ONTARIO PHARMACISTS ASSOCIATION

Advocating Excellence in Practice and Care

Methadone and Buprenorphine/Naloxone Toolkit for Pharmacists

Part B: Buprenorphine/Naloxone

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Disclaimer

These tools have been developed by the Ontario Pharmacists Association (OPA) for pharmacists in Ontario as a general guide to support those wishing to initiate a buprenorphine/naloxone program in their pharmacy setting. The resource materials provided in this toolkit are for general information purposes only and are not meant to be used as a sole clinical decision-making tool.

This toolkit is complementary and is not inclusive of all recommendations and considerations. The information provided is not a substitute for sound clinical judgement from the health care professional. Pharmacists are to exercise their professional judgment in accordance with the Ontario College of Pharmacists (OCP) Standards of Pharmacy Practice. This tool is not a substitute for established clinical practice guidelines or regulatory requirements. It is not intended to supersede or replace guidelines, practice standards, policies or procedures issued by OCP, the Ministry or corporate employers. It is also not intended, and should not be construed, as legal or professional advice or opinion.

While OPA strives to ensure the accuracy of the information provided in this document, information may be subject to change, and it is the responsibility of the user of this document to ensure they have the most up-to-date and complete information from available resources.

Acknowledgement

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Opioid Use Disorder (OUD)

The Centre for Addiction and Mental Health (CAMH) defines Opioid Use Disorder (OUD) as a treatable medical condition characterized by a problematic pattern of opioid use leading to significant impairment or distress. It involves physical and psychological dependence, where individuals continue using opioids despite negative social, physical, or personal consequences.

Key Aspects of OUD according to CAMH:

- Definition: It is a chronic, relapsing condition involving compulsive, or hard-to-control, use of opioids.
- Signs & Symptoms (DSM-5):
  - Loss of Control: Using more or longer than planned, craving opioids, and difficulty cutting down.
  - Functional Impairment: Failing to fulfill major roles at work, school, or home.
  - Physical Dependence: Experiencing tolerance (needing more for the same effect) and withdrawal symptoms (e.g., pain, nausea, agitation) upon stopping.
  - Continued Use: Using despite negative health, social, or dangerous consequences.
- Spectrum of Use: CAMH describes a spectrum from at-risk or hazardous use to severe addiction.

Treatment: Involves evidence-based approaches, primarily Opioid Agonist Therapy (OAT), combined with behavioral and social supports.

The United Nations (UN) addresses opioid use disorder (OUD) primarily through the **United Nations Office on Drugs and Crime (UNODC)**and the World Health Organization (WHO), recognizing it as a critical, chronic, and relapsing health condition rather than just a criminal issue. The UN emphasizes that OUD is a major driver of global mortality, responsible for roughly 70% of the 128,000 deaths attributed to drug use disorders in 2019 (UNODC, *World Drug Report 2023* (United Nations publication, 2023).

Key Findings: Opioid and Stimulant related Harms in Canada July 2024 to June 2025:

17 deaths per day (22% lower than previous 12 months)
14 hospitalizations per day (21% lower than previous 12 months)
59 Emergency Department visits per day (22% lower than previous 12 months)
94 Emergency Medical Services (EMS) responses per day (16% lower than previous 12 months)

53,308 apparent opioid toxicity deaths Jan. 2016 to June 2025
2787 apparent opioid toxicity deaths Jan. to June 2025 of which 97% were accidental
Jan. to June 2025 – 78% apparent opioid toxicity deaths occurred in British Colombia, Alberta and Ontario.
Most apparent opioid toxicity deaths occurred among males (72%) and among individuals aged **30 to 39 years (26%)** so far in 2025 (Jan to Jun)
Of all apparent opioid toxicity deaths so far in 2025 (Jan to Jun), 57% involved fentanyl and 57% involved fentanyl analogues
Of all apparent opioid toxicity deaths so far in 2025 (Jan to Jun), 83% involved opioids that were non-pharmaceutical
Of all apparent opioid toxicity deaths so far in 2025 (Jan to Jun), 68% also involved a stimulant

This update is based on data submitted to or extracted by the Public Health Agency of Canada on or before October 28, 2025
https://health-infobase.canada.ca/substance-related-harms/opioids-stimulants/

Opioid Agonist Treatment (OAT)

Pharmacotherapy is the most effective treatment for opioid use disorder (OUD), and opioid agonist therapy (OAT) saves lives. The mortality risk is significantly reduced for people with OUD while in OAT treatment compared to out of OAT treatment.

Buprenorphine and methadone should both be considered as standard first-line treatment options for OAT. For people who initiate OAT with buprenorphine, clinicians should be aware of the higher risk of attrition after the first month of initiation and offer alternative opioid agonist medications in these circumstances. When considering methadone, clinicians should be aware of the higher risk of mortality during the first month compared with the remainder of the treatment period.

Results from a recent study suggest that any advantages from a reduced risk of mortality with treatment with buprenorphine/naloxone were outweighed by deficits in treatment retention. Evaluated in a jurisdiction where both medications were available in office-based settings, these findings do not support recommendations of buprenorphine/naloxone as first-line treatment over methadone.
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2843176

OAT with slow-release oral morphine should be available and offered as a second-line treatment option as per the 2024 CRISM Nationall Guidelines. The availability of slow-release oral morphine may vary across Canada, but it is recommended that this medication should be make widely available to ensure better equity.
https://www.metaphi.ca/wp-content/uploads/SROM.pdf
https://crism.ca/wp-content/uploads/2024/11/2024-Update-to-CRISM-Update-to-National-OUD-Guideline-20241111.pdf

The approach to providing OAT services is evolving in Ontario. The CPSO Methadone Maintenance Treatment Program Standards and Guidelines from 2011 was rescinded in March 2021. It was perceived that the exceptional status of methadone and the high degree of oversight, disincentivized physicians to offer OAT, thus limiting access for patients. As well, in 2018, Health Canada removed the Section 56 exemption requirement for methadone prescribers – to improve access to treatment.

