



College of Physicians and Surgeons  
of British Columbia

# Methadone for Analgesia Guidelines

December 2016

Updated February 22, 2019

# Methadone for Analgesia Guidelines

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## Table of Contents

<b>Introduction</b> .....	<b>2</b>
<b>Prescribing Methadone</b> .....	<b>3</b>
<b>Patient Assessment</b> .....	<b>4</b>
<b>Opioid Use Disorder and Chronic Pain</b> .....	<b>7</b>
<b>Pharmacology of Methadone</b> .....	<b>8</b>
Side Effects .....	9
<b>Drug Interactions</b> .....	<b>12</b>
<b>Available Strengths and Forms of Methadone</b> .....	<b>14</b>
<b>Switching Opioids</b> .....	<b>15</b>
Indications for Switching Opioids .....	15
<b>Methods for Switching to Methadone</b> .....	<b>17</b>
"Start Low, Go Slow" .....	17
Slow-Switch Method .....	19
PRN Methadone Switch .....	21
<b>Using Methadone Safely: What Can Go Wrong</b> .....	<b>22</b>
<b>Urine Drug Testing</b> .....	<b>23</b>
<b>Appendices</b> .....	<b>24</b>
Appendix A: Links to application forms and relevant documents .....	24
Appendix B: Equianalgesic conversion guides .....	25
Appendix C: Equianalgesic potency of opioids for chronic pain .....	27
<b>Revision History</b> .....	<b>29</b>

# Methadone for Analgesia Guidelines

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## Introduction

Although methadone is most commonly used in the treatment of opioid use disorder, it is also used for the treatment of chronic pain. The Prescription Review Panel of the College of Physicians and Surgeons of British Columbia (the College), in consultation with several experienced prescribers and pharmacists, has developed these guidelines based on best clinical evidence and experience, as a resource for physicians who wish to prescribe methadone for the management of chronic pain.

Methadone is an oral long-acting synthetic opioid. Due to the unique pharmacokinetics of methadone, which has a long and variable half-life and a large volume of distribution, if doses are inappropriately high or increased too rapidly there is a risk of accumulation leading to sedation, respiratory depression and even death. It is a drug that must be used cautiously and doses must be tailored to each patient. It is important that physicians be familiar with methadone's unique attributes before initiating patients on therapy. Inexperienced physicians are encouraged to consult with colleagues who are familiar with the use of methadone, especially if considering a rapid switch method.

Physicians should carefully assess and reassess patients, particularly when initiating methadone therapy, as the risk and onset of respiratory depression is somewhat unpredictable. Particular caution should be exercised in elderly patients, and patients with liver disease. It is important to give consideration to the drug interactions between methadone and other drugs that are metabolized through, or affect the cytochrome P450 pathway. Regular review of PharmaNet facilitates this.

In addition to individualizing treatment, physicians should be careful when switching patients from other opioids to methadone. When compared to other opioids, methadone has more potential drug interactions. The values found in published equianalgesic opioid conversion charts indicate a wide range of possible methadone doses, and it is important to remember that **the equianalgesic dose quoted is an expected end point and not a starting point for a switch**. Again, individual patient responses may vary from those predicted by equianalgesic guidelines.

As with all controlled drugs, physicians should be alert for diversion of their prescriptions of methadone and potentially fraudulent requests for this drug, as this remains a significant concern in the community. Methadone-related deaths are commonly associated with illegal or unauthorized use, or with patients receiving methadone for analgesia.

It should also be clearly understood that not all pain responds to opioids. There is evidence to suggest that some patients with chronic pain may have their pain made worse by taking opioids, because of opioid-induced hyperalgesia. This is manifested by spread of pain outside the localized area of presentation, and increased sensitivity to pain (hyperalgesia) over the whole body. Allodynia may also be present, where normally non-painful sensory stimulus (e.g. light touch) is perceived as painful. When this is identified in a patient already taking a non-methadone opioid, a switch to methadone can relieve the allodynia, start to reverse the hyperalgesia, and facilitate a slow taper off opioids altogether, whilst more appropriate non-opioid and non-pharmacological treatments can be implemented<sup>1,2</sup>.

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<sup>1</sup> Hayes CJ, Painter JT. A comprehensive clinical review of opioid-induced allodynia: discussion of the current evidence and clinical implications. *J Opioid Manag.* 2017 Mar/Apr;13(2):95-103.

<sup>2</sup> Yi P, Pryzbylowski P. Opioid induced hyperalgesia. *Pain Med.* 2015 Oct; 16 Suppl 1:S32-6.

# Methadone for Analgesia Guidelines

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## Prescribing Methadone

On May 19, 2018, Health Canada removed the requirement for physicians to obtain an exemption to prescribe methadone under section 56(1) of the *Controlled Drugs and Substances Act*. There is no longer an application and approval process, and the College no longer maintains a list of methadone prescribers. The College of Pharmacists of British Columbia no longer maintains information on which pharmacies dispense methadone. All BC pharmacies have the option of providing methadone services, but some may choose not to do so.

Physicians wishing to prescribe methadone for analgesia must read and adhere to the College standard *Prescribing Methadone*, and complete the Canadian Virtual Hospice's free, one-hour accredited online course on methadone for pain in palliative care ([www.methadone4pain.ca](http://www.methadone4pain.ca)). Prescribers are also required to familiarize themselves with the College Standard *Safe Prescribing of Opioids and Sedatives*, and to regularly review each patient's PharmaNet profile, to ensure safe prescribing of methadone and to encourage communication with the patient's other health professionals, where necessary.

Physicians looking for resource articles are encouraged to contact the College [library](#). Most articles are provided free of charge to registrants, and monthly automated searches can be customized for the registrant.

Prescriptions for analgesic methadone should be written on a regular controlled prescription form (also known as a duplicate form). Physicians' copies of the controlled prescription forms should be retained with the patient record (not in the prescription pad) and must be identical to the copies issued to the patients.

# Methadone for Analgesia Guidelines

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## Patient Assessment

Methadone may be indicated for management of cancer pain or chronic non-cancer pain (CNCP). It is not a first-line analgesic, nor is it appropriate for acute or unstable pain. It is important to determine and document the patient's diagnosis before establishing a treatment plan which addresses the chronic pain and also takes into account concurrent problems.

An assessment of any patient with chronic pain comprises the following:

1. Pain history – this assessment should include:
  - a. Previous trials of analgesia and non-pharmacologic treatments.
  - b. What the patient is currently taking and its effectiveness in terms of pain and function.
  - c. A brief systems review with particular attention to gastrointestinal, hormonal, and sleep-related symptoms. For example, prior to starting methadone it is important to know if the patient has constipation or symptoms of sleep-disordered breathing.
2. Medical history – review all documentation and previous diagnoses; specific attention to any history of heart disease, arrhythmia, and syncope.
3. Surgical history – review all documentation and previous diagnoses.
4. Psychiatric history – screen for mood disorders, sleep disturbance, trauma history (particularly childhood sexual trauma), personality disorders, limited coping skills.
5. Substance use history – screen for past and current substance use including nicotine, alcohol, over-the-counter medication, medical cannabis, and illicit substances. Structured screening for substances of misuse should include but is not limited to the following:
  - a. Questions pertaining to current and past quantity and frequency of substance use—examples:
    - i. “In the last year, how many times have you had five or more drinks (or, for women, four or more drinks) on one occasion?”
    - ii. “In the last year, have you used substances such as cocaine, heroin, fentanyl or methamphetamine?”
    - iii. “Have you or your family ever felt that you were falling in trouble with use of recreational drugs, including alcohol?”
  - b. Questions pertaining to past history of treatment—example:
    - i. “Have you ever received treatment for substance misuse, such as attending a treatment centre, 12-step meeting or counselling?”
  - c. Questions pertaining to family or patient history of substance misuse—example:
    - i. “Have you or any of your family members ever been diagnosed with substance use problems?”

