Opioid Use Disorder Practice Update

July 12, 2021

In this document:

Overview

On April 14, 2016, the Provincial Health Officer declared a public health emergency under the Public Health Act, following an unprecedented increase in overdose-related harms due to an unregulated, unpredictable, and highly toxic drug supply. In response to this emergency, the Ministry of Health and BCCSU prioritized the development and publication of the provincial *Guideline for the Clinical Management of Opioid Use Disorder*, which was published in February 2017 and officially adopted as the provincial standard in June 2017. The guideline aims to provide comprehensive clinical care guidance and linked education to health care providers across the addiction care continuum in the province, which has improved access to evidence-based treatment for patients and families and reduced the significant harms associated with opioid use disorder in British Columbia. Since publication, evidence, best practices of care, and clinical experience have continued to grow, thus necessitating an update to the guideline to ensure it continues to reflect the most recent, high-quality, and comprehensive evidence on the full continuum of care for opioid use disorder. This update was planned for release in 2020.

However, following the March 17, 2020, BC declaration of a public health emergency due to the COVID-19 pandemic, the BCCSU, Ministry of Mental Health and Addictions, and Ministry of Health mobilized a group of expert clinicians, people with lived experience, and other relevant stakeholders to rapidly develop interim clinical guidance, *Risk Mitigation in the Context of Dual Pandemics,* which built on "*Prescriber Guidelines for Risk Mitigation in the Context of Dual Public Health Emergencies"* from Vancouver Coastal Health Authority. It was recognized that the COVID-19 pandemic would compound the harms and challenges of the toxic drug supply and overdose emergency declared in April 2016, and would increase a number of risks for people who use drugs, including the ongoing risk for overdose and other harms related to the illicit toxic drug supply, the risk of infection and spread of COVID-19 among those with underlying health conditions and who face social marginalization, and risks due to withdrawal for those who must self-isolate or quarantine to prevent the spread of COVID-19. The emergence of the pandemic necessitated that the in-progress update to the *2017 OUD Guideline* be put on hold, in order to respond to the intersection of dual health crises.

Since the public health emergency declaration in 2016, at least 7,300 British Columbians have died from illicit drug toxicity.[1] Recent data from the OUD Cohort[a] indicates that there was a 19.2% increase in

[a] The opioid use disorder (OUD) cohort is an administrative database that captures all BC residents with an indication of OUD since 1996. The cohort is identified using linked population-level administrative databases, capturing provincial health insurance plan registration, physician billing records, hospitalizations, medication dispensations, emergency department visits, perinatal services for all provincial births, mortality and cause of death.

diagnosed (detected) opioid use disorder between September 2018 and September 2020. Overdose continues to be the leading cause of unnatural death in British Columbia, surpassing homicides, suicides, and motor vehicle collisions[2]; life expectancy at birth is declining in British Columbia largely due to the overdose public health emergency.[3] In 2020 alone, an estimated almost 70,000 potential years of life were lost due to illicit drug toxicity deaths in BC, with the average age at death being 43 years old.[4] **The primary driver of this crisis is the growing toxicity and unpredictability of illegally-manufactured and distributed drugs adulterated with fentanyl and other highly potent synthetic opioids.**[5] Higher fentanyl concentrations and an increase in unexpected, dangerous combinations of drugs (e.g., benzodiazepines and fentanyl) have been observed across multiple drug surveillance data sources across the province.[b]

This practice update provides updates on the provision of opioid agonist treatment (OAT) in line with planned updates to the forthcoming provincial *OUD Guideline*, as well as clinical experience and preliminary data from a year of *Risk Mitigation* prescribing and implications for care in order to reduce individuals' risk of overdose and reliance on the illicit opioid supply.

Updates to OAT Practice

Since the 2017 *OUD Guideline* was published, several key updates to OAT practice have emerged, based on both research evidence and clinical experience.

Although current research evidence is limited, clinical experience indicates that some individuals with extremely high tolerance due to fentanyl require significantly higher OAT doses than were common when the drug supply had lower levels of fentanyl adulteration. In addition, although buprenorphine/naloxone may still be considered a preferred first-line medication when feasible (due to its superior safety profile), in practice, offering all 3 oral OAT options, regardless of previous OAT trials, along with education and discussion of the advantages and disadvantages of each medication is a reasonable approach.

