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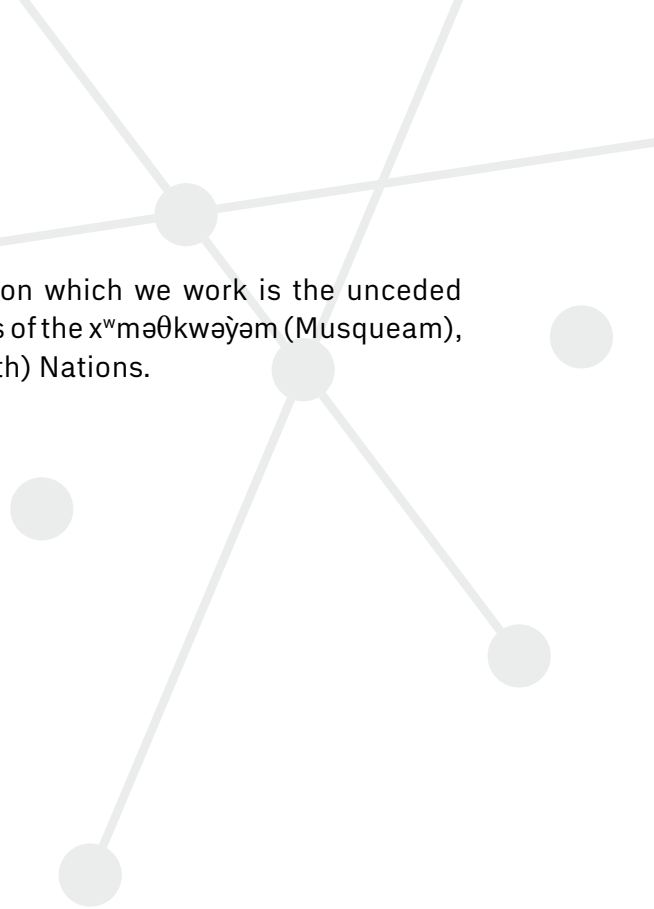
Opioid Use Disorder

Practice Update

January 2022

LAND ACKNOWLEDGEMENT

We would like to respectfully acknowledge that the land on which we work is the unceded territory of the Coast Salish Peoples, including the territories of the x^wməθkwəyəm (Musqueam), Skw̓xwú7mesh (Squamish), and səlililwətaʔ (Tsleil-Waututh) Nations.



IN THIS DOCUMENT

1. [OVERVIEW](#)
2. [PART 1: UPDATES TO OPIOID AGONIST TREATMENT PRACTICE](#)
3. [PART 2: PRESCRIBING OPIOIDS TO REDUCE OVERDOSE RISK AND OTHER HARMS](#)
4. [APPENDIX 1: INFORMED CONSENT](#)
5. [APPENDIX 2: AUTHORSHIP LIST](#)

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 the BC Centre on Substance Use (BCCSU) prioritized the development and publication of the provincial [Guideline for the Clinical Management of Opioid Use Disorder \(2017 OUD Guideline\)](#), 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 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 (OUD) in BC.

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 OUD. 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 and living experience, and other relevant stakeholders to rapidly develop interim clinical guidance, [Risk Mitigation in the Context of Dual Pandemics \(Risk Mitigation\)](#), which built on *Prescriber Guidelines for Risk Mitigation in the Context of Dual Public Health Emergencies* from Vancouver Coastal Health (VCH) 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. These risks include unintentional poisoning, 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, to respond to the intersection of dual health crises.

^a The 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.

Since the public health emergency declaration in 2016, at least 8,574 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 diagnosed (detected) OUD between September 2018 and September 2020. It should be noted, however, that the factors underlying this increase are not well understood—for example, it is unclear whether screening and detection are improving and thus identifying more individuals with OUD, more people are using opioids and developing OUD, or a combination.

Illicit drug poisoning continues to be the leading cause of unnatural death in BC, surpassing homicides, suicides, and motor vehicle collisions²; life expectancy at birth is declining in BC 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

About this Document

This practice update is composed of two parts. The first provides updates on the provision of opioid agonist treatment (OAT) in line with planned updates to the forthcoming provincial OUD Guideline. These updates are based on research evidence published since the *2017 OUD Guideline* was published, as well as clinical experience in BC.

The second part provides an overview of clinical experience and preliminary data from a year of *Risk Mitigation* prescribing, and introduces practice options to reduce individuals' reliance on the illicit opioid supply and related risks, including illicit drug poisoning, outside of the context of risk of COVID-19.^c These practice options, including trialing the prescription of oral hydromorphone and sustained-release oral morphine (M-Eslon) to help separate individuals from the toxic drug supply, do not constitute treatment for OUD. They are, instead, positioned as a harm reduction approach that may be trialed, based on thorough assessment, patient consultation and clinical judgment, in order to reduce the risk of overdose death and other harms for individuals who are not interested in OAT or for those who remain at high risk of overdose despite appropriately dosed OAT. As described in Part 2, these interventions can be paired with OAT and other psychosocial treatment interventions and supports, when appropriate and aligned with individual patient goals. Readers should familiarize themselves with [2017 OUD Guideline](#) before reading this update.

^a It should be noted that the existing evidence on treating OUD 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 This practice update helps enact recent government policy, [Access to Prescribed Safer Supply in British Columbia](#). As part of the development process of this practice update, broad consultation was sought from key stakeholders, including health systems partners, OAT prescribers in BC, and people with lived and living experience. Given the direction of government, review focused on the clinical guidance contained in this document, rather than the concept of prescribing to reduce risks associated with the toxic illicit drug supply.

