



METHADONE

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

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DEA/OD/ODE

Introduction:

Methadone, a pharmaceutical opioid, is currently marketed as oral concentrate (10 mg/ml), oral solution (5 and 10 mg/5ml), tablet (5, 10, and 40 mg), injection (10mg/ml) and powder (50, 100, and 500 mg/bottle for prescription compounding).

According to the National Center for Health Statistics (NCHS) Health E-Stats publication, poisoning deaths increased 66% from 19,741 in 1999 to 32,691 in 2005. During the same time period, methadone deaths increased 468% to 4,462 (14% of all poisonings). 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 those 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 of opioid addiction. In recent years, methadone is also being increasingly prescribed for relief of moderate to severe pain. The number of prescriptions dispensed for methadone products in the U.S. decreased from 4.2 million in 2012 to 3.9 million in 2013 (IMS Health™). Methadone products, when used for treatment of narcotic addiction in detoxification or maintenance programs, shall be dispensed only by pharmacies approved by appropriate regulatory authorities. When used as analgesics, they may be dispensed by any licensed pharmacy. The U.S. aggregate production quota for methadone in 2014 is 31,875 kilograms.

Chemistry/Pharmacology:

Methadone, (RS)-6-(dimethylamino)-4,4-diphenylheptan-3-one, is a synthetic drug with *mu*-opioid receptor agonist activity. 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, 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.

Methadone binds strongly to proteins in various tissues, including the brain. Upon discontinuation of its administration,

low concentrations of methadone are maintained in the body because of 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. 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:

Methadone has abuse potential and may produce psychic and physiologic dependence and tolerance. According to the National Survey on Drug Use and Health, 2.46 million persons age 12 and older in 2012 reported that they used methadone for non-medical purposes at least once in their lifetime, an increase from 2.10 million persons in 2011. The American Association for Poison Control Centers reported 4,693 case mentions (1,893 single exposures) and 51 deaths associated with methadone in 2012. According to the Drug Abuse Warning Network (DAWN), the estimated number of emergency department visits associated with nonmedical use of methadone is 66,870 in 2011. The Medical Examiners Commission Reports released by the Florida Department of Law Enforcement (FDLE) indicate that methadone related deaths in Florida decreased from 954 in 2011 to 750 in 2012.

Illicit distribution:

According to the National Forensic Laboratory Information System (NFLIS) and the System to Retrieve Information from Drug Evidence (STRIDE), 7,183 methadone items/exhibits were identified by federal, state and local forensic laboratories in 2012 and 5,324 in 2013.

Control status:

Methadone is in Schedule II of the Controlled Substances Act.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section, Fax 202-353-1263, telephone 202-307-7183, or Email ODE@usdoj.gov.