# Methadone for Analgesia Guidelines

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6. Family history – including any history of sudden death, which could be from a hereditary long QT syndrome.
7. Social history – specifically, what social supports the patient has, the presence of children or young adults in the house.
8. Physical examination to establish physical function and degree of disability.
9. Laboratory tests and imaging results if required—special attention to hepatic function.
10. ECG – before starting methadone, the prescribing physician should inform patients of arrhythmia risk at high doses (over 120mg/day) and consider undertaking a baseline ECG if a history of arrhythmia or the patient is concurrently on other QT prolonging drugs or electrolyte disturbance. In patients with no other risk factors for cardiac arrhythmia, the threshold for recommending recording an ECG is unclear and there is no universal agreement in the literature.

The following strategies apply to all controlled medication, whether in pill or patch form.

11. Urine drug testing (UDT) – the literature concerning substance misuse demonstrates that self-reports by patients who misuse substances are variable and of questionable validity. Therefore, most experts recommend a urine drug test prior to prescribing opioids. Routine use of UDT on all patients being prescribed opioids will destigmatize the test. Counselling prior to administration of the test is recommended. Ensure that if a patient is already being prescribed an opioid that this information is provided in the request for analysis of the urine specimen, as some synthetic and semi synthetic opioids do not show up on routine screening and must be specifically requested.

Unscheduled urine drug testing can also be considered as part of the longitudinal monitoring process.

12. Pill counts – if methadone is being considered for treatment of CNCP in pill form, the assessing physician should consider undertaking a pill count of the current medication to assess whether it correlates with the last dispense (as per PharmaNet) and the way the patient describes taking it. Any discrepancies should be discussed. Unscheduled pill counts can be a useful strategy for assessing treatment plan adherence. Compliance can be further enhanced by use of blister packing.
13. The assessing physician should obtain collateral information from the patient's usual prescriber/family physician. Any red flags in the patient's care should be considered including running out of medication early, lost medication, stolen medication, over sedation, and sleep apnea.

Once a full patient assessment has been undertaken, a full diagnosis can be made. This should typically identify the source and type of pain (e.g. peripheral nociceptive, neuropathic, mixed nociceptive-neuropathic, non-nociceptive centralized, opioid-induced hyperalgesia, opioid-induced allodynia) as well as any potential allied clinical considerations, and patient goals of treatment (typically based on function and disability reduction). It is important to contact all other prescribers to ensure that all involved agree on the goals of care and prescribing responsibilities.

Ideally, the prescriber of opioids would be the sole prescriber of pain medication for the patient. With most specialist-initiated treatments, once a patient is stable, the family physician assumes ongoing

# Methadone for Analgesia Guidelines

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prescribing for the patient. Similarly, family physicians of patients who require methadone for pain are strongly encouraged to obtain adequate education and training in prescribing methadone for analgesia, to maintain continuity of care. This will also free up specialist clinics to be able to provide consultations for new patients more quickly.

# Methadone for Analgesia Guidelines

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## Opioid Use Disorder and Chronic Pain<sup>3</sup>

Chronic non-cancer pain (CNCP) is a very common condition affecting up to a third of the population. It causes tremendous costs to society, both financially and socially. All patients with CNCP should undergo a thorough evaluation and regular review to make sure that a potentially treatable condition is not missed. Though many patients have identifiable pain generators such as arthritis or spinal degeneration, it can be difficult to identify a cause in some patients.

There are also patients in whom pain is the presenting symptom of psychiatric illnesses such as depression, or social issues (“total pain”). Examples include sleep deprivation, being a victim of domestic violence, or post-traumatic stress disorder. These issues should be identified by thorough patient assessment and ongoing review.

It is important that all patients who are being considered for opioid therapy, and especially those with CNCP, be screened for underlying substance use disorder, including alcohol, prescription medication, or street drugs. **Treatment with an opioid analgesic is not contraindicated in a patient with a history of substance use disorder (SUD), but a comprehensive treatment plan with clear boundaries, which addresses both the chronic pain and SUD, must be developed before medication is provided.** Patients who are already using other substances in a problematic manner may experience further loss of control if they are provided with large dispenses of potent opioids. Engagement in a recovery program is not prerequisite, but strongly recommended for such patients. It is recommended that a physician experienced in addictions assessment and treatment be consulted and that a shared-care treatment and monitoring plan be developed for these patients. If an addictions specialist is not present in your community, support may be obtained by contacting the RACE line ([www.raceconnect.ca](http://www.raceconnect.ca)). At a minimum, the treating physician should keep the patient under close follow-up with periodic objective measurements such as unscheduled urine toxicology and pill counts.

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<sup>3</sup> A detailed treatment of this complex topic is beyond the scope of this guideline.



# Methadone for Analgesia Guidelines

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## Pharmacology of Methadone

Methadone has many characteristics which make it useful for the treatment of chronic pain, particularly its pharmacologic activity in chronic pain syndromes. It is a potent mu ( $\mu$ ) opioid receptor agonist and an NMDA (N-methyl-D-aspartate) receptor antagonist. The NMDA mechanism is thought to play an important role in the prevention of opioid tolerance, potentiation of analgesic effects and for neuropathic pain syndromes.

Methadone is highly lipophilic with rapid absorption in the upper gastrointestinal tract. It has a large initial volume of distribution followed by slow tissue release, as well as a high bioavailability of around 80%. Although its onset of action can be as short as 30 minutes, it should be avoided as a breakthrough or PRN medication due to its long duration of action and potential for dose accumulation. Initial extensive and rapid distribution into body fat occurs within 2 to 3 hours of ingestion, and a subsequent slower elimination phase lasts for 15 to 60 hours<sup>4</sup>. Methadone has no active metabolites and biotransformation is not required for analgesic effect. It is metabolized in the liver primarily through the cytochrome P450 3A4 enzyme, which is a major metabolic enzyme for many other drugs, and is predominantly excreted in feces<sup>5</sup>. Accordingly, careful review of concurrent medications is important when considering methadone as a treatment option.

**Methadone's equianalgesic potency as compared with other opioids can be unpredictable.** Its metabolism does not appear to be affected by mild to moderate hepatic disease, but caution should be exercised in patients with severe or unstable hepatic failure, hepatitis, or people on antiretrovirals for HIV.<sup>6</sup> Methadone has an extremely long and variable half-life (24 to 190 hours depending on the individual), which does not correlate with the observed duration of analgesia (six to 12 hours). This can lead to accumulation, with an increased risk of sedation and respiratory depression if the dose is increased too rapidly. Rapid titration methods used for other opioids, such as morphine and hydromorphone, do not apply to methadone. Methadone dosages should not be increased more frequently than every three to five days except under close supervision, such as on an inpatient or palliative care unit.