PART 1: UPDATES TO OPIOID AGONIST TREATMENT 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 illicit opioid supply was characteristically heroin (i.e., non-pharmaceutical diacetylmorphine) or, at the start of the public health emergency, had lower levels of fentanyl adulteration. In addition, although buprenorphine/naloxone may still be considered a preferred first-line medication due to its superior safety profile, which allows for take-home dosing immediately or soon after initiation, clinicians should carefully assess patients and discuss the advantages and disadvantages of the all 3 oral OAT medications, regardless of the patient's previous OAT trials. Data regarding comparative treatment retention among the 3 oral OAT medications is mixed. For example, a 2021 meta-analysis (N=10 RCTs, 3 observational studies; n=5,065) found that retention rates—both length of time retained in study and presence on final day of study—are generally equal for fixed-dose oral OAT with methadone and buprenorphine/naloxone; however, the average retention rate across studies was highly variable and the evidence quality was rated as low.⁶ Conversely, data from 2012–2018 in BC found that buprenorphine/naloxone was twice as likely as methadone to be discontinued (SROM discontinuation was not reported).⁷ It is not clear, however, if those individuals discontinuing medication transitioned to another OAT medication or discontinued OAT entirely. In addition, Austrian data from 2011–2012 found that SROM had a significantly higher retention rate compared to both methadone and buprenorphine/naloxone.⁸

Prescribers should work with each patient to determine which medication is most therapeutically suitable, based on their circumstances, goals, and previous treatment experiences.

This section provides information on:

- Updates to treatment with buprenorphine/naloxone, including micro-dosing inductions and new formulations ([p. 6](#))
- New methadone formulations ([p. 11](#))
- Updated titration and dosing information for slow-release oral morphine ([p. 11](#))
- Guidance on clinical flexibility in response to local and global emergencies ([p. 12](#))

Buprenorphine/naloxone

This section contains several key updates to inform buprenorphine/naloxone prescribing, including guidance on micro-dosing inductions, information on additional formulations, and information on resources for initiating buprenorphine/naloxone in emergency departments.

Buprenorphine/naloxone Micro-dosing Induction

A variety of methods of transitioning from a full opioid agonist (whether prescribed or illicit) to buprenorphine, a partial agonist, have been described in the literature.⁹ Traditionally, a buprenorphine induction has required a period of abstinence from opioids to ensure that withdrawal is not precipitated. This period can be both time-consuming and challenging for patients,^{10,11} as it requires patients to be in moderate withdrawal prior to induction; if insufficient time has passed since last opioid use,^d the introduction of buprenorphine, a partial agonist with high affinity for the opioid receptor, may cause precipitated withdrawal. A micro-dosing induction that slowly up-titrates small doses of buprenorphine with cessation of all other opioids once a therapeutic dose has been reached has been described in the literature.¹² A 2021 systematic review included 19 case studies/series and 1 feasibility study (n=57).¹³ All 57 patients were able to reach a maintenance dose, and 95% (54/47) did not report precipitated withdrawal during the induction process. Twenty-six patients (46%) were co-prescribed full agonists (including methadone, fentanyl, hydromorphone, and morphine), with the rest continuing to use illicit opioids during the induction period. Although all included patients achieved a maintenance dose, some patients required multiple attempts, and return to illicit opioid use (or relapse) was reported for 5 patients. The median starting dose for studies that did not report precipitated withdrawal was 0.5mg, median duration was 6 days, median maintenance dose was 16mg, and mean rate of dose change to 8mg was 1.36mg/day.¹³ While the findings are promising, it should be noted that the overall quality of included studies was rated as poor, and lack of standardized outcome measures and comparative effectiveness studies limit conclusions regarding effectiveness. There is significant variability and a lack of standardization in the micro-dosing induction protocols reported.¹³

Several case studies and case series have also reported findings in favour of the use of micro-dosing inductions. These include successfully transitioning patients (n=6) onto long-acting subcutaneous^e buprenorphine,^{14,15} a micro-dosing induction paired with assertive community outreach to successfully initiate a patient with multiple past treatment attempts and complex medical comorbidities onto buprenorphine/naloxone,¹⁶ and micro-dosing inductions for individuals prescribed opioids for analgesia.^{17,18}

Research is ongoing to gather high-quality evidence of the efficacy of micro-dosing induction compared to standard buprenorphine induction; two randomized controlled trials are planned

^d 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. Note that 24 hours after last methadone dose may not be sufficient to avoid precipitated withdrawal. Clinicians must ensure that clinical opiate withdrawal scale score is above 12 before administering first buprenorphine/naloxone dose in a traditional induction.

^e Note, extended-release buprenorphine (Sublocade) is available in BC through Special Authority who have been clinically stabilized on 8mg to 24 mg of transmucosal buprenorphine/naloxone for a minimum of 7 days. Sublocade induction through micro-dosing induction would not currently be covered by PharmaCare; however, micro-dosing induction followed by 7 days on at least 8mg buprenorphine/naloxone followed by transition to Sublocade would be eligible for coverage.

to compare micro-dosing inductions with traditional buprenorphine/naloxone inductions, one at Vancouver General Hospital,¹⁹ and one with four sites in BC and Alberta.²⁰

Although the research evidence is limited, clinical practice in many parts of BC now includes using micro-dosing inductions as they reduce the risk of precipitated withdrawal and do not require the patient to experience moderate-to-severe withdrawal. This may increase the likelihood of patient retention and satisfaction. Clinical experience suggests that micro-dosing inductions may be especially helpful for individuals using illicit fentanyl, as clinical experience suggests that the risk of precipitated withdrawal is higher, likely 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-dosing induction protocols. In the absence of said research, many different protocols following the same principles are in use. Clinicians are encouraged to consult the [24/7 Addiction Medicine Clinician Support Line \(24/7 Line\)](#) or [RACEapp](#) when considering a micro-dosing induction. An example protocol follows.