OAT as a Harm Reduction Approach

OAT has been shown to reduce:

- Use of other opioids (Brand et al., 2003; Davioli et al., 2007; Gibson et al., 2008)
- Criminal activity (Lind et al, 2005) as OAT is legal and may keep patients away from the harmful consequences of acquiring and possessing illicit opioids and prescription opioids
- Patient mortality rates (Degenhardt et al., 2011; Gibson et al., 2008; Soyka et al., 2011) compared to people who continue to use illicit opioids
- Injection-related risk (including behaviours and transmission of HIV and sexually transmitted infections (Hart, 2007)
- Cost of law enforcement, health care and social services for patients who are unemployed, homeless or in other difficulties (Hart, 2007)

OAT improves (Brands et al., 2002)**:**

- Physical and mental health
- Social functioning
- Quality of life
- Pregnancy outcomes

In contrast to many short-acting opioids (e.g., heroin), methadone and buprenorphine:

- Are well absorbed and effective orally (methadone) or sublingually (buprenorphine) or subcutaneously (buprenorphine XR injection).
- Take longer (e.g., 30 minutes vs. instantaneously) to produce an effect than opioids that are injected, smoked or snorted
- Are longer acting than other opioids (24 to 36 hours or longer vs. three to six hours) and are administered less frequently
- Do not cause drowsiness or euphoria in patients on an appropriate dose
- Do not cause significant impairment in thinking, behaviour or functioning when taken at an appropriate dose
- Do not dull normal emotions and physical sensations
- Diminish opioid craving
- Decrease drug-seeking behaviour
- Reduce the likelihood of euphoria from other opioids in stable patients
- Continue to be effective with long-term use without dose increases

Limitations to the use of OAT

- Methadone is a high-risk medication with a narrow therapeutic range that can result in opioid overdose, especially at the beginning of treatment. It may prolong QT interval, leading to an increased risk of fatal arrhythmias. Buprenorphine has a lower overdose mortality risk but can still have severe health consequences including death – especially, if misused or combined with other CNS depressants including alcohol.
- People (including health professionals) may inadvertently or inappropriately label patients as 'still addicted', thus stigmatizing them further.
- Program practices may be experienced by patients as demeaning (e.g., observed urine collection, waiting in line at the pharmacy for their dose).
- OAT requires regular visits to the pharmacy, physician,
- Cost may be a barrier for some patients.
- Both buprenorphine and methadone can produce adverse side-effects and may interact with other medications.
- OAT practices may limit patient's 'flexibility' for work or travel.
- There may be limited availability of physicians and pharmacies that offer OAT in some areas
- Pharmacists can aid their patient's recovery by supervising drug administration, monitoring their dosage, communicating with the treatment team, dispensing take-home doses in accordance with established guidelines and providing encouragement and support

CAMH Opioid Agonist Maintenance Treatment: A pharmacist's guide to methadone and buprenorphine for opioid use disorder. Third edition 2015.

Overdose Prevention Sites (which are also referred to as supervised injection services or safe consumption sites) are facilities that fall under the umbrella of harm reduction. These facilities are health services that provide a hygienic environment for people to consume substances under the supervision of medical professionals. In addition to supervised injection, individuals are provided with sterile supplies, education on safer consumption, overdose prevention and intervention, medical and counselling services, and referrals to drug treatment, housing, income support and other services. Overdose prevention sites have been known to reduce costs for the health care system, prevent blood borne illnesses such as HIV or Hepatitis C, helps individuals access supportservices and prevent overdose deaths. In addition, research shows that the existence of an overdose prevention site in a community does not lead to increased crime, and works to decrease public substance consumption. These facilities are helpful in reducing the harms related to substances, particularly opioids. Overdose prevention sites are an evidence-based component to a comprehensive treatment response.

Information on Buprenorphine/Naloxone

Buprenorphine and methadone should both be considered as one of the standard first-line treatment options for opioid agonist therapy. Naloxone is added to buprenorphine to prevent people from injecting it. When the buprenorphine/naloxone pill is dissolved under the tongue, the naloxone doesn't do anything. If the pill is injected, the naloxone can cause withdrawal symptoms or prevent opioids from working.

As a long-acting opioid, buprenorphine prevents withdrawal symptoms and reduces cravings for opioids. It has a high affinity for opioid receptors and blocks the effect of other opioids used concurrently. However, buprenorphine does not cause someone to feel ill if they do use opioids. It has a "ceiling effect' – above a certain dose there is no additional effect which contributes to a lower risk of respiratory depression and overdoses than with other opioids including methadone.

CPSO expects all physicians who prescribe buprenorphine for opioid use disorder treatment to have training/education on addiction medicine generally, prior to initiating buprenorphine treatment. Physicians should collaborate with pharmacists and other members of the patient's interprofessional health care team.