No dose adjustment is needed in mild to moderate renal failure, but when switching to methadone from another opioid in the presence of severe renal impairment, a slow switch and conservative dosing is usually recommended, and the dose then increased according to patient tolerability. Methadone is not removed by dialysis.

Methadone is not effective for chronic pain as a single daily dose and is usually prescribed to be given every eight hours. A small proportion of patients may require a dose every six hours and occasionally patients may find a 12-hour schedule adequate.

Newborns of mothers on methadone treatment for opioid use disorder have better perinatal parameters such as birth weight and head circumference than those of untreated patients with opioid use disorder. However, the balance between risks and benefits of methadone treatment exclusively for

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<sup>4</sup> Thai V, Fainsinger RL. Pain. In: Emanuel LL, Librach LS, editors. Palliative care core skills and clinical competencies. 2nd ed. Philadelphia: Saunders; 2011. p. 95-114.

<sup>5</sup> Kreek MJ, Schechter AJ, Gutjahr CL, Hecht M. Methadone use in patients with chronic renal disease. *Drug Alcohol Depend.* 1980 Mar; 5(3):197-205.

<sup>6</sup> Layson-Wolf, C, Goode JV, Small RE. Clinical use of methadone. *J Pain Palliat Care Pharmacother.* 2002; 16(1):29-59.

# Methadone for Analgesia Guidelines

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analgesia (in the absence of opioid use disorder) in this patient population are different. Patients receiving methadone for analgesia who plan on becoming pregnant should be made aware that the risks to fetus appear small but are probably not zero, and there should be consideration of gradual taper to discontinuation, preferably in advance of pregnancy. If this is not possible, the prescriber should be aware of the physiologic changes in methadone metabolism that occur in pregnancy. These include changes in protein binding, changes in total body fluid, volume and fat, longer gastrointestinal transit time, and induction of CYP3A4, which will affect methadone absorption and distribution. Methadone metabolism increases from the first to the third trimesters, so doses may need to be adjusted to prevent over- or under-medication. It is important to monitor for neonatal withdrawal in the postpartum period, and to be aware of potential for toxicity as the excess fat gained throughout pregnancy is metabolized and releases the stored methadone. Methadone is present in breast milk in only very small amounts, and maternal methadone therapy should not be considered a contraindication to breastfeeding, especially at low doses.<sup>7</sup>

When switching from other opioids, such as morphine, the equianalgesic ratio is quite variable. Extreme caution must be exercised, particularly when the patient is on high doses of the previous opioid. In highly opioid-tolerant patients, the ratio can vary from 25:1 to as high as 200:1. There are a number of published guidelines for conversion from morphine to methadone. No method has been shown to be superior to another by direct comparison, and the method chosen should be appropriate for the circumstances.

See [appendix B](#) for a table of conversion ratios for oral morphine to oral methadone. It is important to note that these conversion guides refer to the expected final stable dosage. **The starting dose should be much lower as the first step of a stepped substitution or “start low, go slow” method of initiation, and gradually increased until better pain control and function is achieved.** See [Switching Opioids](#) for suggested protocols. In an outpatient setting, the preferred method is “start low, go slow.”

## Side Effects

### *Central Nervous System*

CNS side effects include sedation, dysphoria, disorientation, and more rarely, myoclonus, delirium and headache. Sedation tends to resolve within a few days of a dose increase, but may be dose-limiting. Stimulants may be helpful to counteract opioid-induced sedation in patients with a short life expectancy (i.e. in palliative care), but are not recommended for long-term treatment or in the chronic non-cancer pain setting because of the high rate of development of tolerance and the potential for misuse. Patients should be instructed not to drive or operate machinery during the initiation and stabilization phases. Once patients are on a stable dose, however, the use of methadone (or any other long-acting opioid) should not be a barrier to driving. Delirium can be caused by opioid toxicity and is a frequent indication for a switch to methadone, which has a lower potential to cause delirium (see [Switching Opioids](#)).

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<sup>7</sup> Glatstein MM, Garcia-Bournissen F, Finkelstein Y, Koren G. Methadone exposure during lactation. *Can Fam Physician*. 2008 Dec; 54(12):1689–1690.

# Methadone for Analgesia Guidelines

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## Gastrointestinal System

As with any opioid, methadone can cause gastrointestinal side effects such as nausea, constipation, dry mouth, anorexia and (rarely) biliary spasm. Methadone tends to be less constipating than other oral opioids. When switching from other oral opioids to methadone, patients may experience temporary diarrhea and so may need fewer laxatives. Constipation is easier to prevent than to treat so it is advised to discuss bowel regimens with all patients.

## Respiratory System

Respiratory depression may occur in patients whose initial dose of methadone is too high or whose dose is increased too quickly. Respiratory depression is not a concern with chronic stable dosing, unless new medication with the potential to interact has been added (for example, zopiclone for insomnia). Patients with decreased respiratory drive, such as COPD patients with CO<sub>2</sub> retention or those with severe sleep apnea, should be observed cautiously when initiating any opioid, and the dose should be titrated slowly. This concern should not preclude the use of long-acting opioids for dyspnea due to cancer, end-stage COPD, heart failure or other chronic lung diseases, as opioids may offer relief in these situations. Transient pulmonary edema and bronchospasm are rarely seen but can occur with any opioid, including methadone. If patients have a history of true opioid hypersensitivity (e.g. anaphylaxis or urticaria), the initial doses of methadone should be administered under close medical supervision.

## Cardiovascular System

Hypotension and bradycardia can occur and may lead to faintness or syncope. Flushing may occur. Peripheral edema has been reported, usually when high doses are used, and can occur months after commencing methadone.<sup>8</sup>

Unlike other opioids, methadone can cause QT prolongation through interaction with the voltage-gated potassium channels of the myocardium. Patients treated with methadone for pain do not usually require doses over 150 mg/day. There have been some reports of *torsades de pointes* in patients taking high-dose methadone (doses in excess of 150 mg/day). Most of these cases also had other risk factors for cardiac arrhythmia such as pre-existing cardiac disease, metabolic concerns (such as hypomagnesemia from prior use of platin-based chemotherapy and/or malnutrition), or the use of other drugs known to cause QT prolongation. Severe malnutrition due to eating disorders, alcoholism or general debility can cause severe bradycardia and QT prolongation, which increases the risk of arrhythmia. It is recommended that patients who have cardiac disease, other medications or metabolic concerns known to cause QT interval prolongation should have an electrocardiogram prior to starting on methadone (see [Drug Interactions](#)).

If the QTc interval is prolonged to 450-500 ms, then discuss the risks and benefits of methadone (in the context of the patient's goals of care). The QT interval may fluctuate over time, so periodic repeat ECGs are recommended if there is concern about high methadone dosing, other risk factors for arrhythmia, or potential interactions. If QTc >500 ms re-evaluate dose, other contributory factors (e.g. other QTc prolonging drugs, drugs that slow methadone metabolism<sup>9</sup>), and consider specialist consultation.