| Day | Buprenorphine/naloxone Dose | Other Opioids |
|-----|---------------------------------|---------------|
| 1 | 0.5mg/0.125mg twice daily | Continue use |
| 2 | 0.5mg/0.125mg three times daily | Continue use |
| 3 | 1mg/0.25mg twice daily | Continue use |
| 4 | 2mg/0.5mg twice daily | Continue use |
| 5 | 2mg/0.5mg three times daily | Continue use |
| 6 | 4mg/1mg three times daily | Continue use |
| 7 | 12mg/3mg once daily | Stop use |

Additional micro-dosing induction protocols are available from the [BC Pharmacy Association](#), published in the [Canadian Medical Association Journal](#), and reported in peer-reviewed studies (see supplemental material to [Moe J, et al., 2021](#)).

Clinicians may consider co-prescribing a full agonist (e.g., SROM, methadone, or pro re nata [PRN; as needed] hydromorphone) during the micro-dosing induction, if clinically indicated. Initiating a patient onto SROM before the induction can help the patient to avoid illicit opioid use while titrating up the buprenorphine/naloxone dose, and reduce their risk of overdose, and may increase retention in care. See [Oral Hydromorphone to Support OAT Initiation or Maintenance](#) below for more information on prescribing PRN oral hydromorphone to support OAT induction.

Prescribing the micro-dosing induction to be dispensed in blister packaging can help reduce patient confusion regarding doses. An example micro-dosing induction prescription follows.

-----BC CONTROLLED PRESCRIPTION FORM-----

| | | | |
|---|--|--|--|
| PERSONAL HEALTH NO. 1234 567 890 | | PRESCRIBING DATE 28 06 21 <small>DAY MONTH YEAR</small> | |
| PATIENT NAME Generic A Name | | <small>FIRST (GIVEN) MIDDLE / INITIAL LAST (SURNAME)</small> | |
| PATIENT ADDRESS 123 Main Street Victoria BC | | DATE OF BIRTH 03 09 88 <small>DAY MONTH YEAR</small> | |
| <small>Rx: DRUG NAME AND STRENGTH</small> Buprenorphine/naloxone 2mg/0.5mg | | <small>ONLY ONE DRUG PER FORM</small> VOID IF ALTERED | |
| QUANTITY (IN UNITS) 86.5mg <small>NUMERIC</small> | | Eighty-six and one half milligrams <small>ALPHA</small> | |
| THIS AREA MUST BE COMPLETED IN FULL FOR OPIOID AGONIST TREATMENT (OAT) | | | |
| START DATE: 29 06 21 <small>DAY MONTH YEAR</small> | | END DATE: 08 07 21 <small>DAY MONTH YEAR</small> | |
| TOTAL DAILY DOSE Refer to Directions <small>NUMERIC</small> | | NUMBER OF DAYS PER WEEK OF DAILY WITNESSED INGESTION Nil <small>ALPHA</small> | |
| <input type="checkbox"/> NOT AUTHORIZED FOR DELIVERY | | | |
| DIRECTION FOR USE, INDICATION FOR THERAPY, OR SPECIAL INSTRUCTIONS Buprenorphine/naloxone sublingual tablets micro-dosing induction Day 1: 0.5mg twice a day Day 2: 0.5mg three times a day Day 3: 1mg twice a day Day 4: 2mg twice a day Day 5: 2mg three times a day Day 6: 4mg three times a day Day 7: 12mg once daily Day 8-10: 12mg once daily and up to 2 x 2mg/0.5mg tabs as needed Dispense all doses in blister packaging Release June 28 for carry, no witness | | | |
| NO REFILLS PERMITTED VOID AFTER 5 DAYS <small>UNLESS PRESCRIPTION IS FOR OAT</small> | | PRESCRIBER'S SIGNATURE  | |
| PRESCRIBER'S CONTACT INFORMATION Generic Prescriber 123 Health Street Victoria BC V8Z 4H4 | | Tel: 250-999-9911 Fax: 250-999-9119 | |
| | | 91-09898 PRESCRIBER ID 0000000005 FOLIO | |
| PHARMACY USE ONLY | | | |
| <small>RECEIVED BY: PATIENT OR AGENT SIGNATURE</small> | | <small>SIGNATURE OF DISPENSING PHARMACIST</small> | |

PHARMACY COPY - PRESS HARD YOU ARE MAKING 2 COPIES
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An example micro-dosing induction prescription.

Buprenorphine Formulations

Since the publication of the *2017 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 OUD. Sublocade was made available as a provincial drug benefit in BC on April 30, 2020, through PharmaCare Special Authority. Sublocade may reduce patient burden, as it is administered monthly rather than daily. It is currently available for patients who have been clinically stabilized on 8mg to 24mg of transmucosal buprenorphine/naloxone for a minimum of 7 days.

