OPIOID MANAGER

The Opioid Manager is designed to support health care providers prescribe and manage opioids for patients with chronic non-cancer pain. All information is based on the 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain,[1] unless cited otherwise.

This is an update of the original Opioid Manager, released in 2011.

Section A: Important Considerations for Opioid Therapy Trials

- When considering therapy for patients with chronic non-cancer pain, optimize non-opioid pharmacotherapy and non-pharmacological therapy, rather than initiating a trial of opioids.
- For patients starting or continuing an opioid trial, discuss and document patients' goals **(SMART goals: Specific, Measurable, Agreed-upon, Realistic, Time-based),** on a regular basis.

OVERDOSE RISK

- Fatal and non-fatal overdose risk is significant at doses as low as < 20 mg morphine equivalents daily
- Risk of overdose increases in dose
- Risk of overdose increases in patients with active or prior substance use disorder and current serious mental illness

Dose	Fatal overdose	Non-fatal overdose
> 100 mg MED/d	0.23 %/yr	1.8 %/yr
50 – 99 mg MED/d	0.18 %/yr	0.7 %/yr
< 20 mg MED/d	0.1 %/yr	0.2 %/yr

Legend: d = day, MED = morphine equivalent dose, yr = year

CHECKLIST

These are important considerations to discuss and document for patients starting or continuing an opioid trial.

See Appendix A - Checklist for a fillable version of this checklist that can be inserted into the patient medical record.

- ☐ Has non-pharmacological therapy[i] been optimized?
- ☐ Has non-opioid pharmacotherapy[i] been optimized?
- ☐ Stable psychiatric disorder(s) or mental illness?
- ☐ Current or past substance use disorder?
- ☐ Cannabis use?
- ☐ Thorough baseline assessment conducted[ii] (as needed)?
- ☐ Explained potential benefits[i]?
- ☐ Explained adverse effects[i]?
- ☐ Explained risks[i]?
- ☐ Explained opioid safety[i]?
- ☐ Informed consent obtained?
- ☐ Signed treatment agreement[iii] (as needed)?
- ☐ Patient given information handout(s)[ii]?
- ☐ Urine drug screening (as needed)?
- ☐ Naloxone prescription (as needed)?

Non-opioid pharmacotherapy options:[2]

- ☐ General: acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs)
- ☐ Anticonvulsants: carbamazepine, gabapentin, pregabalin
- ☐ Antidepressants: amitriptyline, duloxetine, fluoxetine
- ☐ Topical: topical NSAIDs, topical rubifacients

Non-pharmacological therapy options:[2]

- ☐ Physical activity: aerobic exercise, strengthening exercise, core stabilizing exercise, Tai Chi, yoga, therapeutic aquatic exercise
- ☐ Self-management programs
- ☐ Psychological therapies: cognitive behavioural therapy, mindfulness based interventions, acceptance and commitment therapy, respondent behavioural therapies
- ☐ Physical therapies: manual therapy, transcutaneous electrical nerve stimulation, low level laser therapy

- Active psychiatric disorders (e.g. depression, anxiety disorders or post-traumatic stress disorder) should be stabilized before a trial of opioids is considered for a patient
- Patients with psychiatric disorders report more severe pain, and pain is often resolved or reduced if the psychiatric disorders are well managed

- Opioids are not recommended for patients with current or past substance use disorder (e.g. alcohol use disorder, opioid use disorder)

Clinical pearls

- Opioids may have similar effects on **pain relief** when compared to NSAIDs, tricyclic antidepressants or nabilone
- Opioids may result in similar improvements in **physical function** when compared to NSAIDs, anticonvulsants, tricyclic antidepressants or nabilone

Section B: Opioid Therapy Trial

- This section is intended to support providers starting a patient on opioid therapy. For patients continuing opioid therapy, see **Section C: Maintenance & Monitoring**.
- A reasonable trial of opioid therapy should be accomplished within 3–6 months; opioids provide less pain relief after 3 months, due to tolerance.
- Restrict the prescribed dose to < 90 mg morphine equivalents daily for patients beginning long-term opioid therapy.

