ONTARIO PHARMACISTS ASSOCIATION

Advocating Excellence in Practice and Care

Methadone and Buprenorphine/Naloxone Toolkit for Pharmacists

Part B: Buprenorphine/Naloxone

The Ontario Pharmacists Association wishes to acknowledge the Ministry of Health and Long-term care for funding this initiative.

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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.

Note: During the COVID-19 pandemic, modifications to the standard guidelines have been made in order to reduce community transmission. Please refer to the CAMH document “COVID-19 Opioid Agonist Treatment Guidance” for further information on these modifications to treatment delivery.

Acknowledgement

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Opioid Agonist Treatment (OAT)

What is Opioid Agonist Treatment (OAT)?

It involves the prescribing of methadone, buprenorphine or sustained release oral morphine (SROM) as part of a comprehensive program which ideally includes counselling to help the person in treatment reduce or stop the harmful use of opioids. (Kleber, 2008).

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.

Currently, methadone and buprenorphine are the most prescribed treatment options. Methadone is the most studied and longest used pharmacological treatment for opioid dependence.

A third option, oral sustained release oral morphine SROM (e.g., Kadian®) may be used as OAT in individuals who have not benefited from treatment with first line and second line treatment options (i.e., buprenorphine/naloxone and methadone). This may be used in combination with methadone during the initiation phase for people who use fentanyl. Guide_MethadoneForFentanyl.pdf (metaphi.ca). In Canada, this use is considered **off-label**, and requires careful review of the risks and benefits, fully informed consent of the patient and rigorous clinical documentation.

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.

Recent practice changes for OAT can be reviewed at:
https://pharmacyconnection.ca/update-on-opioid-use-disorder-treatment/

OAT as a Harm Reduction Approach

Any program or policy designed to reduce drug-related harm without requiring the cessation of drug use. Interventions may be targeted at the individual, the family, community, or society (Erickson et al, 2002).

Harm reduction includes both strategies that focus on reducing drug use and those that focus on reducing the harm of drug use.

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 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)

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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 and counsellor.
- 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

Information on Buprenorphine/Naloxone

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.

Buprenorphine/naloxone is rapidly available as the first-line treatment for patients with Opioid Use Disorder. It is recognized that for many patients, any opioid agonist treatment carries a substantially lower risk of adverse events than no opioid agonist treatment.

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.

Recent Canadian guidelines recommend treatment with buprenorphine/naloxone first given its superior safety profile and flexibility in dosing compared to methadone.
(*Bruneau J, Ahamad K, Goyer ME et al. CMAJ 2018 March 5:E247-57*
https://doi.org/10.1503/cmaj.170958)

Initiate opioid agonist treatment with buprenorphine/naloxone whenever it is assessed to carry a lower risk than other agonist therapies because of its pharmacological characteristics and the advantages of more flexible take-home dosing.

META PHI guidelines list both methadone and buprenorphine as first line treatment options for patients who use fentanyl

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 seeing a better side-effect 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, microdose buprenorphine/naloxone or switch to slow-release oral morphine for five days after stopping methadone and before initiating buprenorphine/naloxone.

Induction Phase

Traditional induction typically occurs in an observed clinical setting such as a physician office or pharmacy. 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 required 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.

Prescribe 2-4mg of buprenorphine/naloxone as an initial supervised dose when the patient is in moderate to severe withdrawal (COWS >12). 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

Avoid prescribing more than 12mg total on the first day.

Consider alternative induction approaches such as 'micro-dosing'. Micro-dosing principles are currently not included in any clinical practice guidelines for the management of OUD, rather it is an off-label practice that has been included in clinical practice amongst addiction specialists.

'Micro dosing' – starting with 0.5mg twice per day, with increasing doss 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
OR
'Rapid micro dosing' – administering 0.5-1 mg at shorter intervals, up to 12mg total in a 24-hour period

Macrodosing which is generally done in hospital but allows for up to 32 mg on first day
http://www.metaphi.ca/wp-content/uploads/MacrodosingPrimer.pdf

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

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. In practice, doses higher than 24mg are seen. 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).

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. Communicate 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 - when appropriate to facilitate integration into society and reduce health care burden.

