

# NOVEL PSYCHOACTIVE SUBSTANCES : ORPHINES – BRORPHINE, CYCHLORPHINE, AND BEYOND

APRIL 2026

The Legislative Analysis and Public Policy Association (LAPPA) is continuing to monitor the emergence of novel psychoactive substances (NPS) appearing on the illicit drug market in the United States. The term “novel” does not denote a brand new, never-before-seen substance but rather a substance that is newly available in the drug market. This fact sheet, which is part of a series highlighting these dangerous drugs, is an examination of orphines, which is the name given to the benzimidazol-2-one class of potent synthetic opioids.

Orphines are a class of synthetic opioids first developed by Janssen Pharmaceuticals in the 1960s and were discovered to have anesthetic properties. Specifically, the company synthesized the orphine, “bezitramide,” which it tested in clinical studies in the 1970s and 80s and marketed for chronic pain in Europe under the brand name Burgodin until 2004, when the company removed the drug from circulation following a number of overdoses in the Netherlands. The U.S. Food and Drug Administration never approved bezitramide for use in the U.S. and designated it a Schedule II controlled substance under the federal Controlled Substances Act.<sup>1</sup>

After Janssen pulled bezitramide from the market in 2004, orphines had essentially disappeared. Then in 2018, the synthesis of the orphine brorphine was reported in scientific literature for the first time. The following year, brorphine appeared for the first time in the illicit drug supply in Europe, and in 2020, it appeared in the U.S. illicit drug supply. After being associated with several fatalities, the U.S. Drug Enforcement Administration, in March 2023, added brorphine to the list of Schedule I controlled substances, after the agency had previously issued an order temporarily scheduling the drug in March 2021.<sup>2</sup>

Since the appearance of brorphine in the U.S. illicit drug supply, more orphines have been detected, including Chlorphine, N-Propionitrile Chlorphine (Cychlorphine), 5,6-Dichloro Desmethylchlorphine (SR-17018), Spirochlorphine (R-6890), Spirobrorphine, and 5,6-Dicholoro Brorphine (SR-14968). According to a February 2026 report from the Colombo Plan<sup>3</sup> and the Center for Forensic Science Research and Education (CFSRE), orphines have been identified in 23 states with Illinois and Tennessee experiencing the greatest number of positive reports.<sup>4</sup> Drug policy experts believe that orphines are originating from clandestine laboratories in China and that their sudden rise in the illicit drug market is an attempt by clandestine chemists and international drug trafficking organizations to avoid international legal and regulatory barriers.<sup>5</sup> Following China’s class-wide scheduling of fentanyl compounds in May 2019, the [nitazene](#) class of opioids began originating from China and started appearing in illicit drug markets around the world.<sup>6</sup> Likewise, the rise of orphines has correlated with China’s July 2025 scheduling of the core chemical structure of nitazene compounds.<sup>7</sup>

---

<sup>1</sup> 21 U.S.C. § 812.

<sup>2</sup> Schedules of Controlled Substances: Placement of Brorphine in Schedule I, 88 Fed. Reg. 13,692 (March 6, 2023).

<sup>3</sup> The Columbo Plan is a regional inter-governmental organization of 28 member countries that foster and restore economic and developmental opportunities for countries in the Asia-Pacific region.

<sup>4</sup> “Emergency Global Synthetic Opioid Threats: Benzimidazol-2-ones—The Orphines,” *Center for Forensic Science Research & Education*, January 30, 2026, <https://www.cfsre.org/nps-discovery/public-alerts/emerging-global-synthetic-opioid-threats-benzimidazol-2-ones-the-orphines>.

