkly Rep. 2008 Jul 25;57(29):793-6. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5729a1.htm
- 8. Massey J, Kilkenny M, Batdorf S, Sanders SK, Ellison D, Halpin J, Gladden RM, Bixler D, Haddy L, Gupta R. Opioid Overdose Outbreak West Virginia, August 2016. MMWR Morb Mortal Wkly Rep. 2017 Sep 22;66(37):975-980. https://doi.org/10.15585/mmwr.mm6637a3
- 9. EMCDDA. Public Health England: At least 46 recent overdoses including 16 deaths linked to opioid (heroin) use South London, South East, South West East of England, United Kingdom, 17 August 2021. Email to EWS Network issued on 18 August 2021.
- De Baerdemaeker KSC, Dines AM, Hudson S, et al. Isotonitazene, a novel psychoactive substance opioid, detected in two cases following a local surge in opioid overdoses. QJM. 2023;116(2):115-119. https://doi.org/10.1093/qjmed/hcac039
- 11. Nahar LK, Andrews R, Paterson S. Isotonitazene: a new synthetic opioid in the UK. BMJ. 2021;375:n3143. https://doi.org/10.1136/bmj.n3143
- 12. ACMD. ACMD advice on 2-benzyl benzimidazole and piperidine benzimidazolone opioids. 3 February 2023. https://www.gov.uk/government/publications/acmd-advice-on-2-benzyl-benzimidazole-and-piperidine-benzimidazolone-opioids/acmd-advice-on-2-benzyl-benzimidazole-and-piperidine-benzimidazolone-opioids-accessible-version
- 13. EMCDDA. Heroin adulterated with isotonitazene United Kingdom, May 2021. Email to EWS Network issued on 8 June 2021.
- 14. Frankenmolen PG, Hoogerheide-Wiegerinck CL, van Bakkum FF, Croes EA, Rebel JR, Gresnigt FMJ. Complicaties van vervuilde drugs [Complications of contaminated drugs: how to reduce the number of future victims?]. Ned Tijdschr Geneeskd. 2021;165:D5869. https://www.ntvg.nl/artikelen/complicaties-van-vervuilde-drugs

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