

# Opioids Enabler

## 1. Diagnosis of Opioid Dependence:

### a. Non-prescribed opioids

- DSM criteria:

#### 3 criteria in the same 12 month period:

- Tolerance
- Withdrawal
- Taking larger amounts than intended
- Unsuccessful attempts to quit or reduce
- Time spent acquiring and using
- Neglect of important activities
- Continued use despite known harm

### b. Prescribed opioids: DSM criteria alone can be difficult to apply in patients receiving opioid prescriptions for chronic non-cancer pain.

- List of common aberrant behaviours

#### *Clinical Features of Prescription Opioid Dependence*

Unsanctioned use	Recurrent prescription losses
	Multiple unsanctioned dose escalations
	Binge rather than scheduled use
Alters the route of delivery	Injects, bites or crushes oral formulations
Accesses opioids from other sources	Purchases the drug from the 'street'
	Double doctors
	Goes to walk-in clinics and emergency departments
	Drug seeking
	Dose high or rapidly escalating despite stable pain condition
	Aggressive complaining about the need for higher doses
	Harassing staff for faxed scripts or fit-in appointments
Nothing else 'works'	
Accompanying conditions	Currently addicted to alcohol, cocaine or other drug
	Underlying mood or anxiety disorders not responsive to treatment
Repeated or severe withdrawal symptoms	Marked dysphoria, myalgias, GI symptoms, craving
Social Features	Deteriorating or poor social function
	Concern expressed by family members

Table reproduced from Buprenorphine/Naloxone for Opioid Dependence: Clinical Practice Guideline (CAMH, 2011, p. 101)

## 2. Management of Opioid Dependence:

### a. Non-prescribed opioids:

#### i. Abstinence-based

1. [Home withdrawal mgmt using clonidine](#)

2. Supervised withdrawal management
    - a. [Non-medical](#)
    - b. [Medical](#)
  - ii. Opioid Agonist Treatment<sup>1</sup>
    1. [Buprenorphine/Naloxone](#)
    2. Methadone
  - iii. Psychosocial counselling, in or outpatient treatment programs, mutual aid groups all important components regardless of the above plan.
- b. Prescribed Opioids:
- i. Abstinence-based
    1. [Structured Opioid Therapy \(SOT\) and taper](#)
    2. Home or Supervised withdrawal management (as above)
  - ii. Opioid agonist treatment<sup>1</sup>
    1. [Buprenorphine/Naloxone](#)
    2. Methadone

## Buprenorphine/Naloxone Maintenance:

### Preparation:

1. Patient diagnosed with opioid dependence. Urine Drug Test (UDT) supports self-report
2. Discuss all treatment options (see above), consider contraindications and obtain informed consent:
  - a) Withdrawal Management is less effective, but may be a reasonable option for: Brief duration of dependence, adolescents or young adults, exclusive oral opioids, no major psychiatric co-morbidity, good social supports
  - b) Buprenorphine/naloxone (bup/nlx) may be preferred over methadone: History of or risks for QT interval prolongation, higher risk for methadone toxicity (including lower estimated tolerance), brief duration of dependence, adolescents and young adults, potential for drug interactions.
  - c) Methadone may be preferred over buprenorphine/naloxone: Pregnancy, history of injecting buprenorphine, estimated very high degree of tolerance.
3. Decide whether there are unstable alcohol, benzodiazepine or psychiatric disorders that should be stabilized prior to initiating buprenorphine maintenance.
4. Educate patient on how long they should abstain from opioids prior to their induction (Fig. 1)

#### **Figure 1: Estimated time of abstinence prior to induction**

##### **Short-acting opioids: 6 hrs minimum, 12+ hrs preferable**

*Examples: heroin, oxycodone (e.g., Tylenol 3s, Percocet® or Dilaudid® or sustained-release opioids (ie MSContin®) that are chewed or crushed*