There are no federal or provincial policies governing the prescribing or dispensing of buprenorphine/naloxone.
.
Consider treatment intensity when determining the most appropriate opioid agonist treatment option. Adjust the treatment to accommodate the changing circumstances and preferences of the patient.

Initiate opioid agonist treatment with methadone when treatment with buprenorphine/naloxone is not preferable (e.g., intolerance, patient preference, challenging induction, inadequate response to buprenorphine/naloxone).

Some patients who show a successful and sustained response to methadone may wish to transition to buprenorphine/naloxone. This is an option for patients who:

- Request more treatment flexibility with increased take-home doses
- Are seeking a better and drug-interaction profile
- Wish to withdraw from opioid agonist treatment but have difficulty tapering off methadone and might better tolerate a taper from buprenorphine/naloxone

The decision to transition to buprenorphine/naloxone must be balanced with potential risks of destabilization, which may increase when transitioning from higher methadone doses. To mitigate risk, the methadone should be slowly reduced before making the transition, micro dose buprenorphine/naloxone or switch to slow-release oral morphine for five days after stopping methadone and before initiating buprenorphine/naloxone.

Buprenorphine comes in 2mg, 8mg, 12mg and 16mg tablets combined with naloxone. These tablets must be taken sublingually, as buprenorphine is not readily absorbed when tablets are swallowed. Naloxone is included in the medication only as a deterrent to injection; it is not absorbed when the tablet is taken sublingually or orally and dose not impact the action of buprenorphine or a person's response to other opioid use.

Mechanism of Action

1) High affinity and slow dissociation – Buprenorphine binds strongly to mu-opioid receptors and dissociates slowly, preventing withdrawal symptoms for at least 24 hrs. at an appropriate dose. It blocks the activity of other opioids used concurrently, which makes the use of other opioids less rewarding and is also protective against opioid overdose.
2) Partial opioid agonist – Buprenorphine provides enough opioid agonist activity to prevent withdrawal symptoms and cravings, with less sedation and other side effects than full -agonist opioids.
3) Ceiling effect – Doses beyond 24-32mg do not have additional effects with respect to respiratory depression. As a result, the risk of respiratory depression and overdose is substantially reduced relative to other opioids.

Relative to methadone and other full-opioid agonists, buprenorphine may have a more favourable safety profile, including a lower risk of QT prolongation and lower risk of overdose, especially when combined with alcohol and benzodiazepines.

Induction Phase

Traditional induction typically occurs in an observed clinical setting such as a physician office or pharmacy. In a Home Induction, a person is given a prescription to start at home when they are in withdrawal. Prior to initiating, it is recommended that patients be in at least moderate withdrawal defined by a Clinical Opiate Withdrawal Scale (COWS) score greater than 12. This is to ensure that the full opioid agonist is adequately eliminated to avoid precipitation of opioid withdrawal with buprenorphine/naloxone.

COWS Scale:
https://www.asam.org/docs/default-source/education-docs/cows_induction_flow_sheet.pdf?sfvrsn=b577fc2_2

Patients should wait at least:

- 6-12 hrs. (preferably 12 hrs.) after use of short-actine opioids (e.g., heroin, oxycodone), or
- 12-24 hrs. (preferably 24 hrs.) after the use of a slow-release opioid (e.g., oxycodone controlled-release formulations, or
- 24 hrs. (preferably 36-72 hrs.) after use of long-acting opioid (e.g., transdermal fentanyl, methadone)

Switching from methadone requires that the patient's methadone dose be first tapered down to 30mg or less before buprenorphine treatment is initiated to minimize the risk of precipitated withdrawal. It is recommended to wait at least 3 days after the last dose of methadone before starting buprenorphine/naloxone.

Advise patients that release of opioid withdrawal symptoms generally occur 20-40 minutes after the initial dose of buprenorphine. Review the clinical practice guidelines from CAMH that detail the initiation of buprenorphine/naloxone in the outpatient management of OUD in Ontario.
https://www.camh.ca/en/education/academy/continuing-education-directory/buprenorphine-treatment-for-opioid-use-disorder

Prescribe 2-4mg of buprenorphine/naloxone as an initial supervised dose when the patient is in moderate to severe withdrawal (COWS >13). Up to 6mg is acceptable in clinically required situations but may increase the risk of precipitating withdrawal.

Reassess the patient after one to three hours and prescribe additional observed dose(s) if necessary (COWS >8, symptoms of withdrawal).

- Be careful not to precipitate withdrawal by giving too high a dose or by medicating in the absence of observable withdrawal
- One or two 2mg tabs to take home may be provided if repeated observation is not feasible in the clinical setting, with clear instructions on timing the dose to avoid precipitating withdrawal

It is suggested to avoid prescribing more than 12mg total on the first day.

NB: Pharmacokinetic studies have shown variation depending on the dose combinations of tablets—care is necessary.