This section provides information on updates to treatment with buprenorphine/naloxone, including micro-dosing inductions and new formulations; new methadone formulations; updated titration and dosing information for slow-release oral morphine; a brief overview of enhanced injectable opioid agonist treatment models; and guidance on clinical flexibility in response to local and global emergencies.

Buprenorphine/naloxone Micro-dosing Induction

Traditionally, buprenorphine induction has required a period of abstinence from opioids to ensure that withdrawal is not precipitated. This period[c] can be both time-consuming and difficult for patients.[6,7] A micro-dosing induction that slowly up-titrates small doses of buprenorphine with an abrupt cessation of other opioids once a therapeutic dose has been reached has been described in the literature.[8] Several case studies and case series have been reported (n=74).[8-13] These case reports include individuals on OAT (SROM,[10] methadone,[10] or diacetylmorphine and methadone[8,13]), those using illicit opioids (heroin[8] and

[b] It should be noted that the extant evidence on treating opioid use disorder was developed in the context of wide-spread heroin use and availability, not the more potent fentanyl and analogues that are now ubiquitous in the drug supply in BC and elsewhere. Clinical experience indicates that best practices derived from the evidence regarding treating individuals who use heroin (e.g., dosing, titration) are often insufficient for individuals with extremely high tolerance from fentanyl.

[c] 12–16 hours for short-acting opioids like diacetylmorphine or hydromorphone; 24–72 hours for longer-acting opioids like methadone; ≥24 hours for suspected, confirmed, or unknown fentanyl.

fentanyl[10]), and individuals on opioids prescribed for analgesia.[9] One case study used micro-dosing induction with buprenorphine in a low-threshold community setting to transition 5 patients with OUD to long-acting subcutaneous buprenorphine.[12] A 2021 literature review identified 18 case studies describing the successful transition of 63 patients to buprenorphine using micro-dosing induction techniques.[11] Research is ongoing to gather high-quality evidence of the efficacy of micro-dosing induction compared to standard buprenorphine induction; a randomized controlled trial planned at Vancouver General Hospital will enroll 50 participants with OUD to compare the two induction methods.[14]

Although the research evidence is extremely limited, clinical practice in many parts of BC now includes using micro-inductions as they reduce the risk of precipitated withdrawal and do not require the patient to experience moderate-to-severe withdrawal. Clinical experience suggests that micro-dosing inductions may be especially helpful for individuals using fentanyl, as the risk of precipitated withdrawal is higher due to the pharmacokinetics of fentanyl. Considerably more research is needed to compare traditional inductions to micro-dosing inductions in order to determine comparative efficacy, as well as who is best suited for which type of induction. More research is also needed to determine optimal micro-induction protocols. In the absence of said research, many different protocols following the same principles are in use. An example protocol follows.

Day	Dose	Other Opioids
1	0.5mg/0.125mg bup/nlx BID	Continue use
2	0.5mg/0.125mg bup/nlx TID	Continue use
3	1mg/0.25mg bup/nlx BID	Continue use
4	2mg/0.5mg bup/nlx BID	Continue use
5	2mg/0.5mg bup/nlx QID	Continue use
6	4mg/1mg TID	Continue use
7	12mg/3mg bup/nlx once daily	Stop use

Additional micro-dosing induction protocols are available from the BC Pharmacy Association and published in the Canadian Medical Association Journal.

Buprenorphine Formulations

Since the 2017 publication of the *OUD Guideline*, several additional buprenorphine formulations have become available in Canada.

1. Sublocade

Sublocade is an extended-release formulation of buprenorphine that is administered monthly via abdominal subcutaneous injection for the management of moderate to severe opioid use disorder. Sublocade was made available in British Columbia on April 30, 2020, through Pharmacare Special Authority.

Sublocade is associated with significantly higher treatment retention (almost double; $p<0.0001$) and mean abstinence percentages (over 40%) compared to placebo (5%; $p<0.0001$) in individuals with moderate to severe opioid use disorder.[15] A longitudinal study of extended-release buprenorphine found that 75% of participants who were retained in extended-release buprenorphine treatment for 12 months were abstinent at 12 months compared to 24% of those who were retained in extended-release buprenorphine treatment for 0–2 months ($p<0.001$).[16] Overall, 51% of all participants remained abstinent for 12 months.