##### **Longer-acting opioids: 12 hrs minimum, 24+ hrs preferable**

*Examples: OxyNeo® and other sustained-release opioids that are swallowed whole*

##### **Methadone: 24 hrs minimum, 36 hrs – 3 days preferable**

5. Ensure patient has no intention to drive or operate heavy machinery on their induction day.

### Induction:

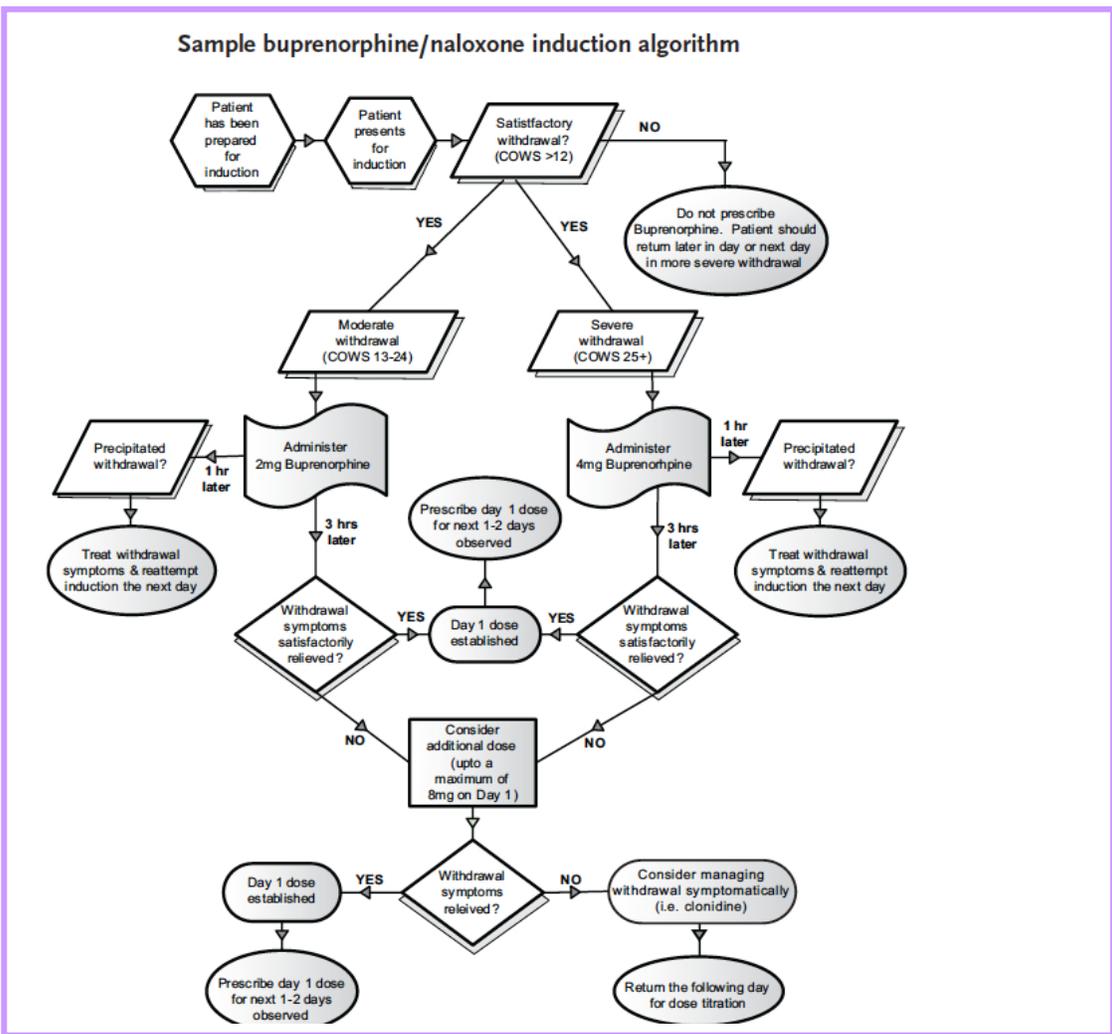
1. Ensure patient is in opioid withdrawal (w/d) of at least moderate severity (COWS >12)<sup>2</sup>
2. If in satisfactory w/d can provide an initial dose of 2mg (COWS 13-24) or 4mg (COWS 25+) or bup/nlx
3. Observe at 1 hour (to assess for precipitated withdrawal) and 3 hrs (to assess for additional doses)<sup>3</sup>
4. Prescription written for 1-2 days for the total dose consumed on day 1. Pt reassessed in 1-3 days.

<sup>1</sup> Methadone can only be prescribed by physicians with a Health Canada Sec 56 exemption. Buprenorphine/naloxone does not require a Health Canada exemption but prescribers with no clinical experience with opioid treatment should consider an accredited buprenorphine prescribing course.