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<sup>8</sup> Mahe I, Chassany O, Grenard AS, Caulin C, Bergmann JF. Methadone and edema: a case report and literature review. *Eur J Clin Pharmacol*. 2004 Feb; 59(12):923-4.

<sup>9</sup> Summaries for patients. QTc interval screening in methadone treatment. *Ann Intern Med*. 2009 Mar 17; 150(6): 1-26.

# Methadone for Analgesia Guidelines

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## *Genitourinary System*

Urinary hesitancy or retention may occur with any opioid, but may be less so with methadone.<sup>10</sup> Chronic use of any opioid can result in hypogonadism, due to central suppression of hypothalamic release of gonadotrophin-releasing hormone (GnRH). GnRH suppression can lead to fatigue, depression, anxiety, decreased muscle mass and reduced libido. Testosterone replacement may be appropriate if testosterone levels are low and patients are symptomatic.

## *Dermatologic System*

Sweating can be a problem with all opioids, and is common with methadone. Pruritus and rashes are seen less frequently with methadone than with other opioids, and methadone may be well tolerated by patients who have allergic reactions to other opioids.

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<sup>10</sup> Gedney JA, Liu EH. Side-effects of epidural infusions of opioid bupivacaine mixtures. *Anaesthesia*. 1998 Dec; 53(12):1148-55.

# Methadone for Analgesia Guidelines

## Drug Interactions

Drugs which interact with methadone generally involve inducers or inhibitors of the cytochrome P450 (CYP) system—mainly CYP3A4 and, to a lesser extent, 1A2 and 2D6. Note that some genetic polymorphism can influence enzyme distribution.

[Appendix A](#) contains a complete list of medications metabolized by cytochrome P450 3A4. This list is divided into inducers, substrates and inhibitors, and should be referred to whenever a new drug is started or when a drug which has been in chronic use is discontinued. Commonly used drugs in each class of interaction are described here.

Inducers of P450 3A4	These drugs will <b>reduce</b> methadone levels—for example, rifampin/rifampicin, phenytoin, carbamazepine. When patients on methadone are initiated on a P450 3A4 inducer, a minor dose increase in methadone may be required.
Inhibitors of P450 3A4	These drugs will <b>raise</b> methadone levels—for example, ketoconazole, fluconazole, fluoxetine, ciprofloxacin and erythromycin. When methadone patients are initiated on a P450 3A4 inhibitor, careful observation is required and, in some instances, the methadone dose may need to be reduced.
Substrates	These drugs <b>compete for metabolism</b> with methadone—for example, nortriptyline and alprazolam. They may or may not also inhibit or induce the enzyme, and changes in dosing should be made if an interaction is suspected.

A link to a list of drugs associated with QT interval prolongation can be found in [appendix A](#). These are some common examples:

Drugs	Examples
antidepressants	amitriptyline, imipramine, nortriptyline, desipramine, doxepin,
antipsychotics	quetiapine, haloperidol, ziprasidone,
antibiotics	erythromycin, clarithromycin
antimalarials	chloroquine
antihistamines	diphenhydramine
antiarrhythmics	quinidine, amiodarone, disopyramide, flecainide, procainamide, propafenone, sotalol

# Methadone for Analgesia Guidelines

Drugs	Examples
others	tacrolimus, arsenic trioxide, quinidine, amiodarone

Patients with impaired liver function should be monitored carefully and methadone doses may need to be reduced as liver function deteriorates. These patients require frequent reassessment.

Acute use of alcohol will potentiate the sedative and respiratory depressant effects of methadone, and patients should be advised to either avoid drinking alcohol or to limit consumption to non-daily use and only 1 standard unit after the initial peak in serum methadone levels (up to 3 hours post-dose). Chronic daily alcohol use outside of safe drinking guidelines will initially induce liver enzymes and tend to reduce methadone levels, but as liver function deteriorates due to chronic disease and/or ongoing alcohol use, methadone will tend to accumulate. Therefore, it is recommended that alcohol be avoided by patients on methadone. In the setting of alcohol use disorder, patients should be detoxified before methadone is initiated as uptake and bioavailability cannot be predicted.

**Benzodiazepine-receptor agonists (i.e. benzodiazepines and “Z-drugs”) and methadone have cumulative toxicity and, when used in combination, enhance respiratory depression, cognitive function, and sedative effects. In particular, benzodiazepines with active metabolites and a long half-life (such as diazepam, which is also metabolized by P450 3A4) should be avoided. Patients using both methadone and a benzodiazepine-receptor agonist require careful monitoring (in general, this combination should be avoided in the CNCP setting).**

When accessing walk-in clinics and emergency rooms patients should always inform new prescribers of all current medications, particularly methadone, so that drug interactions can be prevented.

# Methadone for Analgesia Guidelines

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## Available Strengths and Forms of Methadone

Methadone can be administered orally, sublingually/buccally, topically, and per rectum.

For oral, buccal, and sublingual administration, liquid methadone is most commonly available as Methadose® flavoured oral solution. It can be further diluted in water or any juice (except grapefruit) for enhanced palatability. The usual solution strength is 10 mg/mL, though other strengths may be made available when necessary. When switching to a higher strength, physicians should exercise extra caution, as inadvertent overdose may occur if the higher concentration is not recognized.

The bottle containing the liquid methadone preparation should always be shaken before use. Patients should use a syringe to measure the liquid methadone preparation, to ensure the accuracy of the volume ingested. A spoon or measuring cup should never be used. Depending on the container provided, the patient may need to first pour some into a measuring cup to facilitate use of the syringe. Any remaining liquid should be poured back into the bottle. Patients can also have liquid methadone dispensed in individual doses to facilitate safe administration.

Methadone is also available in tablet form, in 1 mg, 5 mg, 10 mg and 25 mg strengths. These are more expensive than the liquid methadone preparation and are covered by PharmaCare only through the BC Palliative Care Drug Program. Extended health plans may cover the tablet preparation. The use of methadone tablets rather than liquid reduces the likelihood of dosing errors and may be preferred if patients' measuring skills are in doubt or if the liquid methadone preparation is too small to be safely measured, as is usually the case with patients using methadone for pain. Some patients choose to use the liquid when at home but keep tablets for use when out or travelling. It may be more practical for patients being started on methadone to first use the tablets, then switch to liquid to save money if appropriate, once dosing is stable.

Pharmacies can prepare custom-made methadone capsules or suppositories if standard preparations are not satisfactory, such as when patients are unable to swallow and doses are too high to allow buccal or sublingual administration at end of life. It should however be noted that methadone suppositories are not absorbed as effectively as the oral solution administered rectally, and dose adjustments would need to be made accordingly if using custom suppositories. Switching to rectal administration of the oral solution should use the same dose as oral. Effectiveness and side effects should be reassessed and dose adjustments made if needed.

Methadone is easily administered via a gastrostomy or jejunostomy tube, whereas other long-acting opioid preparations may cause blockages or get stuck in such tubes. Short-acting opioids, which require frequent administration, may be impractical.