Consider alternative induction approaches such as:
'Micro dosing' for people who should not undergo withdrawal for medical reasons or who are using opioids with a very long half-life (e.g. methadone or unregulated drugs containing fentanyl) such that waiting for the onset of withdrawal would pose a significant barrier. Most microdosing starts with 1⁄4 of a tablet on the first day and increases from there every day. to a total daily dosage of 12mg over 5-7 days for patents who cannot tolerate the significant period of abstinence needed to start buprenorphine/naloxone with a conventional induction

- https://www.metaphi.ca/wp-content/uploads/ED_OUD_MicrodosingInfo.pdf

OR

'Rapid micro dosing' – administering 0.5-1 mg at shorter intervals, up to 12mg total in a 24-hour period

Macro dosing is for people who do not meet criteria for other methods and for whom delays in treatment pose significant risk (those with very high opioid tolerance and at high risk of not engaging in standard treatment). It is generally done in hospital and allows for up to 32 mg on the first day. Do not use macrodosing in patients at high risk of opioid toxicity.

http://www.metaphi.ca/wp-content/uploads/MacrodosingPrimer.pdf

Suboxone® is now available as a film dosage form. There is evidence to suggest there is a difference in the bioavailability of buprenorphine/naloxone in a film form. Patients starting Suboxone® film should be advised to start taking the product sublingually. Let it dissolve for 15 minutes – do not eat or drink during this time. Once stable and agreeable to the prescriber, the patient may have the option to use the product sublingually or buccally.

Pharmacokinetic studies have shown variation depending on the dose and various combinations – caution must be taken when switching from one dosage form to another. The products are not equally bioavailable nor are they considered to be interchangeable. Patients switching from tablet to film or vice versa should be counselled

to be aware of the potential for variable bioavailability and resulting signs and symptoms that may indicate over or underdose. Best practice, if the prescriber wishes to change the dosage form is to advise to not change the dose as well at the same time—maintain the same dose and allow for time to observe patient response.

Titration and Stabilization Phase

Titrate based on withdrawal symptoms and side effects until an optimal dose has been reached, typically on day 3. Doses may be doubled every day, up to a maximum of 24mg on day 3.

Consider an alternative approach: add up the dose given on day 1 and administer it as the first dose of day 2, followed by additional doses based on the re-emergence of withdrawal symptoms. On day 3, add up the doses administered on day 2 and provide additional doses as necessary. Repeat daily until the patient is stable (no withdrawal, or COWS scores <8 for 24 hrs.) or until a maximum of 24mg per day is achieved. Off label doses up to 32mg per day may be seen (U.S. max dose).

Use slow titration with older adults, patients taking other CNS depressants and patients with questionable opioid tolerance, balancing the risk of lower treatment retention with the risk of over-sedation:

- Increase buprenorphine/naloxone by 2-6mg per day until an optimal dose has been reached (24hrs with no withdrawal symptoms, extinction of cravings to use opioids, absence of toxicity).

The patient should be seen by a member of the health care team to assess effectiveness and safety (e.g., excess sedation). Base reassessment frequency on the intensity of induction.

Maintenance Phase

Use clinical judgment to maintain an optimal individualized daily dose, which is up to a max of 24mg per day.

- If exceeding 24mg in exceptional circumstances, inform the patient that this is a departure from approved doses
  (Limited evidence of a benefit for higher doses & an increased risk of adverse events
  Review the case with an experienced colleague before trialing a dose higher than 24mg per day and attempt to reduce the dose to approved levels (as tolerated) once the OUD has stabilized.

Recognize alternate-day dosing as an option for patients who are clinically stable at doses less than or equal to 12mg per day (i.e., 24mg every other day) and who require less frequent visits to the pharmacy for dosing.

- Balance this with the challenges in managing missed doses. The patient should be reassessed for toxicity/sedation when given this higher dose. Communication between pharmacist and prescriber is critical.
- Take-home doses or switching to an extended-release formulation may be a better approach than alternate-day dosing.

Consider long-acting preparations of buprenorphine – extended release monthly injections (Sublocade®) to enhance medication adherence and convenience for patients who are clinically stable.

Monthly extended-release SC injections (Sublocade®) - Limited use for the management of moderate to severe opioid use disorder as part of a complete treatment plan that includes counselling and psychosocial support in the following adult patients – the patient has been induced and stabilized on an equivalent of 8mg-24mg SL per day for a minimum of seven days.

Discuss switching to buprenorphine injection if the patient also:

- Requires less frequent medication administration
- Is comfortable with an invasive procedure or device
- Patient does not want to administer medications sublingually

Duration of Treatment

Studies have shown that patients are significantly less likely to relapse with long-term treatment. However, medications are just one part of the long-term management of opioid use disorder – counselling, support groups, management of mod and anxiety disorders are all beneficial.

Take Home Doses

Most patients can take home up to one week of buprenorphine from the time they start treatment and move toward monthly pickup, as long as they are stable and managing their medications well. For those patients who have ongoing severe substance use or are unable to store medication safely, consider having buprenorphine doses dispensed daily at the pharmacy until issues are resolved.

Missed Doses

For missed doses with no relapse to full opioid agonist use:

- <5 days – resume previous dose
- >6 days – adjust the dose based on the total daily dose and the number of missed doses

https://www.camh.ca/-/media/files/professionals/canadian-opioid-use-disorder-guideline2021-pdf.pdf

- 2 alternate-day doses – suspend buprenorphine/naloxone until the patient can be reassessed. Then return the patient to a daily dose schedule, possibly at a lowered dose, to restabilize them before resuming an alternate-day schedule.

For missed doses due to relapse or return to full agonist opioid use – advise the patient to stop using buprenorphine/naloxone until they are ready to resume opioid agonist treatment. Schedule a new induction date and return to the process in the 'induction phase'.

https://www.metaphi.ca/wp-content/uploads/ED_OUD_CommunityProvider.pdf

https://www.camh.ca/en/health-info/guides-and-publications/canadian-opioid-use-disorder-guideline

https://pharmacyconnection.ca/opioid-use-disorder-treatment-spring-summer-2020/

Initiating a Buprenorphine/Naloxone Program in Your Pharmacy

Abbreviations:
Ontario College of Pharmacists (OCP); College of Physicians and Surgeons of Ontario (CPSO); Centre for Addiction and Mental Health (CAMH); Clinical Opiate Withdrawal Scale (COWS)

Information to provide to OCP

Unlike methadone, there is no requirement to report to OCP the decision to dispense buprenorphine/naloxone for opioid use disorder treatment.

