



EU EARLY WARNING SYSTEM ADVISORY

Fake oxycodone tablets containing borphine — Slovenia, 2021

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1. Summary and purpose

Borphine is a synthetic opioid monitored by the EMCDDA as a new psychoactive substance. It has been available in Europe since at least March 2020. Its identification has been reported by 4 countries: Belgium, Germany, Slovenia, and Sweden. Similar to other new opioids, borphine is sold as a replacement to controlled opioids on the surface web, darknet markets, and at street-level.

The available information suggests that, similar to fentanyl, borphine is a potent opioid. Overdose may cause life-threatening poisoning from respiratory depression and arrest. Deaths involving borphine have been reported in the United States (20 deaths).

The purpose of this advisory is to:

- Highlight a recent identification of two fake oxycodone tablets containing borphine in Slovenia that were sold on the internet as oxycodone.
- Highlight that borphine appears to be a potent opioid that may pose a high risk of life-threatening poisoning. Deaths have been reported in the United States.
- Request that you report any information you have on borphine to the EMCDDA as soon as possible so that we can improve our understanding of the potential risks. Information should be reported by email to ews@emcdda.europa.eu

2. Advisory

Background



Brorphine is a synthetic opioid monitored by the EMCDDA as a new psychoactive substance [1]. It is structurally related to the internationally controlled opioid analgesic bezitramide [2] that was first reported in the 1960s [3]. Brorphine was first synthesized and reported in the scientific literature in 2018 [4].

The available information suggests that brorphine is a potent opioid [5–7]. As such, its effects are likely to share similarities with fentanyl and other opioid analgesics. These include relaxation and euphoria and, at higher doses, sedation, profound intoxication, and respiratory depression. Overdose may cause life-threatening poisoning from respiratory depression and arrest [8,9].

The notification of brorphine was based on its identification in a seizure of less than 0.05 grams of powder seized by Swedish Police that was collected by the Swedish Post and Telecom Authority on 25 March 2020. The substance was identified in a bag labeled as 'Brorphine 0.05g'. Since then, Belgium, Germany ⁽¹⁾, and Slovenia ⁽¹⁾ have also reported the identification of the substance.

During 2020, brorphine was identified in Belgium in a powder and in the serum of a patient seeking medical help for detoxification [6].

The United States and Canada have reported identifications of brorphine since late 2019. Between June and July 2020, a total of 20 deaths with confirmed exposure to brorphine have been reported in the United States ⁽²⁾. In these cases brorphine was commonly found in combination with fentanyl and flualprazolam. Brorphine was listed in the cause of death for three of the cases. Opioid-related drug paraphernalia was commonly found at the scene and many individuals had a history of drug use, specifically heroin or other opioids [10].

Details of the event

In 2021, Slovenia reported two fake oxycodone tablets containing brorphine collected in January 2021. The fake tablets were round, scored, and blue in colour (Figure 1). The amount of brorphine present in the tablets was not reported. No other substances were detected in the tablets. The tablets were submitted for analysis after a user experienced serious adverse effects. The poisoning was considered non-life threatening but required treatment in hospital. The clinical features of poisoning included prolonged loss of consciousness (approximately 12 hours), rhabdomyolysis and acute kidney failure. Exposure to brorphine was analytically confirmed from biological sample; no other substances were reported. According to the patient, the tablets were bought as oxycodone on the internet (no further details are available).

¹ Brorphine was identified in a test purchase.

² Note: It is not possible to confirm whether the 20 cases reported by Krotulski et al., include some or all of the 7 cases from the United States that we highlighted in EU-EWS-SITREP-2020-0002 and that were reported by the Center for Forensic Science Research and Education (CFSRE):

CFSRE. The rise of brorphine — A potent new synthetic opioid identified in the Midwestern United States. 27 July 2020. [https://](https://www.npsdiscovery.org/wp-content/uploads/2020/07/Public-Alert_Brorphine_NPS-Discovery_072720.pdf)

www.npsdiscovery.org/wp-content/uploads/2020/07/Public-Alert_Brorphine_NPS-Discovery_072720.pdf