When other routes are not available, use of methadone topically may circumvent the need for injections. Specialty pharmacies can compound methadone in Lipoderm®. Pain from malignant wounds can respond well to opioids administered topically. Specialist consultation is advised if considering this.

As with all medications secure storage of methadone is of utmost importance, particularly in households with children who may find its coloring particularly tempting. One teaspoon of methadone would be lethal to a toddler. Secure storage (for example a locked box) can also prevent diversion by others.

Methadone for parenteral injection is no longer available in Canada except by compounding in some specialist centres.

# Methadone for Analgesia Guidelines

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## Switching Opioids

Not only do opioids differ in their effects on opioid receptors, but individuals vary in their ability to metabolize the different opioids. These differences are largely genetically based, through hepatic and renal enzymes or transporter proteins. At present, it is not possible to determine which opioid will best suit an individual other than by individual opioid trial. When initiating a trial, it is important that physicians be prepared to try more than one opioid and are comfortable rotating from one to another until either satisfactory analgesia is achieved or the trial is abandoned. Monotherapy with one opioid (including methadone) is ideal, and one can incorporate other treatment modalities such as non-opioid pharmacotherapy (e.g. neuropathic agents, anti-inflammatories), physical treatments (e.g. physiotherapy, occupational therapy, heat-ice therapy, and intramuscular stimulation), exercise, and psychological treatment.

Morphine is the usual first-line opioid when opioids are indicated for the treatment of chronic pain. The other available long-acting opioids (codeine, oxycodone, hydromorphone, fentanyl, and buprenorphine) may be better tolerated and/or more effective in some individuals but are more expensive and may require PharmaCare authorization. The NMDA-receptor- blocking effect of methadone reduces development of tolerance as compared with other opioids, suggesting that it may be the preferred opioid for long-term use. Methadone may also be considered for morphine-intolerant patients, especially when long-term treatment is anticipated. Methadone and fentanyl are not considered first-line treatments for CNCP (especially in opioid-naïve patients), and except in rare circumstances should be considered only after trials of other agents have been unsuccessful. Examples of such circumstances are a child with continuous pain who is entirely enterally fed, or a person with renal failure and chronic pain.

## Indications for Switching Opioids

1. Inadequate pain control with dose-limiting side effects

This may occur especially with neuropathic pain. Before switching opioids, physicians should perform a detailed pain assessment and consider the use of adjuvant analgesics and other treatments. For example, constipation can usually be well controlled with a good bowel protocol.

2. Confusion, hallucinations or delirium

Although these are often attributable to opioid toxicity, there are many potential causes for delirium in patients with advanced cancer. A clinical assessment and investigation is imperative to exclude other causes before assuming that opioids are responsible. Until these have been excluded, it may be more appropriate to reduce the dose of the opioid.

3. Problems with the route of administration

For children taking opioids for chronic pain from severe medical conditions, liquid administration may be more preferable and/or practical than swallowing tablets. For people with advanced cachexia and little subcutaneous fat, transdermal delivery of fentanyl may be ineffective, and methadone may be an appropriate alternative.

4. Cost



# Methadone for Analgesia Guidelines

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The high cost and (potential lack of) coverage of many long-acting opioids may be a factor in switching to methadone, which is considerably cheaper, especially when high-dose opioid therapy is required.

When switching to a new opioid other than methadone, an up-to-date equianalgesic table should be used, such as the one in [appendix C](#). The patient's total opioid dose should be converted to an oral morphine equivalent using the table. There are a number of ways to switch from another opioid to methadone, each more appropriate for a different degree of urgency. The method chosen should be that most appropriate for an individual, and should take in to account individual physician expertise and experience.<sup>11</sup>

Physicians should ensure that an adequate dose of a short-acting opioid is available when switching opioids, as the equianalgesic ratios can vary between individuals. The dose of the new opioid often needs to be adjusted even when using the ratios suggested. Physicians should also consider the onset of action and clearance of an opioid preparation, so that there is no gap in therapy when switching opioids. This is particularly important with fentanyl patches, which may take up to 24 hours to reach full effect. Methadone usually takes at least three days to reach steady state, and accordingly, toxicity from methadone most commonly occurs between three to five days following a switch (or dose increase). This is why the “start low, go slow” method is recommended unless there is clinical urgency, such as severe opioid toxicity, for example seizures. In this type of situation hospitalization is often unavoidable.

Although the usual dosing for methadone for analgesic purposes is at eight-hour intervals, individual needs may range from every six hours to every 12 hours. Patients should be assessed on an individual basis. In patients who have only intermittent (incident) pain, short-acting opioids such as morphine, hydromorphone, oxycodone (or transmucosal sufentanil) are more suitable.

If possible, patients on high-dose opioid therapy should be admitted to hospital while opioids are being switched. However, switching can be done as an outpatient procedure if **close** supervision is available and if the situation is not acute. Methadone should be started only if the physician is prepared to provide the required close clinical supervision, particularly in the initiation-titration period. Communication about new doses can be complex and confusing for many people, with significant potential for error. Safety parameters that can be employed for outpatient rotation include: family member presence at physician appointments and in the home during first few days of rotation; home care nursing visits; and advice to avoid driving/operating heavy machinery until stable. Use of daily dispensed medication may be appropriate in some circumstances so the pharmacist can review the patient daily until consistent dosing is achieved.

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<sup>11</sup> Perry GF, Portenoy RK. Establishing “best practices” for opioid rotation: conclusions of an expert panel. *J Pain Symptom Manage*. 2009 Sep; 38(3): 418-425.

# Methadone for Analgesia Guidelines

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## Methods for Switching to Methadone

The schedules for switching to methadone described in this chapter represent only a few of the many available. Experienced prescribers generally prefer to switch gradually, over a period of two to three weeks, as this is the safest method. It is important to remember that the equivalence to morphine may vary considerably from one individual to another. For example a person on a high dose of another opioid might need less methadone than expected upon making the switch. The switching method chosen will depend on the circumstances of the individual case. Refer to [appendix B](#) for conversion ratios from oral morphine to oral methadone, and to the equianalgesic chart in [appendix C](#) for conversion between opioids.

### "Start Low, Go Slow"

In an outpatient or non-urgent setting where the reason for switching is not due to toxicity of the prior opioid, the **preferred method** for initiating methadone is the “start low, go slow” method. Methadone is started at a low dose and gradually increased at intervals of no less than three days until good analgesia is achieved. For elderly patients or patients with impaired liver function, this adjustment period should be increased. Doses of only 1 mg to 2 mg every eight hours can be highly effective. Once patients are comfortable, the prior opioid can be slowly tapered to discontinuation. During this taper, the dose of methadone may require further increase, but again should be increased at no less than three-day intervals, and no more than 20% at a time; longer in the elderly or if liver function is impaired, and with smaller increments if the patient is not opioid-tolerant.