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 per day of transmucosal buprenorphine or a minimum of seven days AND the patient is under the care of a healthcare provider with experience in the diagnosis and management of opioid use disorder AND each dose is administered SC in the abdominal region by a certified health care provider who has received instruction and training.
Online training required by manufacturer; must submit certification of training to dispensing pharmacy advised by manufacturer.

No training is required for pharmacists.

Discuss switching to buprenorphine injection if the patient also:

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

Take Home Doses

Urine drug screens should be done at least monthly during induction and dose escalation until the patient has achieved a stable dose. Urine screens are useful to determine take-home dosing

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

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

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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 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

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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 Methadone, Buprenorphine and the Community complimentary online and/or live program

- https://opatoday.com/product/methadone-buprenorphine-and-the-community-live-2022-2023/

OPA Methadone and Buprenorphine/Naloxone Toolkit for Pharmacists

- https://opatoday.com/methadone-and-buprenorphine-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

CPSO Buprenorphine/Naloxone for Opioid Dependence: Clinical Practice Guideline

- http://www.cpso.on.ca/admin/CPSO/media/Documents/physician/your-practice/quality-in-practice/cpgs-other-guidelines/buprenorphine-naloxone-guidelines.pdf

CAMH Opioid Agonist Maintenance Treatment, 3rd edition

- To order - https://store-camh.myshopify.com/products/p6500

Web Resources

- Canada's Mental Health & Addiction Network
- https://www.oha.com/about-oha/Ontario-Hospitals/mental-health-and-addiction-network-(2)

- OPA Professional Development Website
- https://opatoday.com/?s=&filter[taxonomy][content_categories_opa][]=professional-resources

- 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
  - Open Mon – Fri 8:30AM-5PM

- OPA Methadone Drug Information Line
  - 1-888-519-6069 (open M-F 9AM-5PM)
  - Email: methadone@opatoday.com

OPA resources are made possible with the support of the Ontario Ministry of Health and Long-Term Care

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 limitations on:
    - hours when buprenorphine/naloxone is dispensed
    - number of buprenorphine/naloxone clients
    - number of buprenorphine/naloxone clients in 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

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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 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)
  Opioid Agonist Maintenance Treatment by CAMH (see Appendix 5)Optional but best practice
- 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 Suboxone sublingual tab out of the foil or place the generic tablet 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

- Document on the observed dose record, or on the hard copy of Rx, the patient's name, daily dose, date, place and the time of administration noting if a witness or take-home dose was given.
- Record of administration
- No shows/missed doses to be communicated to the prescriber
- Patient receipt showing the dose documented…important when 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
- 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

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, can initiate take homes 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. The usual number of take-home doses can range from one to a recommended maximum of one to two weeks.
- 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, deescalate, 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.

The Ontario Pharmacists Association wishes to acknowledge the Ministry of Health and Long-term care for funding this initiative.

- 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), but a 3-way agreement (physician-pharmacist-patient) is preferred if possible – Best practice
- 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

The Ontario Pharmacists Association wishes to acknowledge the Ministry of Health and Long-term care for funding this initiative.

Buprenorphine/Naloxone Combination Product Dosing Guide

Disclaimer: Individual variability in buprenorphine/naloxone effect and pharmacokinetics need 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 maintenance 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.

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Adverse Effects	Withdrawal Symptoms
• dose related-similar to other opioids • constipation • headache • CNS depression (sedation) • euphoria • sweating • nausea • insomnia • orthostatic hypotension	• headache • GI upset • nausea • diarrhea • runny nose • sweating

Toxic Effects/Severe Symptoms

- Respiratory depression (delayed and prolonged)

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 Opioid Agonist Maintenance Treatment (CAMH) 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 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.

The Ontario Pharmacists Association wishes to acknowledge the Ministry of Health and Long-term care for funding this initiative.

- 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.

A list of medications that can increase or decrease plasma levels/effects of buprenorphine is detailed in Opioid Agonist Maintenance Treatment (CAMH) 2016- Appendix 2, Table A2-5, A2-6 and A2-7, pg. 117-119.

Medications that can decrease buprenorphine levels/effects

- Efavirenz

Medications that can increase buprenorphine levels/effects

- Atazanavir
- Delaviridine
- 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.