Clinical pearls

- Start at lowest available dose of the opioid (remember overdose risk is significant even at low doses)
- In patients with continuous pain including pain at rest, health care providers can prescribe controlled release opioids for both comfort and simplicity of treatment during the day
- Activity related pain might not require sustained release treatment and opioid therapy may be initiated with immediate release alone
- Opioids NOT recommended for initiating a trial of therapy include fentanyl, meperidine, methadone and pentazocine
- Opioids that ARE recommended are listed in the **Suggested Initial Dose and Titration** table
- Oral preparations are preferred
- Prescriptions for chronic pain should be provided by the primary treating provider only, for no more than 28 days at a time

SUGGESTED INITIAL DOSE AND TITRATION[3]

This table provides practical guidance regarding optimal dosing when beginning patients on a trial of opioid therapy. For opioids with multiple dosage forms and singular values in subsequent columns, subsequent column values are applicable across all dosage forms.

Note: Brand names are shown if formulations vary from that of the generic. Reference to brand names does not imply endorsement of any of these products.

Opioid	Dosage forms	Initial dose	Minimum time interval for increase	Suggested dose increase	Maximum dose/day	50 MED	90 MED
Codeine CR	• Tab: 50, 100, 150, 200 mg	• 50 mg q 12 h	• 2 days	• 50 mg/d	• 300 mg q 12 h	• 334 mg/d	• 600 mg/d
Codeine IR	• Tab: 15, 30 mg • Syrup: 5 mg/mL • Elixir: 16 mg/10 mL with Acetaminophen 320 mg • Tab: 8, 15, 30, 60 mg with Acetaminophen 300 mg • Tab: 15, 30 mg with Acetaminophen 325 mg • Tab: 15, 30 mg with Acetylsalicylic acid 375 mg	• 15–30 mg q 4 h prn	• 7 days	• 15–30 mg/d	• 600 mg/d or acetaminophen 4 g/d	• 334 mg/d	• 600 mg/d
Hydromorphone CR, PR	• CR: 3, 4.5, 6, 12, 18, 24, 30 mg • PR: 4, 8, 16, 32 mg	• 3 mg q 12 h, maximum 9 mg/d • 4 mg q 24 h, maximum 8 mg/d	• Minimum 2 days • Minimum 4 days, recommended 14 days	• 3 mg/d • 4 mg/d	• N/A	• 10 mg/d	• 18 mg/d
Hydromorphone IR	• Tab: 1, 2, 4, 8 mg • Syrup: 1 mg/mL	• 1–2 mg q 4–6h prn, maximum 8 mg/d	• 7 days	• 1–2 mg/d	• N/A	• 10 mg/d	• 18 mg/d
Morphine CR, ER	• Tab: 15, 30, 60, 100, 200 mg • Cap (12 h): 10, 15, 30, 60, 100, 200 mg • Cap (24 h): 10, 20, 50, 100 mg	• 10–15 mg q 12 h • 10 mg q 12 h • 10 mg q 24 h	• Minimum 2 days, recommended 14 days	• 5–10 mg/d	• N/A	• 50 mg/d	• 90 mg/d
Morphine IR	• Oral solution: 1, 5, 10, 20, 50 mg/mL • Tab: 5, 10, 20, 25, 30, 50 mg • Cap: 5, 10, 20, 30 mg	• 5–10 mg q 4 h prn, maximum 40 mg/d	• 7 days	• 5–10 mg/d	• N/A	• 50 mg/d	• 90 mg/d
Oxycodone CR with naloxone CR	• Tab: 5/2.5, 10/5, 20/10, 40/20 mg	• 5 mg/2.5 mg q 12 h	• Minimum 1–2 days	• 5/2.5 mg/d	• 80 mg/d oxycodone and 40 mg/d naloxone	• 33 mg/d oxycodone	• 60 mg/d oxycodone
Oxycodone CR	• Tab: 5, 10, 15, 20, 30, 40, 60, 80 mg	• 10 mg q 12 h	• Minimum 2 days, recommended 14 days	• 10 mg/d	• N/A	• 33 mg/d	• 60 mg/d
Oxycodone IR	• Tab: 5, 10, 20 mg • Tab: 5 mg with acetylsalicylic acid or acetaminophen 325 mg • Tab: 2.5 mg with acetaminophen 325 mg	• 5–10 mg q 6 h prn, maximum 30 mg/d • 1–2 tab q 6 h prn • 1–2 tab q 6 h prn	• 7 days	• 5 mg/d	• N/A • Acetaminophen 4 g/d	• 33 mg/d	• 60 mg/d
Tapentadol ER	• Tab: 50, 100, 150, 200, 250 mg	• 50 mg q 12 h	• 3 days	• 50 mg q 12 h	• Not recommended >500 mg/d	• 160 mg/d	• 300 mg/d
Tapentadol IR	• Tab: 50, 75, 100 mg	• 50 mg q 4–6 h prn	• On the first day of dosing, the 2nd dose may be administered 1 hour after the first dose, if adequate pain relief is not attained with the first dose	• 50mg q 4–6 h	• Not recommended daily doses > 700 mg on the first day of therapy and 600 mg on subsequent days	• 160 mg/d	• 300 mg/d
Tramadol CR	• Tab (Zytram XL®): 75, 100, 150, 200, 300, 400 mg • Tab (Tridural®): 100, 200, 300 mg • Tab (Ralivia®): 100, 200, 300 mg • Tab (Durela®): 100, 200, 300 mg	• 150 mg q 24 h • 100 mg q 24 h • 100 mg q 24 h • 100 mg q 24 h	• 7 days • 2 days • 5 days • 5 days	• 75–100 mg q 24 h	• 400 mg/d • 300 mg/d • 300 mg/d • 300 mg/d	• 300 mg/d	• 540 mg/d* • Over maximum dose
Tramadol IR	• Tab: 50 mg • Tab: 37.5 mg with acetaminophen 325 mg	• 25 mg once daily** • 1 tablet q 4–6 h prn	• 4 days • Depends on patient's clinical response	• 25 mg/d • 1–2 tablet(s) q 4–6 h prn	• 400 mg/d • 8 tabs/day or acetaminophen 4 g/d	• 300 mg/d	• 540 mg/d* • Over maximum dose