Sublocade is associated with significantly higher treatment retention (almost double; $p < .0001$) and mean abstinence percentages (over 40%) compared to placebo (5%; $p < .0001$) in individuals with moderate to severe OUD.²¹ A follow-up study included both roll-over patients ($n=113$) and de novo patients ($n=112$) whose first exposure to extended-release buprenorphine was in this phase III open-label long-term study.²² At 12 months of treatment, approximately 60% of rollover and 76% of de novo patients had ceased illicit opioid use. Both rollover and de novo patients had similar retention rates (~51%) and similar participant satisfaction scores.²² 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 ($p < .001$).²³ Overall, 51% of all participants remained abstinent for 12 months. An open-label randomized clinical trial ($n=119$) in Australia comparing patient-reported outcomes for individuals prescribed a different formulation of extended-release buprenorphine (brand name Brixadi) compared to sublingual buprenorphine/naloxone found that extended-release buprenorphine was associated with higher treatment satisfaction ($p = .002$), convenience ($p < .001$), and overall quality of life ($p = .03$) with no significant difference in illicit opioid use measured by self-report or urine drug tests (UDT).²⁴ It should be noted that Sublocade and sublingual buprenorphine/naloxone have not yet been compared in a clinical trial. The evidence base regarding the characteristics of patients who benefit from transitioning to Sublocade is limited and continues to evolve. Discussion of potential risks and benefits, informed consent, and regular follow-up including monitoring for cravings and withdrawal symptoms following initiation of Sublocade should be considered key components of care.

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 OUD. This mode of delivery allows for continuous blood levels of buprenorphine for up to 6 months following implantation.²⁵ 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.²⁵ 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.^{26,27} Probuphine is not covered as a drug benefit 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.^f It is currently approved for use in patients who have sustained stability on sublingual buprenorphine at doses of no more than 8mg.^{25,26} It is currently not recommended for use beyond two 6-month treatment cycles.²⁵

3. Suboxone Film

Suboxone (buprenorphine/naloxone) film is available in BC in 3 dosages.²⁸ Coverage is available through the NIHB and Veterans Affairs Canada; however, Suboxone film is not currently covered by BC PharmaCare.

In a randomized controlled trial, no significant differences in dose effects, adverse effects, or treatment outcomes were identified between Suboxone film and sublingual tablets.²⁹ Some patients may prefer the taste or faster dissolving time of the Suboxone film compared to the sublingual tablet.³⁰ 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 under-dosing,³⁰ 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.³⁰ Consult the product monograph for further information on switching from tablet to film.³¹

Emergency Department Initiation

The emergency department (ED) presents an opportunity to engage patients in evidence-based OUD care and promote harm reduction. People with OUD have high rates of ED utilization.³² A descriptive analysis of the BC Provincial Overdose Cohort reported that over half (60.4%) of 10,455 overdose events from January 1, 2015 to November 30, 2016 had past-year ED utilization.³³ Available evidence demonstrates that ED-based initiation of buprenorphine/naloxone may increase engagement and retention in treatment.³⁴⁻³⁸

Recognizing this opportunity, the BCCSU and BC Patient Safety and Quality Council worked together to launch the Learning about Opioid Use Disorder in the Emergency Department Collaborative (LOUD in the ED). Program faculty developed two key resources: an [OAT Decision Support Tool \(OAT DST\)](#) and two new modules (modules 23 and 24) in the [Provincial Opioid Addiction Treatment Support Program \(POATSP\)](#).

^f Clinicians can find out more information about the Probuphine Education Program by calling 1-844-483-5636.

Methadone

There are now 2 methadone options available as regular PharmaCare benefits in BC. Methadose and Metadol-D are covered as regular benefits for those enrolled in most PharmaCare Plans, including Fair PharmaCare (income-based coverage) and Plan B (Residential Care Facility), Plan C (Income Assistance), Plan G (Psychiatric Medications), Plan P (Palliative Care) and Plan W (First Nations Health Benefits). Methadose was introduced in 2014, replacing 1mg/mL pharmacy compounded methadone. Since this formulation change, some patients who had been stable on compounded methadone 1mg/mL have reported return to illicit opioid use due to inadequate management of withdrawal symptoms.³⁹⁻⁴¹ As a result, in 2019, Metadol-D and Sandoz Methadone (Sterinova) were added as regular benefits and compounded methadone became available as an exceptional, last-resort option for individuals who had trialed regular benefit formulations without success. As of October 1, 2021, Sandoz Methadone (Sterinova) is no longer commercially available. More information can be found in the BCCSU's [OAT Update: Methadone Formulation Options and Interchangeability](#).

In addition, the Ontario-based Mentoring, Education, and Clinical Tools for Addiction—Partners in Health Integration (META-PHI) published [Methadone Treatment for People Who Use Fentanyl: Recommendations](#). This document should not be considered clinical guidance for BC-based prescribers; however, the literature review and recommendations may be informative for prescribers treating patients with high tolerance due to highly-potent fentanyl.

Slow-release Oral Morphine Initiation

Since the *2017 OUD Guideline* was released, 2 additional systematic reviews have been published comparing SROM (brand name Kadian) and methadone.

A 2017 Norwegian systematic review (n=460) compared SROM to methadone and concluded that there is probably little or no difference in treatment retention (moderate certainty); there may be little or no difference in adverse events and illicit opioid use (low certainty); and there is insufficient evidence to determine effect on patient satisfaction and crime.⁴² 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 published trials and unpublished data (n=471) on two outcomes: illicit opioid use and retention in treatment.⁴³ This systematic review included all of the studies included in the 2017 systematic review. 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 noted that the methodological quality of the included studies was low-to-moderate and concluded that, while gaps remain in the evidence base for SROM, it confirmed the apparent non-inferiority of SROM compared to methadone.⁴³

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. Clinical experience in BC

indicates that the titration schedule described in the *2017 OUD Guideline* is often too conservative to retain patients in care. Starting doses as high as 200mg are commonly used, with increases of up to 100mg every 24 to 48 hours.

