Drug Enforcement Administration
Diversion Control Division
Drug & Chemical Evaluation Section

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BRORPHINE

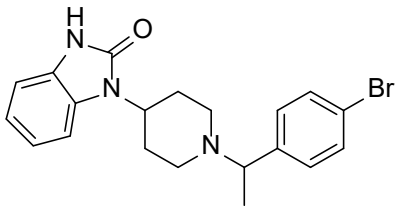
(Chemical name: 1-(1-(1-(4-bromophenyl)ethyl)piperidin-4-yl)-1,3-dihydro-2H-benzimidazol-2-one)

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:

Brorphine (CAS 2244737-98-0) is comprised of three main units: a 4-bromophenethyl group, a piperidine ring, and a 1,3-dihydro-*2H*-benzoimidzole-2-one group. Brorphine is being trafficked as its hydrochloride salt (CAS 2707204-49-5), which would be water-soluble. The chemical structure of brorphine is shown below:



Pharmacology:

In in vitro studies, brorphine, similar to fentanyl, binds to mu-opioid receptors (MOR) and acts as an MOR agonist. It is known that activation of MOR produces several pharmacological effects (including analgesia, euphoria, and respiratory depression), which are expected of brorphine. [1] Consistently, in vivo studies (using animals) have shown that brorphine, similar to other MOR agonists (such as fentanyl), produced analgesic effects and fully substituted for the discriminative stimulus effects of morphine in rodents that were trained to discriminate morphine.

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 an MOR agonist in 2018.

User Population:

Traffickers advertise brorphine as a replacement for fentanyl, which places 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 been discussed in online drug forums (such as Reddit and Erowid), with discussions tailored to effects, dosages, routes of administration, and comparisons of experiences to other synthetic opioids.

International reporting noted an emergency room presentation for opioid withdrawal and subsequent detox of brorphine. [2] According to the NPS Discovery program, twenty drug related deaths involving brorphine occurred between June and July 2020. [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 DEA's National Forensic Laboratory Information System (NFLIS) Drug database, which collects scientifically verified data on drug items and cases submitted to and analyzed by federal, state, and local forensic laboratories, brorphine emerged mid-2019 in the U.S. drug market. There were six reports of brorphine to NFLIS-Drug in 2019, 123 reports in 2020, 22 reports in 2021, 28 reports in 2022, and 11 reports in 2023.

Control Status

Brorphine is a schedule I controlled substance under the federal Controlled Substances Act.

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.

[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. (2018). Optimization of a Series of Mu Opioid Receptor (MOR) Agonists with High G Protein Signaling Bias. *Journal of medicinal chemistry*, *61*(19), 8895–8907. https://doi.org/10.1021/acs.jmedchem.8b01136

[2] Verougstraete, N., Vandeputte, M. M., Lyphout, C., Cannaert, A., Hulpia, F., Van Calenbergh, S., Verstraete, A. G., & Stove, C. (2021). First Report on Brorphine: The Next Opioid on the Deadly New Psychoactive Substance Horizon?. *Journal of analytical toxicology*, *44*(9), 937–946. https://doi.org/10.1093/jat/bkaa094

[3] Krotulski, A. J., Papsun, D. M., Noble, C., Kacinko, S. L., & Logan, B. K. (2021). Brorphine-Investigation and quantitation of a new potent synthetic opioid in forensic toxicology casework using liquid chromatography-mass spectrometry. *Journal of forensic sciences*, *66*(2), 664–676. https://doi.org/10.1111/1556-4029.14623