The evidence base regarding which patients will benefit from transitioning to Sublocade is limited and continues to evolve.

Information on prescribing, dispensing, and applying for coverage request are available in BCCSU's Sublocade (Extended-release Buprenorphine) Information.

2. Probuphine

Probuphine is a buprenorphine subdermal implant used for the management of opioid use disorder (OUD). This mode of delivery allows for continuous blood levels of buprenorphine for up to 6 months following implantation.[17] In Phase III clinical trials, Probuphine was superior to placebo at reducing illicit opioid use over a 6-month period, and non-inferior to sublingual buprenorphine at preventing illicit opioid use over a 4–6 month period.[17] Probuphine (80mg) was approved for use in Canada in April 2018 and is listed for reimbursement (with prior approval) on the federal Non-Insured Health Benefit (NIHB) and Veteran Affairs Canada drug plans.[18,19] Probuphine is not covered by BC PharmaCare at this time. Health care providers must complete a training program for proper insertion and removal of the implant before prescribing Probuphine.[d] It is currently approved for use in patients who have sustained stability on sublingual buprenorphine at doses of no more than 8mg.[17,18] It is currently not recommended for use beyond 2, 6-month treatment cycles.[17]

3. Suboxone Film

Suboxone (buprenorphine/naloxone) film is available in BC in 3 dosages[20]; However, Suboxone film is not currently covered by BC PharmaCare, the Non-Insured Health Benefit (NHIB), or Veteran Affairs Canada.

In a randomized controlled trial, no significant differences in dose effects, adverse effects, or treatment outcomes were identified between Suboxone film and sublingual tablets.[21] Some patients may prefer the taste or faster dissolving time of the Suboxone film compared to the sublingual tablet.[22] Suboxone film produces higher bioavailability of buprenorphine compared to the same dose of the sublingual tablet; as such, switching between the two forms could theoretically lead to inadvertent over- or underdosing, although actual dose changes have not been required in head-to-head trials. For this reason, switching between formulations should be done only with appropriate monitoring for symptoms of over- or under-dosing of buprenorphine.[22]

Methadone Formulations

Since the 2017 publication of the *OUD Guideline*, several additional methadone formulations have become available in BC. More information can be found in the BCCSU's OAT Update: Methadone Formulation Options and Interchangeability.

Slow-release Oral Morphine Initiation

Since the 2017 *Opioid Use Disorder Guideline* was released, two additional systematic reviews have been published comparing slow-release oral morphine (brand name Kadian) and methadone.

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[d] Clinicians can find out more information about the Probuphine Education Program by calling 1-844-483-5636.

A 2017 Norwegian systematic review (n=460) compared slow-release oral morphine to methadone and concluded that there is probably no or little difference in treatment retention (moderate certainty); there may be little or no difference in illicit opioid use (low certainty); there may be little or no difference in adverse events (low certainty); there is insufficient evidence to determine effect on patient satisfaction and crime.[23] Overall, the evidence was assessed as having weaknesses that conferred low certainty in evidence of effect. Thus, the authors were unable to conclude whether SROM and methadone are equivalent. A 2019 systematic review and meta-analysis included both published trials and unpublished data (n=471) on two outcomes: illicit opioid use and retention in treatment.[24] This systematic review included all of the studies included in the 2017 systematic review, as well as additional published and unpublished data. The meta-analysis found no significant differences between SROM and methadone for both outcomes. Results from two studies also suggest that SROM is superior to methadone in reducing opioid cravings; however, this was not included in the meta-analysis. The study authors concluded that, while gaps remain in the evidence base for SROM, this meta-analysis confirms the apparent non-inferiority of SROM with methadone.[24]

There are a variety of dosing schedules described in the literature. Common practice in many clinics differs from the titration schedules described in the literature. The example protocol provided below is based on clinical experience and expertise, and is intended for individuals with known tolerance who are currently using opioids. Clinical discretion and individual circumstances should determine which titration protocol is used and frequent assessment should determine whether titration should be maintained, slowed, or sped up. A patient should be assessed in person or through virtual care prior to any dose increase. An example protocol follows.