Monotherapy with methadone may be enough, but be prepared to provide an agent for adequate treatment of breakthrough pain during the conversion and dose-titration period. This can be an NSAID or acetaminophen, or a short-acting opioid. Methadone is not advised for both continuous pain **and** incident pain because of the potential for accumulation and inadvertent methadone overdose. When other opioids are contraindicated, however, methadone may be used as a breakthrough opioid, but it is prudent to limit each PRN doses to a maximum of 10% of the total daily dose and to no more than three breakthrough doses per day to avoid accumulation. In daily doses of less than 55 mg, methadone is excreted mainly through the liver into the feces.<sup>12</sup> However, urinary excretion of methadone and its metabolites is dose-dependent and may comprise a more significant route of excretion at high dosages. If renal function in patients on a stable dose of methadone deteriorates, and it becomes apparent that there are more side effects consistent with an increasing methadone blood level, it may be necessary to reduce the dose of methadone. Methadone is poorly dialyzed and is the preferred opioid analgesic for patients with pain and renal failure.

This method is appropriate for patients who are extremely intolerant of other opioids or are at high risk for adverse effects (such as those who have had previous anaphylaxis to morphine or COPD patients with a CO<sub>2</sub> retention history from chronic lung disease). It is also the preferred method for opioid-naive patients in exceptional circumstances such as those described above, and for CNCP patients.

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<sup>12</sup> Isaac P, Janecek E, Kalvik A, Zhang M. Opioid agonist maintenance treatment: a pharmacist's guide to methadone and buprenorphine for opioid use disorders 3rd ed. Toronto: Centre for Addiction and Mental Health, 2015.

# Methadone for Analgesia Guidelines

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## Examples

1. Mesothelioma patient with nociceptive and neuropathic pain, and difficulty tolerating opioids. Agrees to try methadone after failure to achieve adequate analgesia with other opioids, including transdermal fentanyl:

Day 1	0.5 mg q8h
Day 4	1 mg q8h (sleep has improved)
Day 7	2 mg q8h
Day 10	3 mg q8h

Dose reassessed every 3 days and increases of 1 mg q8h made until adequate pain control achieved or side effects limit dose. Patient maintains comfort at dose of 3 mg q8h for six months and slowly increases dose as needed due to disease progression. Dose of 10 mg q8h reached after one year and switched to liquid when swallowing becomes difficult. This regimen allows him to pass away peacefully at home.

2. Patient with spinal stenosis:

Week 1	1 mg q8h
Week 2	2 mg q8h
Week 3	3 mg q8h
Week 4	5 mg q8h
Week 5	7 mg q8h
Week 6	9 mg q8h
Week 7	11 mg q8h

Dose reassessed every seven days due to patient frailty and increases (ranging from 1 mg to 2 mg q8h) made until adequate pain control achieved or side effects limit dose. Patient stable on maintenance dose of 11 mg q8h.

3. Patient with peripheral neuropathy following chemotherapy; undergoes tumor-removal surgery which results in radiculopathy. Patient is reluctant to try opioids but has had very limited success with tricyclic antidepressant, gabapentin or pregabalin. Specialist starts methadone:

Week 1	1 mg q8h (no significant analgesia but tolerating well)
Week 2	2 mg q8h
Week 3	3 mg q8h
Week 4	4 mg q8h (pain almost completely controlled)

Dose reassessed every seven days and increases of 1 mg q8h made until adequate pain control achieved or side effects limit dose. Patient is able to decrease dose to 3 mg q8h after six weeks; pain is nearly gone and numbness is bearable. Maintenance dose of 2.5 mg to 3 mg q8h reached and patient is transferred to family physician for ongoing care.

# Methadone for Analgesia Guidelines

Children living with chronic pain from a variety of chronic medical conditions may benefit from long-term opioid therapy, with or without an immediately life-limiting condition. The relatively infrequent dosing schedule of methadone, plus its suitability for administration in flavoured drinks or via enteral feeding tubes make methadone a useful choice of opioid in children as well as in some adults. The "start low, go slow" method of introduction would be important to follow in children, starting with lower doses than in adults, according to body size. If there is no local pediatric specialist available, the physician should consult an appropriate regional specialist.

## Slow-Switch Method

This method is suitable for patients in whom there is greater urgency for a switch, such as in the context of toxicity from the prior opioid, but the patient is otherwise coping and prefers to avoid admission to hospital. A short-acting form of the previous opioid should be available for breakthrough pain or for rescue dosing in case the anticipated methadone dose proves to be inadequate. The advantage of a slow switch method is that the dose of methadone can be adjusted from the planned dose if it appears to be more effective than predicted.

1. Calculate the oral morphine equivalent 24hr total dose using [appendix C](#)
2. Divide this number by the ratio appropriate for this dose range using the conversion ratio table [appendix B](#). This is the **estimated final total** methadone dose.
3. Decide how many steps you will take to complete the switch, no less than 3 steps being recommended.
4. Divide the total daily dose by 3 to give the **estimated final** q8h methadone dose.
5. Further divide the dose by the number of steps to provide the suggested methadone starting dose.
6. Reduce the dose of the prior opioid by 1/number of steps.

## Example

For 450 mg morphine equivalent/24 hours, use a 10:1 conversion ratio

→ estimated final methadone dose would be 45 mg methadone/24 hours

= 15 mg methadone/8 hours  
estimated **final dose**

For 120 mg morphine equivalent/24 hours, use a 5:1 conversion ratio

→ estimated final methadone dose would be 24 mg methadone/24 hours

= 8 mg methadone/8 hours  
estimated **final dose**

# Methadone for Analgesia Guidelines

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## Suppose you choose a 3-step switch:

### Day 1

Calculate the starting equianalgesic dose of methadone using the instructions above, but give only a third of that dose while reducing the dose of previous opioid by a third.

In the first example 15 mg divides exactly by three (i.e. 5 mg q8h). The morphine equivalent would be reduced to 300 mg spread over 24 hours (i.e. 150 mg long-acting q12h or 50 mg short-acting q4h).

In the second example, 8 mg divided by three would suggest a starting dose of 2.5 mg q8h (round down whenever needed for convenience of dosing), the morphine equivalent being reduced to 80 mg spread over 24 hours (40 mg long-acting q12h or 12.5mg short-acting q4h).

### Day 4

Increase the methadone dose to two thirds of the calculated equianalgesic dose and reduce the previous opioid to a third of the pre-switch dose.

In the first example above the methadone would be increased to 10 mg q8h and the morphine equivalent reduced to 75 mg long-acting q12h or 25 mg q4h.

In the second example above the methadone would be increased to 5mg q8h and the morphine equivalent decreased to 40 mg morphine equivalent spread over 24 hours (20 mg long-acting q12h or 7.5 mg short-acting q4h).

### Day 7

Increase the methadone to the full equianalgesic dose (15mg q8h) and discontinue regular administration of the previous opioid. Allow adequate as-needed short-acting opioid as previously described, reminding patients to be cautious using breakthrough as it takes 72 hours for steady state methadone to be achieved.

### Day 10 onward

Adjust the dose of methadone by increments of approximately 20 percent every three to five days until an optimal balance is achieved between analgesia and side effects. Smaller incremental changes may be needed to fine-tune the dosing in very sensitive patients. Methadone dosage should not be increased to control short-lived pain episodes (such as movement-related bone pain in metastatic cancer, or dressing changes), as this may lead to excessive dosing and accumulation. Use a short-acting opioid for these episodes if needed.

