METHADONE (Methadose) Fact Sheet [G]

BOTTOM LINE:
Opioid replacement therapy via methadone reduces or eliminates illicit use of opioids and criminality associated with opioid use, supporting health and social functioning. It is a harm reduction model reducing transmission of infectious diseases such as hepatitis and HIV. Disadvantages include potential for accumulation with repeated doses (which may result in toxicity), interindividual variability in pharmacokinetic parameters, potential for drug interactions, challenges associated with dose titration, stigma associated with opioid replacement therapy, and limited availability of treatment programs (nonexistent in some geographic areas, long wait lists in other areas). Methadone has long been established as an effective treatment of opioid addiction in adults, although federal regulations prohibit most methadone programs from admitting patients younger than 18 years.

PEDIATRIC FDA INDICATIONS:
None.

ADULT FDA INDICATIONS:
Opioid dependence; severe pain.

OFF-LABEL USES:
None.

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

DOSAGE GUIDANCE (ADULTS):
Start 15–30 mg single dose; then 5–10 mg every two to four hours. Adjust dose to prevent withdrawal symptoms; max 40 mg on day 1. 80–120 mg per day is a common maintenance dose for opioid dependence.

MONITORING: ECG.

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; usually 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 ½: 8–59 hours.
- High potential for interactions. Avoid concomitant use with other potent sedatives or respiratory depressants. Use with caution in patients on medications metabolized that are by CYP2D6, inhibit CYP3A4, prolong the QT interval, or promote electrolyte depletion.

EVIDENCE AND CLINICAL PEARLS:
- A few studies in adolescents. Most recently, a 12-month study of 120 adolescents found methadone treatment reduced heroin use, but treatment retention was challenging (similar to adult studies).
- C-II controlled substance; distribution of 40 mg tablets restricted to authorized opioid addiction treatment facilities.
- 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.
- 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.