Training Information for staff

Designated manager and all pharmacists (regular and casual) should be familiar with the principles and practice guidelines on buprenorphine/naloxone. There is no OCP Policy for specific mandatory training, as there is with methadone.

Information for physicians

CPSO expects all physicians who prescribe buprenorphine for opioid use disorder treatment to have training/education on addiction medicine generally, prior to initiating buprenorphine treatment.

Required Documentation

- A written/faxed prescription from any prescriber who is eligible to prescribe narcotics.
- Best practice is a 2-way (Pharmacist-Patient) or 3- way (Pharmacist-Patient-Physician) Treatment Agreement which may include:
    - Expectations of all parties involved
    - Circumstances under which treatment agreement will be in place - “Pharmacy’s rules”
    - Consent to access and share personal health information as it relates to buprenorphine/naloxone treatment
    - Signature of Designated Manager or delegated pharmacist as determined by written policy
    - Signature of the patient
- Patient’s acknowledgement that they may be required to provide photo ID before receiving their buprenorphine/naloxone dose(s)
- Record of dispensing of witness/daily doses and take home/carry doses
- Tracking of missed doses of buprenorphine/naloxone must be readily retrievable using a tracking tool/record of dose administration
- All missed doses should be communicated to the prescriber
- Record of administration to include patient’s name, daily dose*, date, time, and place of observed administration.
  *daily doses can be prepared using different combinations - document for future reference
  e.g., for 12mg, can use [8mg + 2 x 2mg] or [1.5 x 8mg]
- Record of destruction of unused doses must be handled in accordance with applicable laws, standards of practice, and OCP policy

Supplies

- Childproof vial for take home/carry doses
- Patient lockbox, if applicable

Recommended Resources:

OCP Article – Buprenorphine for Opioid Use Disorder Treatment: Focus on New Formulations and Alternative Induction Protocols
- https://pharmacyconnection.ca/opioid-use-disorder-treatment-spring-summer-2020/

OPA's Methadone, Buprenorphine, and the Community
- Webinar and in-person options. See opatoday.com for upcoming sessions.

OPA's Methadone and Buprenorphine/Naloxone Toolkit for Pharmacists
https://www.opatoday.com/methadone-and-buprenorphine-naloxone-toolkit/

CAMH Opioid Use Disorder Treatment (OUDT) Course
https://www.camh.ca/en/education/continuing-education-programs-and-courses/continuing-education-directory/opioid-use-disorder-treatment-oudt-course

CAMH Buprenorphine-Naloxone Treatment for Opioid Use Disorder
https://www.camh.ca/en/education/continuing-education-programs-and-courses/continuing-education-directory/buprenorphine-treatment-for-opioid-use-disorder

CAMH Opioid Agonist Maintenance Treatment, 3rd edition
- To order - https://store-camh.myshopify.com/products/p6500

Web Resources

- OPA Professional Development Website
- https://www.opatoday.com/?s=opioids

- Addiction Treatment Forum
  - http://atforum.com/

- OPA Opioid Substitution Therapies Discussion Forum
  - http://methadoneforum.opatoday.com/

Telephone Resources

CAMH Addiction Clinical Consultation Service
- 416-535-8501, press 2 416-535-8501, press 2 (M-F 8:30AM - 5PM)

Opioid Agonist Therapies Support for Professionals
- Email: methadone@opatoday.com (M-F 10AM – 3PM)

Things to Consider Before Starting to Dispense Buprenorphine/Naloxone

- Pharmacy layout and workflow
- Need for a private area for counseling and witnessing doses
- Staffing impact: adequate personnel, training and competency, professional satisfaction
- Collaborations with buprenorphine/naloxone prescribers
- Reimbursement: will patients pay cash or bill to third party plan?
- Service policies and possible limitations on:
    - hours when buprenorphine/naloxone is dispensed
    - number of buprenorphine/naloxone clients
    - consider the number of buprenorphine/naloxone clients that can comfortably be served in the pharmacy at one time
- Service to buprenorphine/naloxone clients, regularly serviced by other facilities (i.e., guest dosing)
- Harm reduction assessment
- Assess staff competence to deliver buprenorphine/naloxone services in a non-stigmatizing environment
- Procedures to minimize dosing errors and optimize work processes
- Appropriate equipment (e.g., dispensing labels and labeling as regulated, child proof bottles, Information resources, and lockboxes if necessary)
- Dosing documentation logs
- Establish patient care process for patient assessment, dispensing, witnessed administration, and management of difficult situations
- Witnessing buprenorphine/naloxone ingestion requires longer time than methadone ingestion, so, staffing levels will need to be adjusted – where will the patient wait?

