

Benzimidazole-Opioids Other Name: Nitazenes

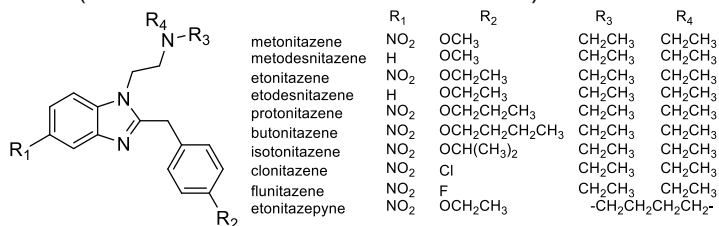
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Introduction:

Recently, a number of synthetic substances of the benzimidazole structural class are being trafficked and abused for their opioid-like effects. In the late 1950s, the pharmaceutical research laboratories of the Swiss chemical company CIBA Aktiengesellschaft synthesized numerous substances in this structural class for use as an analgesic. Since 2019, the abuse of benzimidazole-opioids as evidenced by their identification in toxicology cases, similar to other synthetic opioids, has resulted in adverse health effects including deaths. As the United States continues to experience an unprecedented epidemic of opioid misuse and abuse, the continued evolution and increased trafficking and popularity of new and deadly synthetic opioids from a variety of structural classes, including benzimidazoles, with no approved medical use are a public health concern.

Chemistry:

This class of substances contains a benzimidazole ring with an ethylamine at its 1-position and a benzyl group at its 2-position. Small structural modifications to this scaffold can produce a series of analogous substances, such as the substances listed below (controlled benzimidazoles shown below):



A total of twenty benzimidazole compounds have been identified in forensic reports and toxicology samples to date.

Pharmacology:

Data obtained from pre-clinical studies demonstrate that benzimidazole-opioids exhibit pharmacological profiles similar to that of etonitazene and other mu-opioid receptor agonists. Antinociceptive studies conducted in rodents using known benzimidazole-opioids, demonstrate that, similar to morphine and fentanyl, these substances produced analgesic effects with varying potencies. Data from in vitro studies showed that known benzimidazole-opioids, similar to fentanyl and morphine, bound to and activated the mu-opioid receptor, and thus acted as mu-opioid receptor agonists. It is well established that mu-opioid receptor agonists have a high potential for addiction and can produce dose-dependent respiratory depression and arrest. Abuse of these benzimidazole-opioids has led to their positive identification in several toxicological cases in the United States. Some of these benzimidazole-opioids have been positively identified in numerous post-mortem cases.

User Population:

The population likely to abuse benzimidazole-opioids appears to be the same as those abusing prescription opioid analgesics, heroin, and other synthetic opioid substances. This is evidenced by the types of other drugs co-identified in benzimidazole-opioid drug seizures and in fatal overdose cases. Toxicology analyses co-identified some of these benzimidazole-opioids with other opioids, stimulants, and benzodiazepines. Because abusers of these benzimidazole-opioids are likely to obtain them through unregulated sources, the identity, purity, and quantity are uncertain and inconsistent, thus posing significant adverse health risks to the users. Similar to other mu-opioid receptor agonists, the potential health and safety risks for users of these benzimidazole-opioids are high. The positive identification of benzimidazole-opioids in toxicology and post-mortem cases is a serious concern to the public safety.

Illicit Distribution:

In the illicit drug market, some of these benzimidazole-opioids have been identified in drug seizures. 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, reports of benzimidazole-opioids began to re-emerge in 2019, after several reports of clonitazene and etonitazene in 1999-2004. Since 2019, there have been over 4,300 reports of benzimidazole-opioids to NFLIS-Drug. Furthermore, substances in this class have been co-identified with other psychoactive substances, including illicit opioids, stimulants, and benzodiazepines, in biological fluids. With no approved medical use, the positive identification of these substances in toxicology cases underscore the public health threat associated with their presence in the illicit drug market.

Control Status:

These benzimidazole-opioids are not approved for medical use in the United States. Ten benzimidazole-opioids are controlled in schedule I of the CSA; if others are found to meet the criteria outlined in 21 U.S.C. § 802(32), and it is intended for human consumption, they may be treated as Schedule I controlled substance analogues for the purpose of Federal law pursuant to 21 U.S.C. § 813.

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.