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. To date, there is an absence of evidence to guide titration schedules for SROM. 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. Clinicians are encouraged to consult the [24/7 Line](#) or [RACEapp](#) when determining a titration protocol.

| Day | Slow-release Oral Morphine Dose |
|-----|---------------------------------|
| 1 | 200mg |
| 2 | 300mg |
| 3 | 400mg |
| 4 | 500mg |
| 5 | 600mg |
| 6 | 700mg |
| 7 | 800mg |

The highest dose described in the literature⁹ to date is 1,200mg⁴⁵; however, clinical experience indicates that patients often require doses above 1,200mg to manage cravings and withdrawals, due to high tolerance developed due to fentanyl in the street opioid supply. Prescribers should use caution, with respect to side effects, when prescribing above 1,200mg and clearly document the rationale for doses above 1,200mg.

Increased Flexibility

Events in 2020–2021, including the COVID-19 pandemic and climate emergency-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, facilitating transfer of prescriptions to a new pharmacy, or engaging other health care providers to support medication management. Prescribers are encouraged to consult

⁹ Technically, doses above 1200mg were described in a 2006 prospective, open, non-comparative multi-centre study⁴⁴; however, doses were expressed as a mean plus standard deviation (1104 ±348mg/day). Specific doses, including max dose, were not included.

the [24/7 Line](#) or [RACEapp](#) if needing support to adapt care plans in response to states of emergency or other disruptive events. Exceptions to standard clinical care should be documented, including the rationale, patient discussion, and patient consent.

Urine Drug Testing

The BCCSU published its [Breakout Resource: Urine Drug Testing in Patients Prescribed Opioid Agonist Treatment](#) in July 2021. The document was developed in response to calls from clinicians for more guidance on UDT in the clinical management of OUD. This document reviews the current evidence for UDT, provides an overview of the use of UDT in the primary care management of patients with OUD who are receiving oral OAT (i.e., buprenorphine/naloxone, methadone, or SROM), and offers guidance and general practices for ordering, collecting, and interpreting UDT. Brief guidance on the use of UDT for patients who are receiving injectable OAT is also provided. This UDT breakout guidance effectively replaces the UDT information in the [2017 OUD Guideline](#), and updates the guidance on UDT published in the 2019 [Guidance for Injectable Opioid Agonist Treatment for Opioid Use Disorder](#).

Benzodiazepine-adulterated Opioids

While the vast majority of overdose deaths in BC remain linked to the presence of fentanyl and its analogues in the unregulated drug supply, the use of non-prescribed benzodiazepine receptor agonists is a growing concern, due to the emergence of highly potent “designer benzos,” and the increasing adulteration of the street opioid supply with benzodiazepines and benzodiazepine analogues.⁴⁶⁻⁴⁹ The concurrent use of benzodiazepines and opioids significantly increases the risk of respiratory depression, overdose, and death.⁵⁰⁻⁵³

All patients who use opioids should be offered screening for benzodiazepine use and receive information on the risks of combining opioids and sedatives, whether prescribed or illicit.⁵⁴ Benzodiazepines should be included in UDTs for individuals who use illicit opioids and/or those who are on OAT. However, clinicians and patients should be aware that some benzodiazepines and benzodiazepine analogues (e.g., alprazolam, clonazepam, etizolam, temazepam, triazolam) may not be detected in standard UDTs despite the patient having been exposed.

For more information, including guidance on managing benzodiazepine-opioid withdrawal, see the BCCSU’s [Clinical Bulletin: Benzodiazepines and Opioids](#).

PART 2: PRESCRIBING OPIOIDS TO REDUCE OVERDOSE RISK AND OTHER HARMS

This section of the document describes both clinical experience and preliminary data from over a year of prescribing according to the *Risk Mitigation* interim clinical guidance and helps prescribers more safely and effectively enact the provincial [Prescribed Safer Supply Policy](#). As such, this intervention can be understood as a form of prescribed safer supply; however, this document's scope is limited to the prescription of hydromorphone and M-Eslon as a harm reduction approach to reduce individuals' reliance on the illicit drug supply and associated harms. Prescribed safer supply beyond these 2 medications is out of scope of this document. As outlined in the Prescribed Safer Supply Policy, prescribers operating independently of regional health authorities may prescribe pharmaceutical alternatives according to publicly available clinical documents published by the BCCSU that support the provision of medications to reduce harms associated with illicit opioid use, such as this document. Prescribers must also practice according to their own scope, competence, and clinical judgment. Prescribers should consult the provincial [Prescribed Safer Supply Policy](#) and their local regional health authority for information on facilitating access to prescribed safer supply beyond the scope of this document.

The emerging practice options described in this section do not constitute treatment for OUD and at this time, as evidence is currently limited, should not be considered evidence-based practice. They should, instead, be understood as a harm reduction approach that may help reduce individuals' reliance on the illicit drug supply and, thus, unintentional poisoning or overdose risk. While all individuals with OUD should be offered evidence-based treatment, it is understood that some individuals are not interested in OAT or other psychosocial treatment interventions, while other individuals may continue to experience cravings and withdrawal symptoms despite appropriately-dosed OAT. Using a harm reduction approach to “meet patients where they are at” may help separate people from the toxic drug supply, reduce drug poisoning deaths, other drug-related harms, and engage individuals in care (e.g., primary care, psychosocial supports) who are at high risk of these harms.^h

When considering a trial of prescribed opioids to reduce overdose risk and other harms, a thorough risk/benefit assessment should be performed and documented. Potential risks (e.g., diversion, new-onset OUD) and benefits (e.g., reduced overdose risk, reduced reliance on high-risk and criminalized income generating activities) for both individual patients and the community should be considered.