Role of Pharmacist in Buprenorphine/Naloxone Program

- Assess patient care issues for the safe dispensing of witness doses or take-home doses
    - Monitor for signs and symptoms of intoxication or overdose
    - Observe change in patient's appearance or behaviour
    - Social and housing issues that may require special dispensing needs
    - Process for missed, lost or stolen doses
    - Monitoring of drug interactions
- Positive identification of the patient (e.g., correct patient for the dose prescribed)
- Observe witnessed daily dose
- Provide take-home dose(s)
- Awareness of when buprenorphine/naloxone doses must be withheld, and physician immediately contacted (e.g., symptoms of intoxication such as slurred speech, stumbling gait, confusion, disorientation)
- Provide patient advice and information as necessary (e.g., signs and symptoms requiring immediate attention at various phases of buprenorphine/naloxone use and dosing) – reinforce safety risks
- Diversion alertness
- Determine physician's preferred method of communication especially after hours (e.g., email, cell phone)
- Be familiar with best practices and guidelines for buprenorphine/naloxone dispensing
- Ensure all regulations are met in accordance with the pharmacist's assigned role
- Dispensing and billing roles pending staffing

Role of Pharmacy Technician in Buprenorphine/Naloxone Program

- Enter/process prescriptions
- Prepare individual patient doses
- Report discrepancies to supervising pharmacist (e.g., missing patient documentation, identification discrepancies, interaction codes, unusual patient behaviour)
- Billing/administrative issues as assigned by the pharmacy
- Maintain stock and required supplies
- Check prescriptions for technical accuracy

Buprenorphine/Naloxone Tablet Label Requirements

- **best practices in addition to DPRA requirements for regular prescriptions**

- Specify to “Dissolve tablet under the tongue”
- Total daily dose in mg.
- Ingestion date(s) when specified on prescription order (e.g., patients that receive dose every other day)
- Child-resistant cap for take home doses

Initiating a New Patient

- Copy of picture identification
- Current contact information
- Treatment Agreement (Best Practice): 2-way (pharmacist-patient) or 3way (prescriber-pharmacist-patient) agreement signed by all parties
- Explain hours of operation, usual process/procedure
- Lock box policy (considered best practice)
- Establish and discuss with prescribers (including nurse practitioners) whether patient is in at least moderate opioid withdrawal (i.e., COWS >12) prior to administering first dose
- Counsel on safety and harm reduction including how to recognize and temporarily reverse an opioid overdose by using a Naloxone Kit
  https://www.ocpinfo.com/practice-education/practice-tools/support-materials/naloxone-guidance/?hilite=naloxone
- Notify patient that witnessing dissolving of buprenorphine/naloxone tabs takes longer than methadone ingestion – patient should be prepared to schedule visits to the pharmacy to accommodate this

Physician/Pharmacist Collaboration

- Pharmacy and clinic hours
- After hours contact information for physician and pharmacist
- Pharmacy and clinic procedures
- Consistency in patient messaging and counseling
- Patient care issues
- Is a lock box required? (Considered as best practice)
- How to notify prescriber about missed doses (fax, cell number, email etc.)

Patient Treatment Agreement (Best practice)

- 2-way agreement (pharmacist-patient) or 3-way (prescriber-pharmacist-patient) (sample in Opioid Agonist Maintenance Treatment text by CAMH - Appendix 5)
- Expectation of all parties and consequences may include:
    - Consent to access and share personal health information among health care professionals involved in their care.
    - Pharmacy and clinic hours of operation and procedures
    - Consequences of inappropriate patient behaviors
- Patient care issues
- Need for consistency in timing of doses
- Need for lock box (considered best practice)
- Notice to the patient that missed, lost, stolen or wasted doses will not be replaced without a new prescription
- Inability to have dose if patient appears to be intoxicated
- Procedures for traveling
- Patient's acknowledgement that, if requested, they will be required to provide photo ID before receiving their dose

Witnessing a Dose

- Positive identification of patient (photo ID)
- Pharmacist must assess the patient for signs of intoxication prior to administering the dose
- Press buprenorphine/naloxone sublingual tab into a medicine cup (avoid handling tab)
- Ensure total dose is consumed (be aware of potential for diversion)
- After 1 to 2 minutes, discreetly and respectfully ask patient to lift tongue to display partially dissolved tablet.
- Advise patient not to talk or drink while the tablets are dissolving, as this can result in less of the tablet being absorbed sublingually
- Paper cup to be disposed of in secure pharmacy area
- Pharmacist and/or patient should sign the record of administration (best practice)
- Patient may leave once the tablet is fully dissolved
- To minimize the risk of diversion, the pharmacist may consider "chunking" or "crushing" the dose to speed up dissolution time – there may be a difference in effect in patients receiving crushed or chunked tabs when attending different pharmacies

Documentation

- Record of Administration - Document on the record or on the hard copy of Rx, the patient's name, daily dose, date, place and the time of administration; also note if a witness or take-home dose was given.
- No shows/missed doses to be communicated to the prescriber
- Patient receipt showing the dose documented…this is important when the patient is guest - dosing at another pharmacy as it may be used as evidence of last dose

Dispensing Buprenorphine/Naloxone at a Glance

New patient presents a prescription for buprenorphine/naloxone for opioid use disorder treatment

A Controlled Drugs and Substances Act (CDSA) Prescriber Exemption is not required.

The CPSO expects physicians to undertake training in addictions medicine and buprenorphine/naloxone prescribing.

Prescription should include:

- Dose written in numbers and words (mg of buprenorphine)
- Directions "dissolve under the tongue"
- Start and stop dates (use the word "inclusive" to minimize ambiguity)
- Specific details for days to be observed, or days patient may have take-home doses
- Confirm Narcotics Monitoring System (NMS) requirements and evaluate NMS alerts

It is also recommended that the dispensing pharmacy is specified and a request that the pharmacy notify the physician if the patient misses any doses.