If the dosing strengths of the previous opioid do not allow for adjustments by thirds, or if there is undue anxiety about the switch and no urgency for change, a similar procedure using four or more steps, instead of three, can be applied. **For example**, when switching a patient from transdermal fentanyl at a dose of 100 mcg/hr, the fentanyl can be reduced in 25 mcg/hr increments and the methadone started at one-fourth of the estimated eventual equianalgesic dose.

Example of a patient switching from fentanyl 100 mcg/hr to methadone:

1. Calculate the methadone start dose by calculating oral morphine equivalent and selecting appropriate conversion ratio

# Methadone for Analgesia Guidelines

2. Divide by 3 to give the estimated final q8h methadone dose
3. Decide on how many steps you would like to take to complete the switch.
4. Provide short-acting opioid at approximately 10% of the oral morphine equivalent dose q1h prn

Gradually uptitrate methadone dose to gain analgesia and improve function whilst minimizing side-effects.

For 360 mg morphine equivalent/24 hours, use a 10:1 conversion ratio

→ estimated final methadone dose would be 36 mg methadone/24 hours = 12 mg methadone/8 hours as estimated final dose

Day 1	Fentanyl 75 mcg	Methadone 3 mg every 8 hours
Day 4	Fentanyl 50 mcg	Methadone 6 mg every 8 hours
Day 7	Fentanyl 25 mcg	Methadone 9 mg every 8 hours
Day 10	Fentanyl stopped	Methadone 12 mg every 8 hours

Similarly, reducing from 15mg hydromorphone q12h could be in 5 steps of 3mg each, as Hydromorph Contin comes in strengths that are multiples of 3.

**It is not recommended to start a patient on more than 30 mg/day of methadone even if their previous daily oral morphine equivalent dose is very high. A stepwise approach with close observation is strongly recommended in these circumstances.**

## PRN Methadone Switch

Some protocols suggest the total cessation of the previous opioid while commencing PRN administration of methadone (“stop and go” methods). Although these instructions may appear straightforward and simple for patients to apply, it is possible for patients to inadvertently overdose using this method. This switching method is not recommended unless the prescriber is very experienced with methadone and is able to offer excellent 24hr skilled medical supervision during the switching period. For this reason, this method is not described here. Please consult an appropriate specialist if the situation is urgent (e.g. opioid induced seizures).

# Methadone for Analgesia Guidelines

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## Using Methadone Safely: What Can Go Wrong

Communication errors are the most frequent causes of problems in the initial switching period, especially in the home environment. Write down your instructions and ask for the assistance of home care nurses and pharmacists in ensuring compliance.

Take great care to accurately establish current opioid dosing and use an appropriate conversion ratio, to avoid errors in calculating equianalgesic doses. It is useful to have someone else (such as a pharmacist) check your calculations. Ideally never start with more than 10 mg q8h (refer to [Methods for Switching to Methadone](#) for recommended starting doses). Avoid use of online opioid equianalgesic dose calculators, as they are not always correct with respect to methadone. If the equianalgesic dose and applicable ratio suggest a higher starting dose, go with more steps.

Increasing the methadone dose too quickly can lead to overdose. Allow at least three days (preferably five days) between dose adjustments if possible, and be prepared to reduce the dose as soon as adverse effects occur.

Once on stable dosing, interactions with other medications can have a significant effect on methadone metabolism. If the methadone dose is not adjusted, toxicity can occur. Always check the list of medications metabolized by cytochrome P450 3A4 in [appendix A](#) for possible interactions when prescribing new medications.

Dispensing errors can occur, especially if a different strength of liquid methadone is substituted for the 10 mg/mL strength. If more than one preparation is being used on the same hospital ward, be very careful to administer the correct strength. It would be prudent to differentiate the different strengths by flavour and colour. There is less likelihood of error if tablets are used.

As with all controlled drugs, diversion of methadone and theft can occur if the patient does not live in a safe environment. Patients should be made aware of the risk that their medication may be taken by others for their own use or to be sold on the street, so they can take adequate precautions to keep their medication safe. Locked boxes are a useful means of storing medication, particularly if there are children/young adults or people with a substance use history in the home.

Chronic pain and depression often coexist. Deliberate methadone overdose has been used to achieve suicide, especially when large amounts have been prescribed for non-cancer pain and when there is severe depression. If methadone is to be used for analgesia in these circumstances, limited dispensing and good supervision are required, but should be balanced with the need to avoid unnecessary inconvenience to those with minimal or no risk of overdose. Consider referral to psychiatry for assessment before initiating methadone in someone with active/recent suicidality.

If the switch to methadone is not successful but patients have not been taking their previous opioids for a while they will lose some of their previous opioid tolerance. This may also occur when there has been an interruption in methadone therapy (for example, during a hospital admission for surgery). A return to the pre-switch opioid dose may lead to overdose if loss of tolerance is not taken into account.

Patients are sometimes reluctant to try methadone for analgesia because of the common perception that methadone is only used for treatment of opioid use disorder. Prescriptions should be clearly marked “for pain” to avoid insensitive interactions at the pharmacy or confusion among family members.

# Methadone for Analgesia Guidelines

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## Urine Drug Testing

Urine drug testing (UDT) may not be appropriate in situations where end of life is imminent and/or risk of abuse/diversion is assessed as very low, such as in supervised long-term care or hospice. There is, however, evidence that UDT is a useful tool in the clinical management of patients receiving chronic opioid therapy for any indication, including cancer-related pain. For example, repeated quantitative UDT has been shown to improve chronic pain patient compliance with opioid therapy<sup>13</sup>. Self-reporting of drug use may be unreliable, and the detection of inappropriate use of medications or illicit drugs is important in the early identification of concurrent disorders such as addiction or misuse of medication. Unscheduled counts of pills or liquid volumes and PharmaNet checking can aid in alerting to the possibility of administration errors or diversion<sup>14</sup>.

Prior to initiating a trial of any opioid, patients should be aware that UDT can be a useful tool to increase safety. Contingency plans need to be in place to deal with issues related to addiction or diversion should they occur. UDT can be seen as an objective, non-discriminatory tool for appropriate longitudinal assessment and management of patients' pain and clinical condition, rather than a test whose primary function is to allow or deny opioids to patients.

Urine drug testing should be conducted on a random urine sample that is freshly obtained in the office or laboratory. It is essential that a standard urine collection protocol be in place to ensure reliability of the specimen (see [appendix A](#)). Further information on UDT can be found in the BCCSU guidelines on the clinical management of opioid use disorder, or obtained through the College library. On the laboratory requisition, specify the drugs for which the sample should be screened. This decision may depend on the patient population as well as geographic location because of regional differences in drug use.

Not all drugs in a particular class will be detected by the enzyme immunoassay technique employed by routine drug screens (typically a five-panel screen of opiates, cocaine, amphetamines, benzodiazepines, methadone metabolite). If more thorough investigation is needed, a confirmatory GC-MS (gas chromatography-mass spectrometry) test will be required. This limitation is particularly evident when screening for opioids. The standard immunoassay will only reliably identify natural opioids such as diacetylmorphine (heroin), monoacetylmorphine (first metabolite of heroin), morphine and codeine.