Day	**SROM dose**
1	200mg
2	300mg
3	400mg
4	500mg
5	600mg
6	700mg
7	800mg

There is no maximum dose for SROM; patients with high tolerance may need doses above 1200mg per day to reduce cravings and withdrawal. Clinical experience indicates that patients often require doses above 1200mg due to high tolerance developed due to fentanyl in the street opioid supply.

Models of OAT Provision (Flexible Interdisciplinary Models)

[Note: this is draft text subject to minor updates in the final version]

The 2017 *OUD Guideline* laid out a model of OAT service delivery that includes very specific requirements for pharmacists, including witnessing of doses, ensuring take-home dose security (e.g., labelling, appropriate container), notifying the prescriber of missed doses, and canceling the prescription if a certain number of doses are missed. Although this remains a primary model of OAT provision in BC, new flexible interdisciplinary models have emerged, which help to reduce barriers for individuals who are unable to regularly attend a pharmacy to receive their OAT doses (for example, in rural and remote settings where a community pharmacy requires significant travel and a nurse or other regulated health professionals within their professional scope of practice can perform the required actions). Current models in use and

development are specific to the scope and regulatory structure governing nursing care in community care facilities in BC and follow appropriate federal exemptions for nurses. Any future models that include other regulated health professionals may require additional federal exemptions and confirmation from their regulatory bodies that performing these actions is within scope.

These flexible models serve to reduce barriers to treatment and support continued engagement in care. The models require regulated health professionals, working within their professional scope of practice and within the requirements of the federal regulatory structure and any applicable exemptions, to work closely with the dispensing pharmacy to ensure that the following actions are performed:

- Patient identification
- Patient counselling
- Provision and witnessing of doses
    - May be performed by a regulated health professional practicing within their scope and who is responsible for the patient's care
    - If a regulated health professional is witnessing a dose at a community health facility, the prescription should specify this in the "Directions for Use" portion of the medication
        - An example prescription for 16mg SL buprenorphine/naloxone could read:
          16mg SL once daily
          Dispense all doses in blister package
          Deliver to Pineway Shelter to nursing staff June 12, 2021
          Daily witnessed ingestion by nursing staff
          Rx: June 12–18, 2021
- Take-home dose security
    - Packaging of take-home doses must be performed by the pharmacy, with the doses and any patient instructions provided to the regulated health professional to provide to the patient
    - Take-home doses need to be specified on order/prescription regardless of which health care professional is providing the doses to the patient
- Missed witnessed dose notification
    - The responsible regulated health professional must notify both the prescriber and the pharmacist of any missed witnessed doses
- Prescription cancellation due to missed witnessed doses
    - If enough doses have been missed to require cancellation of the prescription, the responsible regulated health professional must notify the pharmacist, who has the responsibility to then notify the prescriber. A plan will then need to be discussed

- Destruction of missed witnessed doses

    - Missed witnessed doses must not be reused or saved for next day

    - As per current Subsection 56(1) Class Exemption for Nurses providing Health Care at a Community Health Facility, the nurse must return to the supplier for destruction or destroy on-site any unserviceable stock of controlled substances. In the case of on-site destruction, it must be witnessed by the individual destroying the controlled substance and one other nurse, practitioner, pharmacist, pharmacy intern, pharmacy technician or a Health Canada inspector
    - OR:

- The responsible regulated health professional must return to the supplier for destruction or destroy on-site any unserviceable stock of controlled substances. In the case of on-site destruction, it must be witnessed by the individual destroying the controlled substance and one other nurse, practitioner, pharmacist, pharmacy intern, pharmacy technician or a Health Canada inspector

In addition to community models in which the patient receives their OAT medication from regulated health care professionals other than pharmacists, there may be some extraordinary situations when a patient cannot attend the pharmacy (for example, in rural and remote settings with significant barriers to travel or in the case of illness requiring family support). In this case, the patient's representative may pick up and sign for the patient's authorized take-home dose(s) if confirmed in writing by the prescriber.

Increased Flexibility

Events over the past year, including the COVID-19 pandemic and climate change-related phenomena (e.g., wildfire evacuations, weather warnings due to extreme heat), have demonstrated the necessity and feasibility of clinical flexibility that prioritizes patient safety and continuity of care. Patient care should be adapted, as needed, during local or global emergencies and disruptions, to ensure that patients can continue to access life-saving treatment without putting their health at risk (e.g., waiting in extreme heat) or facing unreasonable barriers. Examples of adaptations may include extended carries, reduced urine drug testing, reduced clinic appointments or shifting toward virtual care, and facilitating transfer of prescription to a new pharmacy. Prescribers are encouraged to consult the 24/7 Line or RACE app if needing support to adapt care plans in response to states of emergency or other disruptive events.