<sup>5</sup> *Id.*

<sup>6</sup> *Id.*

<sup>7</sup> *Id.*

Like other mu-opioid receptor agonists,<sup>8</sup> orphines cause central nervous system and respiratory depression. Naloxone can be used to reverse an orphine-involved overdose, but due to the high potency of orphines, multiple doses of naloxone may be needed. Orphines can be difficult to detect because very few toxicology laboratories currently have the ability to detect orphine analogs. Moreover, [drug test strips](#) for orphines do not exist to allow consumers to test for the presence of orphines in their drug products as they can for fentanyl, nitazenes, and [xylazine](#). When orphines are identified, they are often found in combination with other opioids, including fentanyl and nitazene analogs, novel benzodiazepines, such as [bromazolam](#), and stimulants. As of this writing, brorphine is the only recently identified orphine analog that is scheduled as a controlled substance under the federal CSA.

An orphine that has been recently gaining a lot of attention is cychlorphine, which was first detected by the CFSRE in mid-2024. Pharmacological studies of cychlorphine show the drug to be approximately 10 times more potent than fentanyl.<sup>9</sup> The positivity rate of cychlorphine, specifically in fatal drug overdoses, has been increasing since mid-2025. The CFSRE has identified cychlorphine in 25 blood samples from fatal overdoses, with the vast majority of samples submitted in late-2025 and early-2026.<sup>10</sup> The 25 samples originated from eight states (California, Illinois, Louisiana, Nevada, New York, Pennsylvania, Tennessee, and Texas) and three Canadian provenances, with Tennessee exhibiting the highest number of confirmed cases.<sup>11</sup> In 11 of those 25 samples, cychlorphine was the sole opioid identified.<sup>12</sup> The most common co-occurring drugs identified along with cychlorphine among the 25 CFSRE samples were fentanyl and fentanyl analogs, methamphetamine, and novel benzodiazepines.<sup>13</sup> Additionally, in its January 2026 public alert on cychlorphine, the CFSRE reported that NMS Labs, an independent toxicology laboratory, had identified cychlorphine in more than 100 cases.<sup>14</sup>

Cychlorphine is not currently scheduled as a controlled substance on the state or federal levels. In February 2026, Kentucky introduced a bill that would criminalize the importation, sale, distribution, and trafficking of cychlorphine and impose penalties similar to those imposed for the importation, sale, distribution, and trafficking of fentanyl, carfentanil, and other fentanyl analogs.<sup>15</sup> While the Kentucky legislature can impose criminal penalties on a substance, the Kentucky Cabinet for Health and Family Services is the entity responsible for scheduling substances.<sup>16</sup> In March 2026, the Alabama legislature introduced a joint resolution urging the State Committee on Public Health to consider adding cychlorphine as a Schedule I controlled substance.<sup>17</sup>

## CONCLUSION

As clandestine chemists continue to exploit regulatory gaps, the proliferation of orphines, including cychlorphine, will likely continue throughout the U.S. illicit drug market. The high potency of orphines demonstrates the need for enhanced surveillance, increased testing capabilities, and timely public health alerts. While most orphines are currently unscheduled, there will likely be more scheduling actions on the state and federal levels in the near future as more policymakers become aware of orphines and the harm that they pose to public health and safety. LAPP will continue to monitor the spread of orphines and any new regulatory responses.

---

<sup>8</sup> Mu-opioid receptors are a type of receptor in the brain that is responsible for pain control, drug reward, and addictive behaviors. Gavril W. Pasternak and Ying-Xian Pan, “Mu-opioids and Their Receptors: Evolution of a Concept,” *Pharmacological Reviews* 64, no. 4 (October 2013): 1257-1317, <https://doi.org/10.1124/pr.112.007138>.

<sup>9</sup> “Increase in Fatal Overdoses Linked to Novel Synthetic Opioid N-Propionitrile Chlorphine (Cychlorphine),” *Center for Forensic Science Research & Education*, January 2026, [https://www.cfsre.org/images/content/reports/public\\_alerts/Public\\_Alert\\_N-Propionitrile\\_Chlorphine\\_013026.pdf](https://www.cfsre.org/images/content/reports/public_alerts/Public_Alert_N-Propionitrile_Chlorphine_013026.pdf).