<sup>2</sup> Do not provide an initial buprenorphine/naloxone dose if not in at least moderate withdrawal in order to avoid a precipitated withdrawal reaction

<sup>3</sup> Maximum dose on Day 1: 8mg

### Sample buprenorphine/naloxone induction algorithm



Algorithm reproduced from Buprenorphine/Naloxone for Opioid Dependence: Clinical Practice Guideline (CAMH, 2011, p. 85)

### Clinical Opiate Withdrawal Scale (COWS)

Patient's Name: \_\_\_\_\_ Date and Time: \_\_\_\_/\_\_\_\_/\_\_\_\_:\_\_\_\_\_

Reason for This Assessment: \_\_\_\_\_

<p><b>Resting Pulse Rate:</b> _____beats/minute <i>Measured after patient is sitting or lying for one minute</i></p> <p>0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120</p>	<p><b>GI Upset: over last ½ hour</b></p> <p>0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting</p>
<p><b>Sweating: over past ½ hour not accounted for by room temperature or patient activity</b></p> <p>0 no report of chills or flushing 1 subjective report of chills or flushing 2 flush or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face</p>	<p><b>Tremor: observation of outstretched hands</b></p> <p>0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching</p>
<p><b>Restlessness: Observation during assessment</b></p> <p>0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds</p>	<p><b>Yawning: Observation during assessment</b></p> <p>0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute</p>

From: Wesson, DR & Ling, WJ. (2003). *Psychoactive Drugs* 35(2): 253-9 (Used with permission).

## Maintenance:

1. Patient will be seen initially 1-2 times per week and this will gradually lessen to every 1-3 months as the patient stabilizes
2. Dose can be increased 2-4mg at a time until at an adequate maintenance dose  
Adequacy of the dose is determined by:
  - absence of withdrawal for the full 24 hour period
  - improved cravings
  - minimal side effects
3. At follow up visits, patient clinical stability is ascertained using the clinical assessment and urine drug testing.
4. Areas to cover at follow up visits include: adequacy of the dose and side effects, substance use, psychiatric symptoms, employment, social relationships, participation in counselling/mutual aid groups.
5. Once the patient is at a stable maintenance dose consideration can be given to alternate day dosing

## Take-Home Dosing:

6. The prescriber should have a structured approach to deciding about initiating and increasing the number of take-home doses once the patient achieves clinical stability.
7. Take-home doses should not be initiated until the patient has been deemed to exhibit features of clinical stability (Fig 2). Exercise particular caution if patient has recently been suicidal, injecting, has cognitive impairment or unstable housing.

### **Fig 2: Clinical Stability for Take-Homes:**

- No evidence of ongoing problematic substance use, including alcohol
- No evidence of acute or unstable psychiatric symptoms
- Stable behaviour and social situation
- Secure enough housing to safely store the medication.

8. Tighter boundaries should be loosened as the patient displays increased clinical stability (rather than initially looser boundaries being tightened in response to instability).
9. There should be a gradual increase in the number of weekly take-home doses up to a suggested maximum of 1-2 weeks of consecutive take-home doses dispensed between observed doses.
10. Take-home doses should be reduced or eliminated in response to a loss of clinical stability. If a high level of take-home doses are eliminated all at once, and diversion of bup/nlx is suspected, the prescriber should consider reducing the buprenorphine/naloxone dose by 25-50%.

## Missed doses<sup>4</sup>:

Usual dose	Number of consecutive days missed	New starting dose
> 8 mg	> 7 days	4 mg
> 8 mg	7 days or less	8 mg
6-8 mg	6 or more days	4 mg
2-4 mg	6 or more days	2-4 mg

## Methadone Maintenance Treatment (MMT):

### Methadone Initiation and Maintenance<sup>5</sup>:

1. Separate Health Canada exemptions for addiction and pain treatment
2. Factors favouring methadone over buprenorphine maintenance:
  - a. Failure or adverse effects with Buprenorphine
  - b. Previous intravenous buprenorphine use
  - c. High risk for treatment drop-out
  - d. Pregnancy (also safe during breastfeeding)
3. Starting methadone maintenance dose up to 30 mg maximum
4. Can be increased by up to 10 to 15 mg every 3 to 5 days during stabilization phase or 5-7 days if doses above 80 mg

<sup>4</sup> **Used with permission:** Lintzeris N, Clark N, Winstock A, Dunlop A, Muhleisen P, Gowing L, Ali R, Ritter A, Bell J, Quigley A, Mattick RP, Monheit B, White J. National clinical guidelines and procedures for the use of buprenorphine in the treatment of opioid dependence. 2006. Canberra: Commonwealth of Australia. [cited 2011, August 8]. Available from: [http://www.health.gov.au/internet/drugstrategy/publishing.nsf/Content/9011C92D2F6E1FC5CA2575B4001353B6/\\$File/bupren.pdf](http://www.health.gov.au/internet/drugstrategy/publishing.nsf/Content/9011C92D2F6E1FC5CA2575B4001353B6/$File/bupren.pdf)

<sup>5</sup> CPSO Methadone Maintenance Treatment Program Standards and Clinical Guidelines, 4th Edition, February 2011.