Clinical Experience from Risk Mitigation Prescribing

Clinical experience and initial evaluations of the implementation of the *Risk Mitigation* interim clinical guidance have revealed several key lessons, which inform this practice update.

Using PharmaNet[25] and other Ministry of Health[26-28] data available through the BCCDC COVID-19 Cohort (BCC19C),[e] an estimated 6,498 people were dispensed Risk Mitigation Guidance (RMG) prescriptions from March 27 2020 to February 28, 2021.[f] Opioid medications were dispensed to 3,771 persons (58.0%), stimulant medications were dispensed to 1,220 persons (18.8%), alcohol withdrawal management medications were dispensed to 1,431 (22.0%) persons and benzodiazepines were dispensed to 784 persons (12.1%). Overall, there were 179,349 unique medication dispensations, more than 70% of which were for opioids, and approximately 20% of which were for stimulants.

Preliminary data from the BC COVID-19 Cohort indicates that, of 6,498 persons who were dispensed RMG medications from March 27, 2020 to February 28, 2021, 82 persons died during that period. Of the persons who died, 33 (40%) were prescribed opioids only, 9 (11%) were prescribed stimulants or stimulants and

[e] All inferences, opinions, and conclusions drawn in this report are those of the BCCSU, and do not reflect the opinions or policies of the Data Steward(s).

[f] The BCC19C was established at the Provincial Health Service Authority (PHSA) as a surveillance platform to integrate various datasets including data on BC-wide laboratory tests, COVID-19 surveillance case data, HealthLink 811 calls, prescription drug dispensations, medical visits, ambulance dispatches, Intensive Care Unit (ICU) admissions, and mortality—ß all integrated with existing administrative data sources such as the Chronic Disease Registry, hospital admissions and the Provincial Client Roster.

opioids, 6 (7%) were prescribed alcohol withdrawal medications and another RM medication (unspecified), and the rest (34; 42%) were prescribed only alcohol withdrawal medications or only benzodiazepines. Of the 82 persons who died, 7 had an active dispensation on the day they died (n=4 opioids; n=3 alcohol withdrawal management medications). The cause of death for a high proportion of deaths (n=37; 45%) is not specified due to the lag in Vital Statistics data. Of those deaths where cause is specified (n=45; 55%), none were due to illicit drug toxicity death. Among persons who received *Risk Mitigation* prescriptions that were not active on the day they died, the average length between prescription end date and death was 41 days for stimulant medications, 56 days for opioid medications, 86 days for benzodiazepine medications and 72 days for alcohol withdrawal management medications.

In addition, a mortality rate for persons who received *Risk Mitigation* prescribing has been found of 13.2 deaths per 1,000 person years. This rate includes individuals prescribed a variety of classes of medications (opioids, stimulants, benzodiazepines, and alcohol withdrawal medications). Due to this, it is challenging to compare the mortality rate to that faced by individuals who primarily use opioids. However, the following comparisons may be useful to help contextualize what is known at this point about *Risk Mitigation* reducing mortality. Cohort data from Vancouver, BC, has found a mortality rate of 22.7 per 1000 person years between 2006 and 2017 for people who inject drugs[29] and 12.7 per 1000 person years for individuals who used opioids daily or received OAT[g] between 2005 and 2017,[30] while a 2019 meta-analysis (n=150,253) of cohort studies of individuals on buprenorphine/naloxone or methadone found a crude mortality rate of 16 deaths per 1,000 person years,[31] and a 2020 meta-analysis (n=229,274) of 101 cohorts of people with OUD involving illicit opioids found a crude mortality rate of 18.7 per 1000 person years.[32] In addition, a retrospective cohort study using the BC Provincial Overdose Cohort found a 12-month crude mortality probability of approximately 5% for individuals who had visited the emergency department with an overdose-related visit in the previous 12 months,[33] which accords with a cohort study out of Ontario that similarly found that 5% of individuals who had attended the ED for non-fatal opioid overdose within the past year had died of any cause (1.9% of opioid-related causes).[34]