Prescribing opioids to reduce an individual's use of toxic street drugs, overdose risk, and other harms represents a novel approach with a limited evidence base. As part of offering this intervention, prescribers should:

- Stay up to date on relevant provincial policies and published clinical bulletins, practice updates, and clinical guidance from the BCCSU

^h See First Nations Health Authority's [Policy on Harm Reduction—Indigenous Harm Reduction](#) for more information on the expansion of a safer supply of pharmaceutical alternatives to the toxic drug supply to communities that choose to provide pharmaceutical alternatives to their members in ways that are culturally safe.

- Practice within their scope and individual competence
- Offer and facilitate access to wraparound care, according to patient needs and preferences
 - o Where possible, prescribers are encouraged to work within programmatic services that can provide wraparound care
 - o Where not possible, prescribers should ensure they are offering, making referrals, and facilitating access to wraparound care, in collaboration with their patient

Clinical Experience from Risk Mitigation Prescribing

Clinical experience and initial evaluationsⁱ of the implementation of the *Risk Mitigation* interim clinical guidance inform this practice update.

Using PharmaNet⁵⁵ and other Ministry of Health⁵⁶⁻⁵⁸ data available through the BC Centre for Disease Control (BCCDC) COVID-19 Cohort⁵⁹ (BCC19C),^k *Risk Mitigation Guidance* (RMG) opioid medications were identified as having been dispensed to 3,771 persons from March 27, 2020 to February 28, 2021.^k

Preliminary data from the BC COVID-19 Cohort indicates that, of 6,498 persons who were dispensed all RMG medications^l from March 27, 2020 to February 28, 2021, 82 people died during that period. Of those who died, 33 (40%) were prescribed RMG opioids only and 9 (11%) were prescribed RMG stimulants or stimulants and opioids. The rest (28%) were prescribed other medications under the *Risk Mitigation* interim clinical guidance. No individuals who died were prescribed both benzodiazepines and opioids.

In addition, a mortality rate for people who received *Risk Mitigation* opioid prescribing has been found of 11 deaths per 1,000 person years. While direct comparisons are not possible, for perspective, cohort data from Vancouver, BC, has found a mortality rate of 22.7 per 1,000 person years between 2006 and 2017 for people who inject drugs⁶⁰ and 12.7 per 1,000 person years for individuals who used opioids daily or received OAT^m between 2005 and 2017.⁶¹ A 2019 meta-analysis (n=150,253) of cohort studies following individuals who received buprenorphine/naloxone or methadone treatment found a crude mortality rate of 16 deaths per 1,000 person years, a rate that included individuals in treatment during the study and both in and out of treatment during the follow-up period.⁶² 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 1,000 person years.⁶³ 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

ⁱ 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).

^j The BCC19C was established at the Provincial Health Service Authority 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 admissions, and mortality—all integrated with existing administrative data sources such as the Chronic Disease Registry, hospital admissions, and the Provincial Client Roster.

^k Note: The data presented here is preliminary and incomplete and does not include interpretation. More complete data, including qualitative findings and interpretation, will be forthcoming from the BCCDC COVID-19 Cohort.

^l Other medications prescribed according to the *Risk Mitigation* interim clinical guidance included in the BCC19C cohort include stimulants, alcohol withdrawal medications (carbamazepine, gabapentin, and clonidine), and benzodiazepines.

^m Specifically, this cohort reported using opioids daily or receiving OAT in the 6 months prior to their baseline survey AND did not sero-convert to HIV+ during the follow-up period.

department for an overdose in the previous 12 months,⁶⁴ 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).⁶⁵

More recent data from BC Coroner's Service and the BCC19C shows that 2,423 people died of illicit drug toxicity in BC from March 1, 2020, to May 31, 2021.^{59,66} Hydromorphone was detected in 5.9% of illicit drug toxicity deaths (n=142) during this time. In addition, the monthly proportion of individuals with hydromorphone detected in post-mortem toxicology has remained relatively stable, with a range of 0 to 8.2% detected January 1, 2019–February 28, 2020 and 2.7–9.3% detected March 1, 2020–May 31, 2021.^{59,66} Of the 5.9% of deaths where hydromorphone was detected, the vast majority included both hydromorphone and fentanyl (4.2% of total deaths, n=101) while hydromorphone without fentanyl or fentanyl analogues was detected in 1.7% (n=41) of total deaths. In a majority of these cases where fentanyl was not detected, hydromorphone was detected in combination with other substances, including morphine, etizolam, flualprazolam, and alcohol. A recently released knowledge update from the BCCDC that includes this data concludes that *Risk Mitigation* prescribing is not a direct contributor to the rising rates of illicit drug toxicity death in BC, and that fentanyl and its analogues remain the main contributors to illicit drug toxicity deaths.⁶⁶

Several limitations to this data are also noted.^{59,66} Hydromorphone toxicology data from the BC Coroners Services was not linked to PharmaNet, which makes it impossible at this time to determine whether the hydromorphone detected post-mortem was prescribed to the decedent. Hydromorphone is prescribed in BC outside the context of *Risk Mitigation* prescribing (e.g., analgesia, injectable OAT); hydromorphone toxicology data cannot be confirmed to reflect hydromorphone that was prescribed through *Risk Mitigation* rather than for other reasons. And, finally, toxicology data is derived through post-mortem testing of blood, tissue, or urine samples. Due to similar metabolization, it is possible that the detected hydromorphone originated from heroin or morphine (including SROM), rather than the consumption of hydromorphone.^{59,66}

Additional, preliminary, data on *Risk Mitigation* prescribing through the Victoria Safer Alternatives for Emergency Response (SAFER) initiative, a flexible, community-based, safer supply project in Victoria, is available.⁶⁷ The program developed prescribing protocols, based on the *Risk Mitigation* interim clinical guidance. Preliminary findings found that 54% of participants (n=49/72) self-reported reductions in potential harms from substance use including decreased cravings, decreased withdrawal symptoms, increased safer use practices (e.g., decreasing injection drug use), and reduced use of illicit substances.⁶⁷ In addition, 53% of participants self-reported at least one positive social or health outcome enabled by involvement in the SAFER program, including improved wound healing and fewer abscesses, improved mental health, increased connection to healthcare, improved engagement in health maintenance (e.g., routine blood work, prenatal care), reduced reliance on the street economy, increased connection to social supports, and improved overall function.⁶⁷ A full evaluation of the Victoria SAFER initiative is currently underway.