Legend: ~ = approximately equal to, cap = capsule, CR = controlled release, d = day, ER = extended release, g = gram, h = hour, IR = immediate release, MED = morphine equivalent dose, mg = milligram, mL = milliliter, µg =microgram, N/A = not available, PR = prolonged release, prn = as needed, q = every, SL = sublingual, tab = tablet

*The maximum recommended daily dose of tramadol is 300 mg – 400 mg depending on the formulation.

**Cut tablet in half to start at 25 mg. Pharmacy can cut tablets in half if required.[3]

Note: Information on the buprenorphine transdermal patch and buprenorphine/naloxone sublingual tablets is available in **Section D: Switching** and **Section E: Tapering**, respectively. Buprenorphine/naloxone sublingual tablets are NOT recommended for an initiation trial of opioid therapy.

Section C: Maintenance & Monitoring

- This section is intended to support providers with patients continuing opioid therapy.
- Monitor and document a patient's response to the opioid therapy through regularly scheduled appointments.

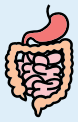
INITIATION, MAINTENANCE & MONITORING

These are the key elements to document upon initiating a trial of opioid therapy (3–6 month) and on an ongoing basis for monitoring purposes.

See **Appendix B - Initiation, Maintenance & Monitoring Chart** for a fillable version of this table that can be inserted into the patient medical record.