NB: Buprenorphine/naloxone is not officially approved for treatment of pain in Canada

Wastage and Destruction

Health Canada no longer requires prior authorization requests for the local destruction of Narcotics and Controlled Drugs

- http://www.ocpinfo.com/practice-education/practice-tools/fact-sheets/destruction/

Prescription Labelling Requirements

Label must include:

- "Dissolve under the tongue"
- Total daily dose in mg.
- Usual prescription labelling requirements

For take home doses include:

- Child resistant vial
- Lockbox (best practice)
- Usual auxiliary labelling for opioid narcotics
- Ingestion dates for take home doses

Take-Home Doses

- Do not dispense buprenorphine/naloxone take home doses unless authorized by prescriber
- Usually, prescriber can initiate take home dose(s) after 2 months of clinical stability
- Provide tablets to patient in childproof vial

- Once patient qualifies, the take home dose schedule is defined by the prescriber. Most patients can take home up to one week of buprenorphine from the time that they start treatment and move toward monthly pickup, as long as they are stable and managing their medications well https://www.metaphi.ca/wp-content/uploads/ED_OUD_CommunityProvider.pdf
- If applicable, explain benefits of a locked box to the patient

Initiating a New Patient

NOTE: ALL staff in a pharmacy that serves methadone/buprenorphine patients should be trained to communicate effectively and are given the necessary skills to reason, de-escalate, and be empathetic to patients that have unique needs. The needs of such patients may differ from those that they may be used to interacting with.

- Collect patient information including date of birth, drug allergies, medical history, current medications including OTC's, use of alcohol and cannabis
- Request a copy of picture identification
- Ensure correct contact information is recorded (home, work, cell phone number, address)
- Collect a signed 2-way agreement (pharmacist-patient); however, a 3-way agreement (physician-pharmacist-patient) is preferred if possible
- Explain the pharmacy's hours of operation, usual process and procedures
- If the pharmacy is closed on a given day, other arrangements must be made, and proof of last dose must be presented

Minimizing Risk

- Use childproof vials for take home doses
- Positively identify all patients (photo ID)
- Confirm the dose with the patient before it is consumed
- If a patient is receiving buprenorphine/naloxone from two different pharmacies, have an effective communication system to ensure communication of all doses received, dose changes or missed doses.
- Advise patients that relief of opioid withdrawal symptoms usually begins 20-40 min. after the initial dose of buprenorphine
- Advise patients that serious respiratory depression has occurred when combined with CNS depressants including other opioids, alcohol, benzodiazepines, certain antidepressants, sedating antihistamines and barbiturates

Contraindications:

- Allergy or sensitivity to buprenorphine or naloxone
- Acute severe hepatitis, or severe liver dysfunction or failure
- Acute intoxication/impaired level of consciousness
- Severe respiratory compromise
- Unable to give informed consent due to psychosis or other causes

Note: Opioid withdrawal can exacerbate unstable cardiac, respiratory and psychiatric conditions.

Buprenorphine/Naloxone Combination Product
Pharmacology & Additional Information

Disclaimer: Individual variability in buprenorphine/naloxone effect and pharmacokinetics needs to be considered when dosing buprenorphine/naloxone. There is no induction dose considered to be absolute safe for all patients. Health professionals are advised to use their professional judgment and refer to available literature when dosing buprenorphine/naloxone.

Some Important Dosing Facts About Buprenorphine/Naloxone

- Buprenorphine is a partial mu agonist at opioid receptors
- Buprenorphine is a partial agonist and has a 'ceiling effect' to its opioid agonist effects at higher doses, therefore making it safer in overdose and reducing its potential for abuse
- Serious respiratory depression has occurred when combined with CNS depressants including other opioids, alcohol, benzodiazepines, certain antidepressants, sedating antihistamines, and barbiturates
- For patients with children, the use of child proof vials and lockboxes for take home doses can prevent accidental overdoses
- The effectiveness of opioid agonist therapy is tied to adequacy of dosing. Adequate dosing can result in treatment retention and reduction in illicit opioid use.
- Buprenorphine has a very high binding affinity for the opioid receptor and can precipitate withdrawal in patients who have recently used other opioids with lower affinities, including morphine or methadone.
- Wait to initiate therapy with buprenorphine/naloxone until at least 6 to12 hours (best is 12 hours) after use of short-acting opioids; or at least 12 to 24 hours or longer (best is 24 hrs.) after use of slow-release opioid; 36-72 hours after long-acting opioid (e.g. transdermal Fentanyl®, methadone)
- For those patients switching from methadone to buprenorphine, it is preferable to wait 3 or more days after last dose of methadone; in addition, the transition should occur after having tapered methadone dose to 30mg or less to minimize risk of precipitated withdrawal

Note: A micro dosing approach in which buprenorphine/naloxone initiation overlaps with administration of initial opioid may be preferred for patients to avoid withdrawal symptoms.

