

METHADONE

(Trade Names: Methadose[®], Dolophine[®];
Street Names: Fizzies, Amidone, Chocolate Chip Cookies)

Introduction:

Methadone is a pharmaceutical opioid that is primarily used in detoxification or maintenance programs to treat opioid addiction. Methadone is currently available as an oral concentrate (10 mg/ml), oral solution (5 and 10 mg/5ml), tablet (5, 10, and 40 mg), injection (10 mg/ml), and powder (50, 100, and 500 mg/bottle for prescription compounding).

In November 2006, the Food and Drug Administration (FDA) issued a public health advisory stating that methadone use in pain control may result in life-threatening cardiac and respiratory changes and deaths. FDA further advised that methadone doses for pain relief should be carefully selected, slowly titrated, and carefully monitored by the prescribing physician. As of January 1, 2008, manufacturers of 40 mg methadone hydrochloride dispersible tablets have voluntarily agreed to restrict distribution of this formulation to only hospitals and facilities authorized for detoxification and maintenance treatment of opioid addiction. The 40 mg methadone product is not FDA-approved for use in the management of pain.

Licit Uses:

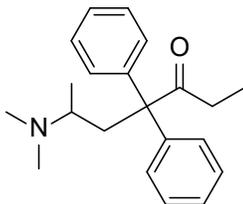
Methadone has been used for over forty years, primarily as a detoxification and maintenance treatment for opioid addiction.

Methadone products, when used for the treatment of narcotic addiction in detoxification or maintenance programs, should be dispensed only by pharmacies approved by appropriate regulatory authorities. When these products are used as analgesics, they may be dispensed by any licensed pharmacy.

In recent years, methadone has been increasingly prescribed for relief of moderate to severe pain. According to the IQVIA National Prescription Audit™, total prescriptions for methadone dispensed in the United States peaked in 2010 at approximately 4.4 million and then decreased each year to approximately 1.4 million in 2022, 1.3 million in 2023, and 1.2 million in 2024.

Chemistry:

Methadone is a synthetic drug. It is chemically known as (*RS*)-6-(dimethylamino)-4,4-diphenylheptan-3-one. The CAS number for methadone is 76-99-3. The molecular weight is 309.45 g/mol, with a molecular formula of C₂₁H₂₇NO. The chemical structure of methadone is shown below:



Pharmacology:

Methadone is a *mu*-opioid receptor agonist that binds strongly to proteins in various tissues, including the brain. Methadone has abuse potential and may produce psychic and physiologic dependence and tolerance. Upon discontinuation of its administration, low concentrations of methadone are maintained in the body due to the slow release of methadone from tissue binding sites. Notable features of methadone are its efficacy by the oral route, its prolonged duration of action in suppressing withdrawal symptoms in physically dependent individuals, and its tendency to produce persistent effects with repeated administration.

Pharmacological and toxic effects, abuse, and dependence liabilities of methadone are qualitatively similar to those of other schedule II opioid analgesics, such as morphine and oxycodone. Analgesic activity of racemic methadone is entirely due to its *l*-isomer, which is 8 to 50 times more potent than *d*-isomer. The *d*-isomer lacks significant respiratory depressant action and addiction liability but possesses antitussive activity. The analgesic effect of 8 to 10 mg of methadone is almost equivalent to that of 10 mg of morphine. With respect to total analgesic effects, methadone given orally is one-half as effective as its intramuscular administration. Pain relief from a dose of methadone lasts about 4 to 8 hours, but the drug may stay in the body for 8 to 59 hours.

Acute overdose of methadone, similar to morphine, can produce severe respiratory depression, somnolence, coma, skeletal muscle flaccidity, cool clammy skin, constricted pupils, reduction in blood pressure and heart rate, pulmonary edema, and death.

Pure opioid antagonists such as naloxone are specific antidotes against respiratory depression from methadone overdose

Illicit Uses:

America's Poison Centers reported that in 2022, methadone was associated with 1,731 case mentions, 864 single exposures, and 7 deaths. In 2017, methadone was associated with 2,611 case mentions; 1,054 single substance exposures; and 16 deaths.

The National Center for Health Statistics (NCHS) reported that in the United States, overdose death estimates involving methadone decreased by 14% from the 12-month periods ending December 2017 (3,308 deaths) and December 2019 (2,843 deaths). This estimate then increased by 34% for the 12-month period ending December 2021 (3,815 deaths) and subsequently decreased by 8% for the 12-month period ending December 2023 (3,501 deaths). For the 12-month period ending September 2024, NCHS estimated that 3,291 overdose deaths involved methadone.

User Population:

The 2023 National Survey on Drug Use and Health indicated that 206,000 people (aged 12 and older) reported misusing methadone in the previous year; consistent with results from 2022.

Illicit Distribution:

The Drug Enforcement Administration's National Forensic Laboratory Information System (NFLIS) Drug database collects scientifically verified data on drug items and cases submitted to and analyzed by participating federal, state, and local forensic laboratories. NFLIS-Drug received over 109,000 reports of methadone, with 1,483 reports of methadone in 2020; 1,108 in 2022; and 784 in 2024 (reports still pending).

Control Status:

Methadone is controlled in schedule II of the Controlled Substances Act.