

Methadone Fact Sheet

Facts about the Use of Methadone for Chronic Pain

- Synthetic, highly lipophilic opioid
- Schedule II substance
- Mechanisms of action: muopioid agonist; monoamine reuptake inhibitor; N-methyl-D-aspartic acid (NMDA) antagonist
- May not prescribe for opioid detox or maintenance, write “for pain” on prescription
- Recommended dosing: Start low, go slow
 - Opioid-naïve patient: Starting dose, 2.5–5 mg 8–12 (up to 24) hr for 4–7 days
 - Frail patient older patient: 2.5 mg once or twice daily
 - Converting from morphine to methadone: Suggested dosing guide³

Total Daily Oral Morphine Dose	% of Morphine Dose
<100 mg	33%
101-300 mg	20%
301-600 mg	10%
601-800 mg	8%
801-1000 mg	7%
>1000 mg	5%
>2000 mg	Consult pain specialist

- Duration of analgesia is approximately 3-6 hrs; typically extends to 6-12 hr with repeated dosing
- Due to its long half-life ($t_{1/2} = 22$ hrs), plasma levels may take 5-7 days to stabilize
- Side effects include pruritus, nausea, constipation, confusion, sedation, sweating, flushing, and respiratory depression
- Inexpensive compared with opioids (30-day supply: \$8.00)
- Discontinue methadone slowly: 1-2 mg/wk

Cautions Regarding the Use of Methadone for Chronic Pain

- Titrate slowly, analgesic effect does not peak for 3-5 days after dose changes
- Elimination half-life (8-59 hours) is longer than its duration of analgesic action (4-8 hours)
- In chronic use, methadone may be retained in the liver and then slowly released, prolonging the duration of action despite low plasma concentrations
- Use logarithmic conversion, relatively small doses of methadone may have analgesic efficacy of larger doses of morphine
- Cross-tolerance, as with all opiates, is incomplete. It is recommended that the initial dose is 50-75% of the equianalgesic dose.³
- Methadone’s peak respiratory depressant effects occur later and persist longer than its peak analgesic effects
- Methadone can cause serious cardiac conduction effects, including QT interval prolongation and torsades de pointes
- Methadone label revised by FDA due to reported deaths from respiratory depression and cardiac arrhythmia
- Potential for drug interactions as metabolized by the cytochrome P450 system
- Changes in gastric pH or P-glycoprotein activity by affect absorption
- Caution is recommended when methadone is prescribed with benzodiazepines

References:

1. <http://www.fda.gov/cder/drug/InfoSheets/HCP/methadoneHCP.htm>
2. Toombs JS, Kral LA. Methadone treatment for pain states. American Family Physician. 2005;71(7):1353-8. <http://www.aafp.org/afp/20050401/1353.html>
3. Gazelle G and Fine PG. Fast Facts and Concepts #75: Methadone for the treatment of pain, 2 nd Edition. July 2006. End-of-Life Physician Education Resource Center: <http://www.eperc.mcw.edu>.