Pharmacology of Buprenorphine (sublingual tablets)

- Buprenorphine is a synthetic opioid, acting as a partial mu agonist at the mu-opioid receptors of the CNS and peripheral tissues
- As a partial agonist, buprenorphine has a ceiling effect to its opioid agonist effects at higher doses, making it safer in overdose & reducing its potential for abuse
- Poor oral bioavailability due to extensive first-pass metabolism
- Administration sublingually once per day or every other day
- Absorption: rapid with sublingual administration
- Onset of effects: 30-60 minutes
- Time to peak plasma concentration: 90 minutes
- Peak clinical effects: 1-4 hrs.
- Duration of effects: 48-72 hrs.
- Time to steady state: 5-10 days
- Elimination Half-life: 28-37 hrs.
- May be associated with fewer and less severe drug interactions when compared with methadone.
- Metabolized primarily by CYP 3A4; lesser by CYP 2C8

Pharmacology of Naloxone

- An opioid antagonist with a relatively short half-life that is included with buprenorphine to deter misuse of buprenorphine through injecting or snorting of the sublingual tablets.
- Poor oral bioavailability. No clinically significant effects when taken sublingually
- Naloxone is used intravenously, intramuscularly or intranasally to treat opioid overdose.

Toxic Effects/Severe Symptoms

- Respiratory depression (delayed and prolonged)

Adverse Medication Effects	Withdrawal Symptoms
• dose related-similar to other opioids • constipation • headache • CNS depression (sedation) • euphoria • excessive sweating • nausea & vomiting • insomnia • orthostatic hypotension • dry mouth • changes in sex drive • drowsiness • light-headedness • weight gain •	• headache • GI upset/abdominal cramps • nausea • diarrhea • runny nose • excessive sweating • uneasiness • yawning • tears • goosebumps • craving the drug

Buprenorphine/Naloxone Drug Interactions

Pharmacists are encouraged to regularly access the most up-to-date information on drug interactions from reliable drug information sources as part of their clinical assessment and new information is becoming known daily.

Appendix 2 in the 3rd edition of CAMH Opioid Agonist Maintenance Treatment is not exhaustive. Pharmacists are encouraged to regularly access the most up-to-date information on drug interactions from reliable drug information sources as part of their clinical assessment and new information is becoming known daily.

An additional resource is the mobile APP – Opioid Drug Interactions by PCM Scientific.

Pharmacists and Buprenorphine/Naloxone Drug Interactions

- Keep an accurate, updated medication profile, including OTC, herbal and illicit drugs
- Develop a working knowledge of buprenorphine/naloxone drug interactions
- Watch for additive toxicity, particularly with CNS depressants
- Need quick access to current list of interactions
- Determine clinical significance of drug interaction.
- Use alternative, non-interacting drugs when possible
- If potentially interacting drug must be used, adjust buprenorphine/naloxone dose based on patient response
- Make dose adjustments slowly and in small increments to avoid toxicity. Severity of signs/symptoms of withdrawal or over sedation may help determine extent of dose change required
- If potential increase in buprenorphine/naloxone levels, advise patient in advance of signs or symptoms to watch for and what to do
- When possible, avoid concurrent administration of drugs with overlapping side effect profiles
- Consider pre-existing disease states as an alternative cause for symptoms, other than a drug interaction.
- In some cases, adverse drug reactions can be resolved by altering dosing schedule
- Consider complexity of prescribed regimens on patient adherence
- Patients should be carefully monitored when starting or discontinuing a medication that may interact with buprenorphine/naloxone

Patients and Buprenorphine/Naloxone Drug Interactions

- Provide all health care providers with an updated list of all medications used (including OTC, herbal and illicit drugs)
- Carry a list of all current medications on a Medication Record
- Consult with their doctor or pharmacist before taking any OTC, herbal or dietary supplements
- Advised of hazards of using illicit or drugs intended for someone else
- Patients who are on an interacting medication should be educated about the importance of adhering to their medication regimen
- Counselled to quickly report any sudden or unexpected signs/symptoms of buprenorphine/naloxone withdrawal or overmedication
- If potential increase in buprenorphine/naloxone levels, advise patient in advance of signs or symptoms to watch for and what to do.
- Verbally instruct on what the drug is for, how to take it, and how to reduce the risk of side effects or interactions

- Special consideration for patients with liver or kidney disorders, pulmonary or heart ailments, pregnancy
    - Note: buprenorphine is contraindicated in patients with severe hepatic impairment
- Instruct client in advance on what to do in an emergency if their supply of buprenorphine/naloxone and/or other medications runs out

Pharmacodynamic Interactions of Buprenorphine/Naloxone

Additive Effects:

- When combined with a medication or illicit drug that has similar pharmacological profile, the effects may be additive – e.g., Potentiation of CNS or respiratory depressant effects, constipation, nausea or urinary retention.
- CNS depressant effects of alcohol and benzodiazepines are additive when combined with buprenorphine – putting patients at increased risk of respiratory depression and sedation which can result in death.
- OTC medications containing dimenhydrinate and diphenhydramine can be abused and are problematic when used by patients on buprenorphine.
- Anticholinergic medications can potentiate the effects on the bowel, causing increased risk of severe constipation, possibly leading to paralytic ileus. It can also increase the risk of urinary retention.
- Due to buprenorphine's powerful affinity for the mu-opioid receptor, when it is used in the presence of other opioids it may cause these opioids to be displaced leading to acute withdrawal symptoms (precipitated withdrawal).

Pharmacokinetic Interactions

- Buprenorphine is metabolized by CYP3A4 and to a lesser extent by CYP2C8.

Medications that can decrease buprenorphine levels/effects

- Efavirenz

Medications that can increase buprenorphine levels/effects

- Atazanavir
- Erythromycin
- Fluoxetine
- Indinavir
- Itraconazole
- Ketoconazole
- Nelfinavir
- Ritonavir

Buprenorphine effects on other drugs

- Lopinavir
- Nelfinavir

Check with your Drug Information Centre or an online reference for current, up to date information.