<sup>10</sup> *Id.*

<sup>11</sup> *Id.*

<sup>12</sup> *Id.*

<sup>13</sup> *Id.*

<sup>14</sup> *Id.*

<sup>15</sup> H.B. 750, 2026 Gen. Assemb., Reg. Sess. (Ky. 2026).

<sup>16</sup> See KY. REV. STAT. ANN. § 218A.040 (West 2025).

<sup>17</sup> H.J.R. 281, 2026 Leg., Reg. Sess. (Ala. 2026).

## RESOURCES

Andrews, Emily. “Orphines: A Rising Group of Synthetic Opioids.” *Talking Drugs*, January 27, 2026. <https://www.talkingdrugs.org/orphines-a-rising-group-of-synthetic-opioids/>.

Aussem, Pat. “Orphines: New Opioids Stronger Than Fentanyl—What Parents Should Know.” *Partnership to End Addiction*, March 2026. <https://drugfree.org/article/orphines-new-opioids-stronger-than-fentanyl-what-parents-should-know/>.

Burley, Brandon. “New Synthetic Opioid Linked to 19 Tennessee Deaths Exposes Limits in Detection and Legal Clarity.” *Tennessee Lookout*, March 2, 2026. <https://tennesseelookout.com/2026/03/02/new-synthetic-opioid-linked-to-19-tennessee-deaths-exposes-limits-in-detection-and-legal-clarity/>.

Choi, Joseph. “What to Know About Cychlorphine, the Synthetic Opioid 10 Times Stronger than Fentanyl.” *The Hill*, March 12, 2026. <https://thehill.com/policy/healthcare/5779927-potent-opioid-cychlorphine-alarm/>.

Singer, Jeffery A. and Josh Bloom. “Meet the Drug War’s Latest Creation: Cychlorphine.” *The Hill*, March 37, 2026. <https://thehill.com/opinion/healthcare/5803049-cychlorphine-emerges-illicit-market/>.

Sprague, Jon E., et al. “Non-fatal Opioid Overdose Associated Predominantly with the, Benzimidazolone, Cychlorphine.” *Clinical Toxicology* 64, no. 2 (2026): 146-147. <https://doi.org/10.1080/15563650.2025.2594070>.

UNODC Laboratory and Scientific Service. “Increasing Nitazene and Orphine Analogues.” *United Nations Office on Drugs and Crime*, February 25, 2026. <https://www.unodc.org/LSS/Announcement/Details/e69b2ff5-5b91-4eea-8e1f-802ca7ad5080>.

UNODC Laboratory and Scientific Service. “Orphine Analogues.” *United Nations Office on Drugs and Crime*, last accessed April 3, 2026. <https://www.unodc.org/LSS/SubstanceGroup/Details/09f4734d-aadb-44a0-aa76-2e8816b1cc02>

## ABOUT THE LEGISLATIVE ANALYSIS AND PUBLIC POLICY ASSOCIATION

The Legislative Analysis and Public Policy Association (LAPPA) is a 501(c)(3) nonprofit organization whose mission is to conduct legal and legislative research and analysis and draft legislation on effective law and policy in the areas of public safety and health, substance use disorder, and the criminal justice system.

LAPPA produces up-to-the-minute comparative analyses, publications, educational brochures, and other tools ranging from podcasts to model laws and policies that can be used by national, state, and local criminal justice and substance use disorder practitioners who want the latest comprehensive information on law and policy. Examples of topics on which LAPPA has assisted stakeholders include naloxone laws, law enforcement/community engagement, alternatives to incarceration for those with substance use disorder, medication for addiction treatment in correctional settings, and the involuntary commitment of individuals with alcohol or substance use disorder.

For more information about LAPPA, please visit: <https://legislativeanalysis.org/>

© Legislative Analysis and Public Policy Association - This project was supported by the Model Acts Program, funded by the Office of National Drug Control Policy, Executive Office of the President. Points of view or opinions in this document are those of the author and do not necessarily reflect the official position or policies of the Office of National Drug Control Policy or the United States Government.