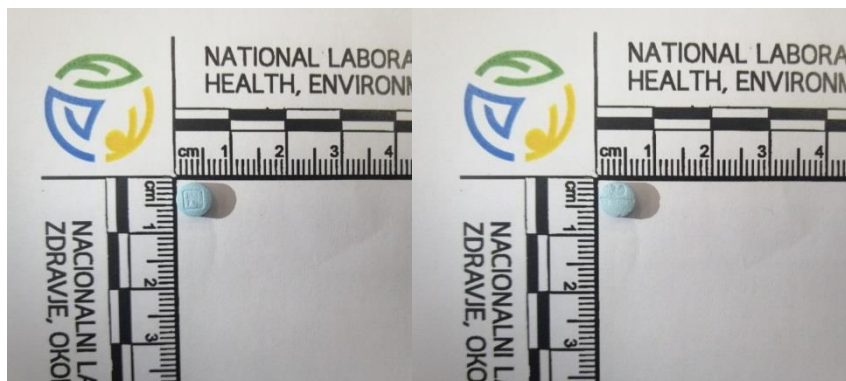


Figure 1. Fake oxycodone tablets that contained buprenorphine submitted for analysis in Slovenia in January 2021.

The prevalence of fake tablets containing buprenorphine in Europe is unknown. In the last few years, the EMCDDA issued a number of advisories to the EWS Network on fake medicines containing new opioids [11–13]. Given the international supply chains for such fakes, including on darknet drug markets, the availability elsewhere cannot be excluded.

Risks to users

Fake medicines are typically visually indistinguishable from legitimate products. Only chemical analysis can determine the contents. People using such fakes will be unaware of both the substances they contain and the amount. This poses an inherent risk to the individual. Fake medicines containing new opioids have caused large numbers of severe and fatal poisonings, including mass poisonings, in the United States and Canada in the past few years [14–17]. In some cases, mass poisonings have stressed the capabilities and resources of first responders, emergency departments, and intensive care units, and have led to the rapid depletion of supplies of naloxone [17]. It is of particular concern considering the ongoing COVID-19 pandemic.

The risk of poisoning may be greater by the unintentionally high doses that users may take, especially when combined with other substances. Similarly to other opioids analgesics, the use of buprenorphine with other central nervous system (CNS) depressants, including other opioids, sedatives/hypnotics, alcohol, pregabalin, gabapentin, tranquillisers, and sedating anti-histamines, is likely to produce additive depressant effects which can increase the risk of life-threatening respiratory depression and arrest. The timely administration of the antidote naloxone has been shown to be effective in reversing respiratory depression caused by potent opioid analgesics [18,19].

The risk of poisoning includes both current high risk opioid users and other groups who may have no or limited tolerance to opioids, including 'recreational' users. Recreational users are less likely to be aware of the risk of overdose and are unlikely to have access to community opioid overdose prevention programmes, including take-home naloxone programmes [20,21].



3. Action required

The EMCDDA requests that the Network report to the EMCDDA any identifications of brorphine, especially first identifications in country (FICs), in a timely manner in order to help us understand the risks this substance may pose to Europe. Information should be reported through the EDND or by email to:

ews@emcdda.europa.eu

Further information on the procedures and specific types of information that should be reported is available in the operating guidelines and guidance notes for the European Union Early Warning System:

http://www.emcdda.europa.eu/publications/guidelines/operating-guidelines-for-the-european-union-early-warning-system-on-new-psychoactive-substances_en

4. Further information

Further information on brorphine is available in the EDND profile:

<https://ednd2.emcdda.europa.eu/ednd/substanceProfiles/1108>

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.³

6. References

1. EMCDDA. Formal notification of 1-[1-[1-(4-bromophenyl)ethyl]-4-piperidinyl]-1,3-dihydro-2H-benzimidazol-2-one (brorphine) by Sweden as a new psychoactive substance under the terms of Regulation (EU) 2017/2101. EU-EWS-RCS-FN-2020-0013. 04 June 2020.
2. INCB. Yellow list: List of narcotic drugs under international control. 58th edition. July 2020. <https://www.incb.org/incb/en/narcotic-drugs/Yellowlist/yellow-list.html>

