
METHADONE (Methadose) Fact Sheet [G]

Bottom Line:

Methadone is a long-acting opioid agonist that is one of the mainstays of opioid use disorder (OUD) treatment, along with buprenorphine. Compared to patients not in treatment, those receiving methadone have lower all-cause mortality, rates of transmissible diseases, criminal convictions, suicide, and even cancer. Methadone for OUD must come from a federally regulated opioid treatment program (OTP), or “methadone clinic.” Patients start out by going to the clinic daily, which can be an inconvenience. Disadvantages include the potential for diversion and the possible accumulation of doses due to its long half-life.

FDA Indications:

Opioid dependence; severe pain.

Dosage Forms:

- **Tablets (G):** 5 mg, 10 mg, 40 mg (scored).
- **Oral solution (G):** 10 mg/5 mL, 5 mg/5 mL.
- **Oral concentrate (G):** 10 mg/mL.

Dosage Guidance:

Start 15–30 mg single dose; then 5–10 mg every two to four hours until cessation of withdrawal symptoms; max 40 mg on day 1. Maintenance treatment: Increase daily dose by 5–10 mg every two to three days until the patient is no longer experiencing opioid cravings; 80–120 mg per day is a common maintenance dose for opioid dependence.

Monitoring: ECG if cardiac disease.

Cost: \$

Side Effects:

- Most common: Constipation, dizziness, sedation, nausea, sweating.
- Serious but rare: May prolong the QT interval and increase risk for torsades de pointes; caution in patients at risk for QT prolongation, especially with doses >100 mg/day. Severe respiratory depression may occur; use extreme caution during initiation, titration, and conversion from other opioids to methadone. Respiratory depressant effects occur later and persist longer than analgesic effects, possibly contributing to cases of overdose.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Opioid agonist.
- Metabolized primarily through CYP2B6, 2C19, and 3A4 (major); inhibits CYP2D6; t_{1/2}: 8–59 hours.
- High potential for interactions. Avoid concomitant use with other potent sedatives or respiratory depressants. Use with caution in patients on medications that are metabolized by CYP2D6, inhibit CYP3A4, prolong the QT interval, or promote electrolyte depletion.

Clinical Pearls:

- Schedule II controlled substance; distribution of 40 mg tablets restricted to authorized opioid addiction treatment facilities.
- Currently, may only be dispensed according to the Substance Abuse and Mental Health Services Administration's (SAMHSA) Center for Substance Abuse Treatment (CSAT) guidelines. Regulations vary by area; consult regulatory agencies and/or methadone treatment facilities. Advocacy efforts to expand methadone treatment beyond federally regulated opioid treatment programs have escalated, particularly after relaxed flexibilities during COVID-19 showed positive outcomes.
- Methadone accumulates with repeated doses; dose may need reduction after three to five days to prevent CNS depressant effects.

Fun Fact:

A persistent but untrue urban legend claims the name “Dolophine” was coined in tribute to Adolf Hitler by its German creators. The name was in fact created after the war by the American branch of Eli Lilly, and the pejorative term “adolphine” (never an actual name of the drug) didn't appear in the US until the early 1970s.