- ☐ Date (patient seen)
- ☐ Opioid prescribed
- ☐ Daily dose, frequency and timing
- ☐ Daily morphine equivalent dose
- ☐ Date of new dose to be administered
- ☐ Status of patient goals
- ☐ Pain intensity (Brief Pain Inventory[iv])
- ☐ Functional status changes
- ☐ Adverse effects (e.g. fatal and non-fatal overdose, motor vehicle accident, addiction, sleep apnea, osteoporosis, drowsiness, constipation, dizziness/vertigo, hypogonadism/sexual dysfunction, vomiting, nausea, opioid induced hyperalgesia, dry skin/pruritis)
- ☐ Presence of clinical features of opioid use disorder (see **Clinical Features of Opioid Use Disorder** table)
- ☐ Date and result of last urine drug screening
- ☐ Naloxone prescription written
- ☐ Tapering offered
- ☐ Non-pharmacological therapies being used for pain
- ☐ Non-opioid pharmacotherapy being used for pain

Clinical pearls

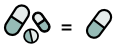


- Opioids increase the risk of gastrointestinal adverse events vs. non-opioid therapy alone (64 more events per 1000 patients treated)
- Identify the lowest effective dose for patients continuing opioid therapy

Section D: Switching

- Consider switching opioids if problematic pain and/or adverse effects persist.
- While switching over to the new opioid, it is important to warn the patient (and family, caregivers or friends) about signs of overdose: slurred or drawling speech, emotional lability, ataxia, "nodding off" during conversation or activity.
- Consider a 3-day follow-up to assess withdrawal symptoms and pain; contact the patient 3 days after starting the new opioid to check for signs of over-sedation and to ensure that pain relief is at least comparable to the pre-switch treatment.
- Switching opioids may be done as a way of facilitating a dose reduction.

MORPHINE EQUIVALENCE TABLE



Opioid conversion table.

Opioids* Oral preparations (mg/d)	To convert to oral morphine equivalent, multiply by:	To convert from oral morphine, multiply by:
Buprenorphine[3]	• 5 µg/h patch = 9–14 mg MED/d • 10 µg/h patch = 18–28 mg MED/d	• 15 µg/h patch = 27–41 mg MED/d • 20 µg/h patch = 36–55 mg MED/d[4,5]
Buprenorphine/naloxone SL[3]	16 mg SL = 90 mg MED	
Codeine	0.15 (0.1–0.2)	6.67
Hydromorphone	5.0	0.2
Methadone	Dose equivalents unreliable	
Morphine	1.0	1
Oxycodone	1.5	0.667
Tapentadol	0.3–0.4	2.5–3.33
Tramadol**	0.1– 0.2	6
Fentanyl[6]***	60 –134 mg morphine = 25 µg/h patch 135–178 mg morphine = 37 µg/h patch 180–224 mg morphine = 50 µg/h patch 225–269 mg morphine = 62 µg/h patch 270 –314 mg morphine = 75 µg/h patch 315–359 mg morphine = 87 µg/h patch 360–404 mg morphine = 100 µg/h patch	

When to switch opioids:

- Uncontrolled pain
- Intolerable adverse effects
- Switching route of administration (e.g. oral to transdermal)

How to switch:

The two methods for switching opioids are presented below. There is no evidence that favours one method over another. Careful attention must be taken when swiching an opioid to ensure the patient is seen each week and understands prescription instructions.

- **Method 1:** Decrease the total daily dose of the current opioid by 25–50% and convert to new opioid equivalent dose.
- **Method 2 (Cross Taper Method):** Decrease the total daily dose of the current opioid by 10–25% per week while titrating up the total daily dose of the new opioid weekly by 10–20% with a goal of switching over 3–4 weeks (also consider dose formulations available). Consider more regular (e.g. weekly) follow-ups, weekly dispensing and/or dosette/blisterpack if required.

See Appendix C - Switching Opioids for succinct steps and examples on how to switch opioid therapies, and fillable switching templates that can be completed and inserted into the patient medical record.

Legend: h = hour, MED = morphine equivalent dose, mg = milligram, mL = milliliter, µg = microgram, SL = sublingual

*Conversion ratio for opioids are subject to variations in kinetics governed by genetics and other drugs.

**The maximum recommended daily dose of tramadol is 300 mg–400 mg depending on the formulation.

***The information provided can be used to determine the morphine equivalents for a patient on fentanyl. If used for switching opioids the dose conversions are for **unidirectional conversion to fentanyl** in patients for chronic use and not opioid naive patients. The dose conversions were **not intended to convert patients from fentanyl to other opioids**; doing so may result in overdose and toxicity.