Oral Hydromorphone to Support OAT Initiation

The inclusion of oral hydromorphone prescribing in the *Risk Mitigation* interim clinical guidance has been used by clinicians to trial PRN (*pro re nata*; as needed) prescribing of opioids to support initiation of oral opioid agonist treatment (OAT). Clinical experience indicates that hydromorphone PRN has allowed patients to titrate their OAT dose up without needing to access the illicit drug supply, or to access it minimally to manage cravings and withdrawal symptoms during titration, which decreases the risk of overdose and supports continued engagement in care. Although not an evidence-based practice, some clinicians have that reported their patients are benefitting significantly from this approach and significantly reducing their use of illicit opioids and, thus, overdose risk, as well as increasing retention in care until titrated to a therapeutic dose. Evaluation data from the OUD Cohort up to September 30, 2020 found that 96% of all individuals who were dispensed opioids through *Risk Mitigation* prescribing had ever been on OAT prior to their first RM dispensation. More recent data (up to February 28, 2021) found that 68% of persons dispensed prescription opioids through *Risk Mitigation* prescribing had been dispensed OAT in the 30 days prior to first *Risk Mitigation* dispensation. Among those not prescribed OAT in the 30 days prior to RMG, almost 2% received an OAT dispensation on the same day as their first RM

[g] Specifically, this cohort reported using opioids daily or received OAT in the six months prior to their baseline survey AND did not sero-convert to HIV+ during the follow-up period.

dispensation, almost 15% were dispensed OAT within 7 days of receiving their first RM dispensation, and approximately 15% were not dispensed OAT within 30 days of their first RM dispensation.

When initiating OAT, it may be appropriate to co-prescribe oral hydromorphone if the patient is concerned about cravings or withdrawal symptoms and is at risk of accessing the illicit supply to ameliorate them while titrating their dose up. In this case, co-prescribing oral hydromorphone may help reduce overdose risk.

- Opioid agonist treatment initiation and titration should follow the *Provincial Guideline* or updated guidance above; oral hydromorphone prescribing may follow the hydromorphone dosing protocol below:
    - Prescribe oral hydromorphone 8mg tablets (1–3 tabs q1h as needed up to 14 tablets), provided daily

Using Hydromorphone or M-Eslon to Reduce Overdose Risk

Clinical experience suggests that some individuals have been able to reduce their reliance on the illicit drug supply and thus reduce their risk of overdose through the prescription of oral hydromorphone and/or sustained-release oral morphine (M-Eslon), while other individuals have not benefitted from this intervention. It is recognized that expanded options including higher potency medications and a variety of formulations are urgently required in order to help reduce individuals' reliance on the illicit drug supply and overdose risk. Until provincial protocols to guide the provision of pharmaceutical alternatives to reduce risk of overdose and drug-related harms are available, clinical judgment paired with thorough assessment and patient preference may indicate that trialing prescription of oral hydromorphone and/or M-Eslon is a reasonable approach to reduce risk of overdose and reliance on the illicit drug supply for individuals at high risk of overdose.

Hydromorphone may be prescribed as an adjunct to OAT, where a patient has experienced some benefit from OAT but continues to rely on the illicit drug supply to some extent; hydromorphone and/or M-Eslon may also be prescribed to individuals who are not currently receiving OAT, are not interested in starting OAT or other forms of addiction treatment, and are at high risk of overdose from the illicit opioid supply. For individuals interested in starting OAT, see Oral Hydromorphone to Support OAT Initiation, above.

Assessment

The following considerations for eligibility should be assessed and documented in the patient's health record:

- Ongoing active opioid use
  AND
- At high risk of overdose or other harms related to illicit opioid use

Assessment for eligibility should include the following:

- Active substance use assessment (i.e., type of substance, quantity used, frequency of use)
  - Note: Not all patients who qualify for these medications will meet a diagnosis of opioid use disorder. For example, individuals who use opioids intermittently may be at high risk of overdose due to the highly toxic illicit drug supply
- Substance use and treatment history
- History of overdose and other drug related harms (e.g., infections, criminalization)
- Comorbid mental and physical conditions
- Prescribed medication(s)
- Current access to a prescriber (i.e., GP, addiction medicine physician, nurse practitioner)

Dosing

If clinical judgment and patient preference indicate that a trial of oral hydromorphone is appropriate, the following protocol may be used:

