

# The Role of Methadone in the Management of Chronic Non-Malignant Pain: Specific Considerations

## Overview

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Although the literature on methadone for non-malignant pain is scanty and based on case studies, the increasing use of methadone for this purpose requires recommendations to guide practice. There is extensive literature on the use of methadone as a potent analgesic agent for cancer pain and therefore recommendations for the use of methadone in the management of chronic non-malignant pain must be extrapolated from the cancer pain literature.

Methadone is a synthetic opioid analgesic with excellent oral bioavailability, a side effect profile similar to other opioid analgesics and a duration of action of at least eight hours with repetitive dosing. These qualities make it an attractive drug for outpatient pain management. Methadone also has an opioid receptor profile different from that of morphine and has N-methyl-D-aspartate (NMDA) antagonist activity that may confer advantages over morphine. However, experience in the use of methadone for cancer pain has revealed that methadone is far more potent as an analgesic agent than has been suggested by equianalgesic tables derived from single dose studies. With repetitive dosing, methadone is approximately ten times more potent than indicated in these standard tables. The main reason for this is probably the long elimination half-life of methadone (24-36 hours) which allows for much higher drug levels to be reached than could be predicted from single dose studies. This has obvious clinical implications since methadone takes 5-7 days to reach steady state at any particular dose. Therefore, the use of methadone as an analgesic agent requires the same pain assessment skills as for any other opioid drug, but even greater scrutiny in patient monitoring of analgesic and side effects.

## Methadone use in the Management of Chronic Non-Malignant Pain

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In Canada, methadone is available at low cost as an elixir which is usually made up at a concentration of 1 mg/ml. In opioid-naive patients or patients taking codeine preparations, methadone 2.5 mg q8h is safe and usually well-tolerated. For patients already on a major opioid analgesic like oxycodone or morphine, a reasonable starting dose of methadone is 5 mg q8h with dose increments of 5 mg q8h every 5-7 days. A general rule is to provide careful dose titration until adequate pain relief is achieved or side effects limit further dose escalation. However, one should look for a graded analgesic response to incremental dosing. The absence of a graded analgesic response may mean that the patient is not

opioid-responsive. Patients should be seen weekly during the titration phase and every month or two during the maintenance phase.

For patients being switched from relatively large doses of an opioid analgesic (> 200 mg oral morphine or morphine equivalents daily), the table below should be used to calculate equianalgesic doses. For patients taking more than 500 mg oral morphine or morphine equivalents daily, the conversion to methadone should be staged with a third of the anticipated methadone dose being introduced every five days so that the entire conversion takes fifteen days. The dose of the previous opioid is decreased by a third every five days in inverse fashion.

### Equianalgesic Doses of Common Opioid Analgesics Relative to Oral Methadone with Repetitive Dosing

Drug	Per Os (PO)	Intramuscular/Subcutaneous
Methadone	2 mg	
Morphine	30 mg	10 mg
Hydromorphone	8 mg	2 mg
Oxycodone	15 mg	

Patients and co-habitants should be warned about potential side effects (especially drowsiness and respiratory depression) and the possibility that side effects can continue to evolve for five to seven days after each dose adjustment. The spouse or significant other should be available at least twice daily to monitor for toxicity. Since drowsiness commonly precedes respiratory depression, they should be instructed to call the prescribing physician if drowsiness develops to obtain advice about further dosing. This obviously requires physician availability 24 hours a day during the titration phase. Elderly patients (over the age of 65), patients with severe lung disease and patients who cannot be adequately monitored at home should be considered for inpatient initiation of methadone treatment.

*Note: The CPSO involvement in the opioid dependence program mentioned is unrelated to the use of Methadone for analgesic purposes. If a physician wishes to obtain a permit to prescribe Methadone for analgesic purposes, he or she needs to apply to the Office of Controlled Substances in Ottawa (613) 946-5139*