SUGGESTED INITIAL DOSE AND TITRATION FOR BUPRENORPHINE TRANSDERMAL PATCH[3]

The buprenorphine transdermal patch is indicated for the management of pain severe enough to require daily, continuous, long-term opioid treatment and for which alternative options are inadequate. It can be prescribed to opioid naive patients.

Opioid	Dosage forms	Initial dose	Minimum time interval for increase	Suggested dose increase	Maximum dose/day	50 MED	90 MED
• Buprenorphine*	• Patch: 5, 10, 15, 20 µg/h	• 5 µg/h every 7 days	• 7 days	• 5 µg/h every 7 days	• 20 µg/h every 7 days	• 20 µg/h[4,5]*	• Not available

Legend: h = hour, MED = morphine equivalent dose, µg = microgram

*The oral morphine to buprenorphine transdermal patch ratio can range from 75:1 to 115:1, therefore the mid-point of this range (i.e. 95:1) is suggested.

Section E: Tapering

- Consider a discontinuation of the opioid therapy if improvement in pain or function is not achieved.
- Consider tapering opioids to the lowest effective dose for patients with a prescribed dose ≥ 90 mg morphine equivalents daily.
- Opioid withdrawal symptoms are unpleasant, but not life-threatening. What is life-threatening with opioids is overdose. Careful consideration needs to be taken with patients who are pregnant; severe, acute opioid withdrawal has been associated with premature labour and spontaneous abortion.
- Careful attention must be taken when tapering an opioid to ensure the patient is seen each week and understands prescription instructions.

WHEN TO CONSIDER TAPERING OPIOIDS

	Examples and consideration (if applicable)
Pain condition resolved	• Patient receives definitive treatment for condition • A trial of tapering is warranted to determine if the original pain condition has resolved
Risks outweigh benefits	• Overdose risk has increased • Clear evidence of diversion • Clinical features of opioid use disorder have become apparent (see **Clinical Features of Opioid Use Disorder** table)
Adverse effects outweigh benefits	• Adverse effects impairs functioning below baseline level • Patient does not tolerate adverse effects • Non-adherence to the treatment plan
Patient requests	• Patient requests opioid prescription to be tapered or stopped
Medical complications	• Medical complications have arisen (e.g. hypogonadism, sleep apnea, opioid induced hyperalgesia)
Opioid not effective	• Opioid effectiveness = improved function or at least 30% reduction in pain intensity • Opioid being used to regulate mood rather than for pain control • Pain and function remains unresponsive • Periodic dose tapering or cessation of opioid therapy should be considered to confirm opioid therapy effectiveness • Consider that tapering can result in withdrawal mediated pain that can present as increased pain for the patient; this should not be taken as evidence confirming opioid effectiveness for pain
≥ 90 Morphine equivalent dose	• For patients with chronic non-cancer pain who are currently using ≥90 mg morphine equivalents daily tapering opioid to the lowest effective dose with potential discontinuation is suggested • For patients with chronic non-cancer pain who are using opioids and experiencing serious challenges in tapering, referral to a formal multidisciplinary program or interprofessional coordinated multidisciplinary collaboration is strongly recommended

How to taper – the essentials

How do I stop? The opioid should be gradually tapered rather than abruptly discontinued. Patients should be actively engaged in a discussion about the merits of gradual dose reduction, including the potential for better pain control and quality of life. See Opioid Tapering - Information for Patients.[v]

How long will it take to taper the opioid? Tapers can usually be completed between 2 weeks and 4 months. For some patients on very long-term, high dose opioid therapy, it may take longer.

When do I need to be more cautious when tapering? In patients who are pregnant; severe acute opioid withdrawal has been associated with premature labour and spontaneous abortion. Also in patients with acute coronary disease, or severe/unstable psychiatric disorder(s) or mental illness.