5. Consecutive missed doses may require 50% dose reduction or restarting at 30 mg or less
6. Take home doses are earned with stable methadone dose, no problematic substance use including alcohol (monitored by UDT), stable housing and stable mental health and safely stored in a locked box
  - a. Maximum 6 take-home doses per week with possible special carries for travel
  - b. Consent to communicate with other opioid or benzodiazepine prescribers required
  - c. Take home doses reduced with instability of above criteria or concern for diversion

#### **Methadone Drug Interactions:**

1. Exercise caution with central nervous system (CNS) depressants (alcohol, benzodiazepines, non-benzodiazepine hypnotics, antipsychotics, antidepressants, sedating antihistamines) and whenever possible avoid these during periods of methadone dose adjustment
2. Consider additive similar effects (constipation, urinary retention)
3. Be aware of combined risk factors for QTc prolongation<sup>5</sup>:
  - a. Low potassium level (caused by diuretics)
  - b. Medications that inhibit CYP 3A4, 1A2, 2D6, 2D8, 2C9/2C8, 2C19 and 2B6<sup>6</sup> (HIV antivirals, antifungals, calcium channel blockers, fluoroquinolone antimicrobials, antidepressants, contraceptives)
  - c. Medications that prolong QTc (cardiac medications, antipsychotics, macrolides antimicrobials, anti-nausea drugs such as domperidone) <http://www.azcert.org/medical-pros/drug-lists/printable-drug-list.cfm>

#### **Methadone Toxicity:**

1. Characterized by decreased LOC, respiratory depression and pinpoint pupils
2. May not become apparent for 5 to 9 hours post ingestion
3. May be alert during conversation but succumb to respiratory depression during sleep
4. Can occur after other medication changes, despite a stable methadone dose
5. Refer to the emergency department and keep patient awake if concerned for toxicity

#### **Acute Pain Treatment in MMT<sup>5</sup>:**

1. If pain not severe, try non-opioid treatments as first line
2. MMT patients are tolerant to opioid analgesic effects and may require higher, more frequent doses
3. Methadone doses may be split, if eligible for take-home doses, for increased analgesic effect
4. Avoid the previous opioid of abuse, try weak opioids (codeine, tramadol) first then morphine preferred over oxycodone or hydromorphone for acute pain if strong likelihood of benefit for nociceptive or neuropathic pain
5. Dispense small amount of opioids at once, and begin to taper/discontinue as soon as acute pain resolving
6. Opioids not justified for analgesia with acute flares of fibromyalgia or low back pain
7. Communication with the methadone prescriber to coordinate pain treatment is essential

#### **Concurrent Mental Health Disorders<sup>5</sup>:**

1. Mood and anxiety disorders are several times more prevalent in MMT patients than in the general population
2. Little evidence to support antidepressant therapy for major depressive and dysthymic disorders in MMT patients<sup>7</sup>
3. Consider referral for psychiatric assessment and treatment if persistent symptoms after initial trial of therapy
4. Benzodiazepine use in MMT patients is associated with increased psychological distress, risk for overdose, higher risk of suicidal behaviour, violence, impaired attention and memory, impaired driving and risk for continuing poly-drug use with a negative to no impact on treatment retention. For those MMT patients on chronic benzodiazepines, benzodiazepine tapering may be and discontinuation may be beneficial.

<sup>6</sup> Bhushan M. Kapur; Janine R. Hutson; Tamanna Chibber; Adriana Luk; Peter Selby. Methadone: a review of drug-drug and pathophysiological interactions. *Critical Reviews in Clinical Laboratory Sciences* (August 2011), 48 (4), pg. 171-195

<sup>7</sup> Pedrelli P, Iovieno N, Vitali M, Tedeschini E, Bentley KH, Papakostas GI. Treatment of major depressive disorder and dysthymic disorder with antidepressants in patients with comorbid opiate use disorders enrolled in methadone maintenance therapy: a meta-analysis. *J Clin Psychopharmacol*. 2011 Oct;31(5):582-6.