Prescribe oral hydromorphone 8mg tablets (1-3 tabs q1h as needed up to 14 tablets) [h]

AND/OR

Prescribe M-Eslon 80-240mg PO BID provided daily (avoid sprinkling doses)

- **Note:** Doses should be started at the lower end of the range unless there is a known tolerance and up-titrated based on patient comfort, withdrawal symptoms, and cravings
- It may be helpful to prescribe a long-acting opioid in conjunction with a short-acting opioid for those not on OAT

The assessment and informed consent process should include a discussion of the potential risks and benefits of this intervention, as well as a discussion of continuing care. This should include a discussion of patient goals, as well as which clinical and psychosocial parameters would indicate that the patient is benefitting from the intervention, and which clinical and psychosocial parameters would indicate that the patient is not benefitting from the intervention, and how the treatment plan would change if the patient is not benefitting.

Assessment and Continuing Care

Following an initial trial period (i.e., 2–4 weeks), a thorough assessment of clinical and psychosocial indicators, as well as patient goals, should be performed, to determine whether the patient is benefitting from the intervention. The results of this assessment along with expert consultation, where appropriate, and patient preference should inform the decision to continue or discontinue this intervention. Clear indication of patient benefit, supported by clinical judgment and aligned with patient goals, supports the continuation of this intervention.

Indications that the patient is benefitting

Clinical

- Reduction or cessation of illicit substance use
- Reduced risk of overdose
- Lack of cravings
- Management of withdrawal symptoms
- Improved overall wellbeing
- Consistent[i] urine drug tests positive for prescribed medications[j]

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[h] Note, this maximum dose may be exceeded, based on clinical judgment, if there is clear clinical indication of benefit.

[i] Monthly or more frequent UDT may be appropriate, based on clinical judgment

[j] Note that consistent urine drug tests positive for prescribed medications **and** negative for illicit substances are *not* required in order to continue this intervention. Given the extremely high potency opioids in the illicit drug supply, many individuals may continue to use a combination of prescribed hydromorphone and illicit opioids. It is recognized that each dose of prescribed, regulated opioids reduces risk of overdose.

Psychosocial[k]

- Reduced need to engage in high-risk and criminalized activities (e.g., sex work) to support substance use
- Seeking or gaining employment or volunteer activities
- Integrating new activities
- Reconnecting with family and friends (e.g., improved social functioning)
- Attaining safe housing and accessing other social services

Indications that the patient is not benefitting

Clinical

- No change or increased intensity of illicit substance use
- No change or increased overdose risk
- Ongoing cravings and withdrawal symptoms
- Urine drug tests consistently negative for prescribed substance or other indications of diversion
- No change in wellbeing
- Consistently missed doses

If thorough assessment of patient-identified goals and indicators of clinical and psychosocial stability indicate that the patient is not benefitting from the intervention despite attempts at optimizing dosing and psychosocial supports, it may be appropriate to discontinue the intervention and explore alternative harm reduction, treatment, and recovery options. Alternative options may include initiating opioid agonist treatment, increasing existing OAT dose, tapering hydromorphone dose, referral to an existing pharmaceutical alternative or safe supply program, or a combination. It may also be appropriate, based on clinical judgement, to trial another opioid medication covered under the forthcoming Pharmaceutical Alternatives policy. The assessment, treatment plan, and rationale should be documented in the patient's medical record. It may be helpful to consult the 24/7 Line for assistance in determining whether the intervention is or is not beneficial, and next steps.

Peer Navigators and Advocacy

Clinical experience from the past year indicates that the inclusion of peer navigators and patient advocates on the care team can help support engagement in care, including both continued engagement with prescribing to reduce reliance on the illicit drug supply and with substance use disorder treatment. Peer navigators and advocates can support engagement in care in the following ways:

- Outreach
- Explaining interventions and treatment options and what to expect
- Completing intake forms in a setting that is comfortable for the patient
- Supporting patients to attend appointments (including reminders, providing rides)

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[k] Structural barriers such as lack of affordable and accessible housing or suitable employment may make these difficult to achieve for individuals who are otherwise benefitting from the intervention. Improvements in these domains are not required, but—where possible—may be additional indications that the patient is benefitting and should continue to receive this intervention.