How do I taper the dose? Example tapering approaches are presented below. There is no evidence that favours one approach over another.
For additional details and a template please see the Opioid Tapering Template.[vi]

- Gradually reduce dose by 5–10% of morphine equivalent dose every 2–4 weeks with frequent follow-up. Switching from immediate release to controlled release opioids on a fixed dosing schedule may assist some patients in adhering to the withdrawal plan.
- Switch opioid to methadone or buprenorphine/naloxone preparations and then gradually taper (see **Morphine Equivalence** table and **Suggested Initial Dose and Titration for Buprenorphine/Naloxone Sublingual Tablets** table).
- Reduce the opioid dose rapidly over a few days/weeks or immediately. This method must be carried out in a medically supervised withdrawal centre as it may result in severe withdrawal symptoms.

Tips for tapering fentanyl transdermal patch

- Converting fentanyl to other opioids is not recommended as conversions are unreliable, and doing so may result in overdose and toxicity
- Consider reducing fentanyl by 12–25 µg/h patches every 2–4 weeks
- Consider adding immediate release oral opioid for pain relief (e.g. morphine IR 5 mg qid prn up to a maximum dose of 20 mg/d, may be required at lower doses of fentanyl for breakthrough pain)
- Once fentanyl is at the lowest available dose (e.g. 12 µg/h every 72 hours), stop the fentanyl transdermal patch and only use the immediate release oral opioid for pain relief
- **Note:** It takes 17 hours or more for the fentanyl serum concentration to decrease by 50% after patch is removed

Clinical features of opioid use disorder[7] (see full table[ii])

- Altering the route of delivery*
- Accessing opioids from other sources*
- Unsanctioned use
- Drug seeking
- Repeated withdrawal symptoms
- Accompanying conditions
- Social features
- Views on the opioid medication

*Behaviours more indicative of addiction than the others.

Legend: d = day, h = hour, IR = immediate release, mg = milligram, µg = microgram, prn = as needed, qid = 4 times a day
Recommendations in the above table have been developed in part from a consensus of expert opinion.

SUGGESTED INITIAL DOSE AND TITRATION FOR BUPRENORPHINE/ NALOXONE SUBLINGUAL TABLETS[3]

Buprenorphine/naloxone sublingual tablets are indicated for substitution treatment in patients with problematic opioid drug dependence. It is also used to taper opioids.

Opioid	Dosage forms	Initial dose	Minimum time interval for increase	Suggested dose increase	Maximum dose/day	50 MED	90 MED
• Buprenorphine/ naloxone SL*	• SL: 2/0.5, 8/2 mg	• 4–12 mg on day 1, maintenance dose of 12–16 mg	• Daily	• Guided by clinical and psychological status of the patient	• 24 mg/d	• 9 mg SL	• 16 mg SL

Legend: d = day, MED = morphine equivalent dose, mg = milligram, SL = sublingual
*Health care providers do not require an exemption to prescribe buprenorphine. Providers who wish to use buprenorphine for substitution treatment in patients with problematic opioid drug dependence should obtain knowledge regarding its intended impacts, side effects and role in addiction treatment.[vii]

Supporting Material

[i] **Management of Chronic Non Cancer Pain - Appendices**
cep.health/cncp

[ii] **Management of Chronic Non Cancer Pain**
cep.health/cncp

[iii] **Opioid Medication Treatment Agreement**
http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b05.html

[iv] **Brief Pain Inventory (BPI)**
http://nationalpaincentre.mcmaster.ca/documents/brief_pain_inventory.pdf

[v] **Opioid Tapering - Information for Patients**
http://nationalpaincentre.mcmaster.ca/documents/Opioid%20Tapering%20Patient%20Information%20(english).pdf

[vi] **Opioid Tapering Template**
https://cep.health/clinical-products/opioid-tapering-template/

[vii] **FAQ About Prescribing Buprenorphine**
https://www.cpso.on.ca/CPSO/media/documents/Methadone/FAQs-Prescribing-Buprenorphine.pdf

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[1] Michael G. DeGroote National Pain Centre, McMaster University. The 2017 Canadian guideline for opioids for chronic non-cancer pain. [cited Sept 5, 2017]. Available from: http://nationalpaincentre.mcma ster.ca/opioid/

[2] Centre for Effective Practice. Management of chronic non cancer pain (Appendix). 2017; [cited Sept 27, 2017]. Available from: cep.health/cncp

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