The synthetic and semi-synthetic opioids (methadone, fentanyl, oxycodone, hydromorphone) require GC-MS testing for their identification. Similarly, the benzodiazepine immunoassay may not identify two of the most commonly prescribed benzodiazepines (lorazepam and clonazepam), therefore these should also be identified by GC-MS.

Urine specimens for drug testing are retained in the laboratory for up to 14 days so the ordering physicians can review results with the toxicologist and order confirmatory tests when required. It is advisable to make the purpose of testing clear on the requisition to avoid delay and potential for potentially damaging miscommunication with the patient.

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<sup>13</sup> Knezevic NN, Khan OM, Beiranvand A, Candido KD. Repeated quantitative urine toxicology analysis may improve chronic pain patient compliance with opioid therapy. *Pain Physician*. 2017 Feb; 20(2S):S135-S145.

<sup>14</sup> Hamill-Ruth RJ, Larriviere K, McMasters MG. Addition of objective data to identify risk for medication misuse and abuse: the inconsistency score. *Pain Med*. 2013 Dec; 14(12):1900-7.



# Methadone for Analgesia Guidelines

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## Appendices

### Appendix A: Links to application forms and relevant documents

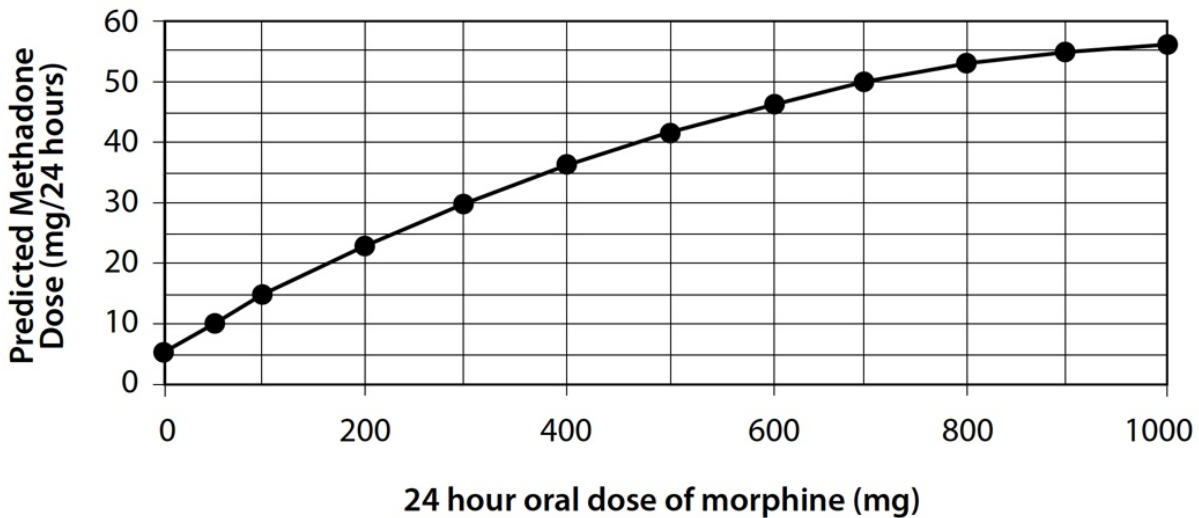
- [\*Prescribing Methadone standard\*](#)
- [\*Methadone for Pain in Palliative Care online CME\*](#)
- [\*Safe Prescribing of Opioids and Sedatives standard\*](#)
- [\*Non-Prescription Naloxone Now Available Outside of Pharmacies\*](#)
- [\*Take-home naloxone kits now available at community pharmacies\*](#)
- [\*Medications metabolized by cytochrome P450 3A4\*](#)
- [\*Drugs associated with QT interval prolongation\*](#)

# Methadone for Analgesia Guidelines

## Appendix B: Equianalgesic conversion guides

Here are two recommended tools for estimating the final predicted equianalgesic dose of methadone when switching from another opioid. This nomogram depicts the ratio as a continuous variable and the table below provides an alternate means to check your estimation. One would need to extrapolate between steps in the table.

### Methadone Conversion Nomogram – Final Predicted Dose



Adapted from Toombs J Oral methadone for chronic pain. A practitioner’s Guide. 2008 Pain Treatment Topics.

Daily oral morphine equivalent (mg)	Conversion ratio of oral morphine: oral methadone Ayonrinde
30-100	3:1
101-300	5:1
301-600	10:1
601-800	12:1
801-1000	15:1
>1000	20:1

Ayonrinde OT et al. The rediscovery of methadone for cancer pain management. Med J Aust. 2000 173:356-540.

**\* Maximum recommended starting dose = 30 mg/day**

# Methadone for Analgesia Guidelines

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- This conversion guide applies to the maintenance dosage. The starting dose should be much lower and gradually increased until analgesia is achieved.
- For switching protocols, refer to [Switching Opioids](#).
- In an outpatient setting, the preferred method is to "start low, go slow."
- This suggested conversion guide has no relevance in the initiation of methadone for opioid dependence and should not be used for that purpose.

# Methadone for Analgesia Guidelines

## Appendix C: Equianalgesic potency of opioids for chronic pain

Doses in each column are equianalgesic and interchangeable at the doses shown, with the cautions mentioned below.

Equianalgesic doses of opioids may vary considerably from those predicted and should be modified according to response.

	Drug	Examples	PO Dose	Schedule
Morphine	Immediate release	MOS, MSIR	20 mg	q4h
	Sustained release	M-Eslon, MS Contin Kadian	60 mg	q12h
Codeine	Immediate release		120 mg*	q4h
	Sustained release	Codeine Contin	360 mg	q12h
Oxycodone	Immediate release	Supeudol, Oxy-IR	15 mg	q4h
	Sustained release	OxyNeo	45 mg	q12h
	Combination products	Oxycocet/Percocet (+Acetaminophen)	15 mg*	q4h
Hydromorphone	Immediate release	Dilaudid	4 mg	q4h
	Sustained release	Hydromorph Contin	12 mg	q12h

### \*Cautions:

- For transdermal delivery drugs (i.e. fentanyl, buprenorphine) consult a pharmacist
- Doses of codeine above 300 mg/12 hrs are not recommended. Tramadol is considered approximately equivalent to codeine, so one Tramacet would be equivalent to one Tylenol #3. If higher doses are needed, a switch to a strong opioid such as morphine is recommended. The maximum recommended dose of acetaminophen is 4,000 mg/day, or 12 x Tylenol #3.

# Methadone for Analgesia Guidelines

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- To make 15 mg of oxycodone using a combination preparation would require three tablets q4h, which may become toxic due to the ASA or acetaminophen content. Pure oxycodone or other opioids are recommended in this situation.
- Previous opioid should be tapered over first 12 hours of fentanyl as absorption is delayed.

**Note:** All content in this guideline is consistent with the [Methadone4Pain.ca](http://Methadone4Pain.ca) module.

# Methadone for Analgesia Guidelines

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## Revision History

**Effective:** December 7, 2016

**Updated:** January 12, 2017; June 5, 2017; November 20, 2017; June 4, 2018; February 22, 2019