Preliminary evaluation data from VCH indicates that 4,225 individuals underwent eligibility assessment for *Risk Mitigation* prescribing between March 24, 2020 and May 6, 2021,⁶⁸ identified through electronic medical records.ⁿ Of these 4,225 individuals, 2,425 (57%) were found eligible

and prescribed medications according to the *Risk Mitigation* interim clinical guidance (“RM clients”), while 1,800 individuals were not eligible (“non-RM clients”). Vancouver Coastal Health’s evaluation includes both RM clients and non-RM clients. The vast majority of eligible clients were prescribed hydromorphone alone (65.5%), a very small number were prescribed M-Eslon alone (1.4%), 5.1% were prescribed hydromorphone and M-Eslon, and 15.9% were prescribed a combination of stimulants and hydromorphone and/or M-Eslon (an additional 12.0% were prescribed stimulants only).⁶⁸ In comparison to assessed individuals who were not found eligible for *Risk Mitigation* prescriptions, *Risk Mitigation* clients had a higher proportion of active OAT prescriptions (34.3% vs. 9.2%) or a recent history of OAT (15.7% vs. 4.2%) at the time of their eligibility evaluation. Over 75% of all RM clients had a history of receiving OAT in the 6 months prior to the identification of their eligibility for *Risk Mitigation* prescribing. Additionally, compared to non-RM clients, a higher proportion of RM clients received a prescription for OAT in the 30–60 days following their eligibility assessment for *Risk Mitigation* (55.5% vs. 10.4%). Close to 58% of RM clients who did not have a recent history of OAT (in the previous 30 days) received an OAT prescription within one week of engagement in *Risk Mitigation* prescribing while only 6.1% of non-RM clients were engaged in OAT in the week following their evaluation.

Oral Hydromorphone to Support OAT Initiation or Maintenance

The inclusion of oral hydromorphone prescribing in the *Risk Mitigation* interim clinical guidance has been used by clinicians to trial PRN prescribing of hydromorphone to support initiation of oral 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 reported that their patients are benefitting substantially from this approach, including reducing their use of illicit opioids and increasing retention in care until titrated to a therapeutic OAT 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 RMG dispensation. More recent data (up to February 28, 2021) found that 68% of people dispensed prescription opioids through *Risk Mitigation* prescribing had been dispensed OAT in the 30 days prior to first RMG dispensation. Among the 32% not prescribed OAT in the 30 days prior to RMG, almost 2% received an OAT dispensation on the same day as their first RMG dispensation, almost 15% were dispensed OAT within 7 days of receiving their first RMG dispensation, and approximately 15% were not dispensed OAT within 30 days of their first RMG 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 illicit drug poisoning risk.

ⁿ Data sources include Vancouver Community Analytics Tool, VCH Profile EMR, Acute, ED datamarts.

- Opioid agonist treatment initiation and titration should follow the [2017 OUD Guideline](#) or updated guidance above; oral hydromorphone prescribing may follow the hydromorphone dosing protocol below:
 - o Prescribe oral hydromorphone 8mg tablets (1–3 tablets q1h as needed up to 14 tablets), provided daily
 - o Some patients will naturally taper their hydromorphone use as they reach a maintenance OAT dose, other patients may continue to use oral hydromorphone to manage ongoing cravings and withdrawal symptoms.
 - o Clinical judgment should be used to determine whether continued prescription of hydromorphone is appropriate, prioritizing safety of both the individual and the community

It may also be appropriate to trial co-prescription of oral hydromorphone for individuals who are experiencing benefit and satisfied at their current maintenance dose of oral OAT but continuing to experience cravings and/or withdrawal symptoms that they manage with illicit opioids, increasing overdose risk.

- Prescribe oral hydromorphone 8mg tablets (1–3 tabs q1h as needed up to 14 tablets), provided daily
 - o Note: Prescribe according to use. For example, if illicit use is infrequent, dispensing every day may not be required

Using Hydromorphone or M-Eslon to Reduce Overdose Risk for Individuals Not on OAT

Client audience: Individuals who are not interested in OAT or other psychosocial treatment interventions, including recovery-oriented care, or able to access other prescribed safer supply options through health authority-funded or run programs who are at high risk for overdose. 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. 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). However, clinical experience also indicates that there have been negative UDT in patients prescribed hydromorphone, with some anecdotes of diverted hydromorphone.⁶⁹

Until provincial protocols are available to guide the provision of additional pharmaceutical alternatives, it is the opinion of the authors of this practice update^o that clinicians should use clinical judgment including thorough assessment, consideration of patient preference, and consideration of the harms associated with potential diversion to determine whether trialing prescription of oral hydromorphone and/or M-Eslon is appropriate. Individuals who received prescribed oral hydromorphone and/or M-Eslon through *Risk Mitigation* prescribing who are have benefitted from this prescribing (see, [Assessment of Benefit and Continuing Care](#) below) should continue to receive this prescribing as it aligns with their goals and preferences.

^o See [Appendix 2](#) for authorship list.