³ http://www.emcdda.europa.eu/about/national-focal-points-contact-information_en



3. Janssen PAJ. Benzimidazoliny piperidines. US Patent. 1965; US 3196157A.
<https://patents.google.com/patent/US3196157A/en>
4. Kennedy NM, et al. Optimization of a series of mu opioid receptor (MOR) agonists with high G protein signaling bias. *J Med Chem.* 2018;61(19):8895–907.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6386185/>
5. Vandeputte M, et al. In vitro functional characterization of a panel of non-fentanyl opioid new psychoactive substances. *Arch Toxicol.* 2020;94:3819–3830. <https://doi.org/10.1007/s00204-020-02855-7>
6. Verougstraete N, et al. First report on buprenorphine: the next opioid on the deadly new psychoactive substances' horizon? *J Anal Toxicol.* 2020;44(9):937–46. <https://doi.org/10.1093/jat/bkaa094>
7. US DEA. Buprenorphine: three factor analysis. <https://beta.regulations.gov/document/DEA-2020-0038-0003>
8. Pattinson KT. Opioids and the control of respiration. *Br J Anaesth.* 2008;100(6): 747–58.
<https://doi.org/10.1093/bja/aen094>
9. White JM, et al. Mechanisms of fatal opioid overdose. *Addiction.* 1999; 94(7): 961–72.
<https://doi.org/10.1046/j.1360-0443.1999.9479612.x>
10. Krotulski AJ, et al. Buprenorphine—Investigation and quantitation of a new potent synthetic opioid in forensic toxicology casework using liquid chromatography-mass spectrometry. *J Forensic Sci.* 2020.
<https://doi.org/10.1111/1556-4029.14623>
11. EMCDDA. EU Early Warning System Advisory. Fake medicines (Xanax and OxyContin tablets) containing fentanyl — Sweden, November 2017–January 2018. EU-EWS-RCS-AD-2018-0001. 09 February 2018.
12. EMCDDA. EU Early Warning System Advisory. Fake oxycodone tablets containing methoxyacetylfentanyl — Sweden, 2018. EU-EWS-RCS-AD-2018-0003. 04 May 2018.
13. EMCDDA. EU Early Warning System Advisory. Fake Percocet tablets containing fentanyl — London, United Kingdom, December 2018. EU-EWS-RCS-AD-2018-0004. 11 December 2018.
14. US DEA. Counterfeit prescription pills containing fentanyl: a global threat. 2016.
<https://www.dea.gov/sites/default/files/docs/Counterfeit%2520Prescription%2520Pills.pdf>
15. Edison L, et al. Notes from the field: counterfeit Percocet-related overdose cluster — Georgia, June 2017. *MMWR Morb Mortal Wkly Rep.* 2017; 66(41):1119–20.
<http://dx.doi.org/10.15585/mmwr.mm6641a6>
16. Arens AM, et al. Adverse effects from counterfeit alprazolam tablets. *JAMA Intern Med.* 2016;176(10):1554–5. <https://doi.org/10.1001/jamainternmed.2016.4306>
17. Sutter ME, et al. Fatal fentanyl: one pill can kill. *Acad Emerg Med.* 2017;24(1):106–13.
<https://doi.org/10.1111/acem.13034>



18. Kim HK, et al. Reducing the harm of opioid overdose with the safe use of naloxone: a pharmacologic review. *Expert Opin Drug Saf.* 2015;14(7):1137–46. <https://doi.org/10.1517/14740338.2015.1037274>
19. Boyer EW. Management of opioid analgesic overdose. *N Engl J Med.* 2012;367(2):146–55. <https://doi.org/10.1056/NEJMra1202561>
20. EMCDDA. Preventing fatal overdoses: a systematic review of the effectiveness of take-home naloxone. Publications Office of the European Union, Luxembourg. 2015. <https://doi.org/10.2810/396726>
21. EMCDDA. Preventing opioid overdose deaths with take-home naloxone. Publications Office of the European Union, Luxembourg. 2016. <https://doi.org/10.2810/357062>