- Accompanying patients to appointments, if requested
- Facilitating access to treatment, harm reduction, and primary care services (e.g., vaccination)
- Providing advocacy when individuals encounter challenges accessing treatments or interventions

Patient Education and Informed Consent

The informed consent process should include a discussion and documentation of the potential risks and benefits of pandemic prescribing, as well as a discussion of continuing care. This should include a discussion of patient goals, as well as which clinical and psychosocial parameters would indicate that the patient is benefitting from the intervention, and which clinical and psychosocial parameters would indicate that the patient is not benefitting from the intervention, and how the treatment plan would change if the patient is not benefitting.

When counselling on routes of administration, oral ingestion of prescribed hydromorphone and/or M-Eslon is recommended, as this is the lowest risk route of ingestion. However, education on harm reduction should be provided, as many patients will choose other routes of use. See Safer Tablet Injection: A Resource for Clinicians Providing Care to Patients Who May Inject Oral Formulations for more information.

Prescribers should also provide education on the risk of ingesting multiple CNS depressants (e.g., opioids and benzodiazepines or alcohol).

Appendix: Informed Consent

Seeking informed consent to trial an intervention requires disclosing the relevant information that will allow the patient to make a voluntary choice to accept and consent or decline the intervention. More information on informed consent is available through the Canadian Medical Protective Association's *Consent: A Guide for Canadian Physicians*. This appendix provides a brief overview of the informed consent process, and a template that may be used to guide and document the process.

The informed consent process should include a description of the proposed intervention, including potential risks and benefits; a description of eligibility; a description of engagement with care during the intervention; and a description of what indicators would indicate that the patient is benefitting from the intervention and should continue to receive it, as well as what indications would indicate that the patient is not benefitting from the intervention and alternative harm reduction, treatment, and recovery options should be explored instead. This conversation should be thoroughly documented in the patient's medical record.

Informed Consent Template

1. Provide a description of the intervention
   The specific intervention (e.g., co-prescription of hydromorphone to support OAT initiation, prescription of hydromorphone to reduce reliance on toxic drug supply and overdose risk) should be described, including the limited evidence base supporting it, and potential benefits (e.g., reduced reliance on toxic drug supply, reduced overdose risk, increased OAT retention) and risks (e.g., known risks associated with opioid prescribing, injection-related risks if applicable)) should be described.

2. Describe eligibility
   Eligibility considerations for this intervention include:
   Ongoing active opioid use
   AND
   At high risk of overdose or other harms related to illicit opioid use

3. Describe engagement with care during intervention
   Specific follow-up will depend on clinical judgment and the individual patient.
   Items for discussion should include:
   a. *Frequency of follow-up,*
   b. *Frequency of dispensation of medications (e.g., daily dispensation vs. take-home doses)*
   c. *Frequency of urine drug testing.*
   d. *Expectation that patient will work together with prescriber on agreed upon plan for amount of engagement around care that would help ensure continuation of prescriptions, and what will happen if agreed upon plan is not met (e.g., consistently missed doses, missed follow up appointments may result in prescription being cancelled)*

4. Describe indications that patient is benefitting or not benefitting from intervention
   Clinical and psychosocial indications of benefit such as reduction or cessation of illicit substance use, reduced risk of overdose, and reduced need to engage in high-risk and criminalized activities should be described. Clinical and psychosocial indications of a lack of benefit such as no change

or increased intensity of illicit substance use, no change or increased overdose risk, and no improvement in employment, volunteering, or housing should also be described. Indications of benefit should be tailored to the individual patient; patient should be invited to describe ways that they would know they are benefitting from the intervention (e.g., less engagement in marginalized income-generating activities, experiencing less withdrawal), which should be documented in the patient's medical record and revisited on follow up.

5. Describe options if patient does not benefit from intervention
   If thorough assessment of patient-identified goals and indicators of clinical and psychosocial stability indicate that the patient is not benefitting from the intervention despite attempts at optimizing dosing and psychosocial supports, it may be appropriate to discontinue the intervention and explore alternative harm reduction, treatment, and recovery options.

   Alternative options may include initiating opioid agonist treatment, increasing existing OAT dose, tapering hydromorphone dose, referral to an existing pharmaceutical alternative or safe supply program, or a combination.

6. Ensure patient understands the above information, and seek consent or refusal of care

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