

July 2021

Brorphine

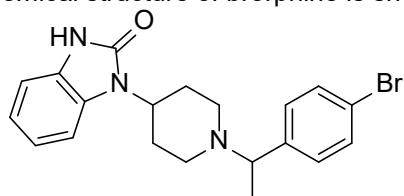
(chemical name: 1-(1-(1-(4-bromophenyl)ethyl)piperidin-4-yl)-1,3-dihydro-2H-benzimidazol-2-one)

Introduction:

Brorphine is a potent synthetic opioid recently encountered as both a single substance of abuse and in combination with substances such as heroin and fentanyl. The availability of synthetic opioids continues to pose an imminent hazard to public safety. Adverse health effects associated with the abuse of synthetic opioids and the continued evolution and increased popularity has been a serious concern in recent years. The United States continues to experience an unprecedented epidemic of opioid misuse and abuse. The presence of new synthetic opioids with no approved medical use exacerbates the epidemic. The introduction of a new synthetic opioid to the illicit market is harmful and causes deep concern. While toxicologists develop methods for detection this compound may be underreported.

Chemistry:

The chemical structure of brorphine is shown below.



Brorphine (CAS 2244737-98-0) is comprised of three main units: a 4-bromophenethyl group, a piperidine ring, and a 1,3-dihydro-2H-benzimidazole-2-one group. Brorphine is being trafficked as its hydrochloride salt (no current CAS), which would be water-soluble.

Pharmacology:

In *in vitro* studies, brorphine, similar to fentanyl, binds to mu-opioid receptors and acts as a mu-opioid receptor agonist. Activation of mu-opioid receptors by brorphine has been shown to involve recruitment of beta-arrestin-2, a regulatory protein. It is known that activation of mu-opioid receptor produces several pharmacological effects to include analgesia, euphoria, and respiratory depression as would be anticipated for brorphine.¹

Licit Uses:

Brorphine has not been approved for medical use in the United States, and there are no published studies on safety for human use. Brorphine has no industrial use. Brorphine was first reported in the scientific literature as a mu-opioid receptor agonist in 2018.

User Population:

Traffickers advertise brorphine as a replacement for fentanyl putting the user at serious risk. The population likely to abuse brorphine appears to be the same as those abusing prescription opioid analgesics, heroin, tramadol, fentanyl, and other synthetic opioids. This is evidenced by additional drugs identified in brorphine seizures.

Like many other synthetic opioids, brorphine is abused as a recreational drug. Brorphine has become frequently discussed in online drug forums, with discussions tailored to effects, dosages, routes of administration, and comparing experiences to other synthetic opioids. These discussions on forums such as Reddit and Erowid have increased since mid-2019.

International reporting notes an emergency room presentation for opioid withdrawal and subsequent detox of brorphine.² According to the NPS Discovery program, between June and July 2020, seven drug related deaths involving brorphine occurred.³ DEA encourages law enforcement and public health to remain on the lookout for related events and would be appreciative of any adverse event reporting connected to brorphine.

Distribution:

According to the NFLIS data, in mid-2019 brorphine emerged in the United States' drug market. According to NFLIS, federal, state, and local forensic laboratories have identified six reports of brorphine in 2019, 112 reports in 2020, and 12 reports in 2021, as of June 2021.

Control Status

Brorphine is a Schedule I controlled substance under the Federal Controlled Substances Act.

3. Krotulski, A. J.; Papsun, D. M.; Noble, C.; Kacinko, S. L.; Nelson, L.; Logan, B. K. Public Health Alert: The Rise of Brorphine - A Potent New Synthetic Opioid Identified in the Midwestern United States. July 2

1. Kennedy, N. M.; Schmid, C. L.; Ross, N. C.; Lovell, K. M.; Yue, Z.; Chen, Y. T.; Cameron, M. D.; Bohn, L. M.; Bannister, T. D. Optimization of a Series of Mu Opioid Receptor (MOR) Agonists with High G Protein Signaling Bias. *J. Med. Chem.* **2018**, *61* (19), 8895-8907.
2. Verougstraete, N.; Vandeputte, M. M.; Lyphout, C.; Cannart, A.; Hulpia, F.; Van Calenbergh, S.; Verstraete, A. G.; Stove, C. First Report on Brorphine: The next Opioid on the Deadly New Psychoactive Substances' Horizon? *J. Anal. Toxicol.* **2020**.
<https://doi.org/10.1093/jat/bkaa094>.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; Fax 571-362-4250, telephone 571-362-3249, or E-mail DPE@dea.gov.