Oral hydromorphone and/or M-Eslon[®] may be prescribed to individuals who are not currently receiving OAT, are not interested in starting OAT or other forms of substance use disorder treatment, and are at high risk of poisoning from the illicit opioid supply.

Assessment

The following considerations for eligibility should be assessed and documented in the patient's health record when considering a trial of hydromorphone and/or M-Eslon prescribing to reduce reliance on the illicit drug supply and overdose risk, including prescribing hydromorphone to support OAT initiation:

- Ongoing active opioid use
- AND
- At high risk of illicit drug poisoning 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, route of administration, frequency of use)
 - Note: Not all patients who qualify for these medications will meet a diagnosis of OUD. For example, individuals who use opioids intermittently may be at high risk of poisoning 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, psychiatrist, addiction medicine physician, nurse practitioner)
- Patient goals (e.g., reduce use, stop use, safer use, manage cravings and withdrawal symptoms)
- Potential indicators of benefit (see [Assessment of Benefit and Continuing Care](#) below, which may help guide discussion indicators that patient is benefitting from the intervention)

[®] Note that patients prescribed SROM or sustained-release oral morphine (Kadian or M-Eslon) may have a positive UDT result for hydromorphone due to high morphine levels; morphine is metabolized to hydromorphone by a minor pathway, which may be detected in individuals taking high doses of oral morphine. See the BCCSU's [Urine Drug Testing: Breakout Resource](#) for additional information regarding UDT for individuals with OUD, including information on cross-reactivity and confirmatory testing.

Dosing

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

- Prescribe oral hydromorphone 8mg tablets (1–3 tablets q1h as needed up to 14 tablets)⁹

AND/OR

- Prescribe M-Eslon 80–240mg orally twice daily (avoid sprinkling doses)
 - o 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
 - o It may be helpful to prescribe a long-acting opioid in conjunction with a short-acting opioid for those not on OAT
 - o Note: Multiple long-acting opioid formulations should not be prescribed concurrently. For this reason, extreme caution should be used if M-Eslon is being considered in conjunction with oral OAT

Frequency of dispensation should be guided by clinical judgment, prioritizing patient and community safety. Generally, daily dispensing should be prescribed. Exceptions should be documented.

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. In addition to reviewing patient goals, this should include a discussion of which clinical and psychosocial parameters would indicate that the patient is benefitting from the intervention, 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 of Benefit and Continuing Care

If the above assessment indicates that a trial of hydromorphone or M-Eslon prescribing is appropriate, an initial trial period (i.e., 2–4 weeks) should be followed by a thorough assessment of clinical and psychosocial indicators, as well as patient goals, to determine whether the patient is benefitting from the intervention. The results of this assessment along with expert consultation (e.g., addiction medicine specialist, [24/7 Line](#)), where appropriate, and patient preference should inform the decision to continue or discontinue this intervention. With patient consent, other care team members (e.g., outreach workers, social workers, primary care providers, family members) may also provide information relevant for decision making. Clear indication of patient benefit, supported by clinical judgment and aligned with patient goals, supports the continuation of this intervention. It should be noted, however, that not all of the potential benefits listed below may emerge in the initial 2- to 4-week period following initiation; it may take some time for clinician and patient to determine an optimal dose, to access relevant psychosocial supports, and for the patient to begin to stabilize. Clinical discretion should be used to determine whether a continued trial is appropriate. Patients' individualized goals regarding their health and substance use should be continually re-assessed, and treatment plans adjusted accordingly.

⁹ Note, this maximum dose may be exceeded, based on clinical judgment, if there is clear clinical indication of benefit. Clinical exceptions, including rationale, should be documented.

INDICATIONS THAT THE PATIENT IS BENEFITTING

Clinical

- Reduced (or cessation of) illicit substance use
- Reduced risk and incidence of overdose due to reduction or cessation of illicit opioid use
- Reduced cravings
- Reduced potential communicable disease exposure and infection
- Reduced emergency department or acute care usage
- Increased engagement in primary care and other health services
- Management of withdrawal symptoms
- Patient report of improved overall wellbeing
- Urine drug tests consistently positive for prescribed medications^r

Psychosocial^s

- Reduced need to engage in high-risk and criminalized activities (e.g., sex work) to support substance use
- Maintaining, seeking, or gaining employment or volunteer activities
- Improved attitude toward self
- Ability to set and meet goals in major areas (e.g., personal health, career)
- Enrolled in education or training programs
- 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
- No change in wellbeing or social functioning
- Consistently missed doses
- Development or worsening of mental or physical health conditions associated with prescribed medications

^r Note that UDTs consistently 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. In the case of UDTs negative for the prescribed substance (e.g., hydromorphone), prescribers should use clinical judgement to determine if it is appropriate to continue prescribing based on an assessment of the risks and benefits and discussion with the patient. It is recognized that each dose of prescribed, regulated opioids reduces risk of overdose.

^s 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.

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 OAT, increasing existing OAT dose, tapering hydromorphone dose, referral to an existing pharmaceutical alternative or safer supply program, bed-based treatment options, or a combination. It may also be appropriate, based on clinical judgement, contact regional health authorities to determine availability of safer supply programs, which may have additional opioid medication options. 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.

Evaluation

Clinicians prescribing hydromorphone to reduce risk of overdose and other harms must become part of the provincial evaluation outlined in the [Prescribed Safer Supply Policy](#), through two avenues:

1. All safer supply prescribing will be captured in the health administrative data from PharmaNet.
 - a. Dispensation of prescribed safer supply to individuals at pharmacies or clinic settings will be recorded in PharmaNet, which will be used to support provincial evaluation and monitoring efforts.
 - b. Prescribers must indicate on the prescription that the drug is prescribed safer supply (see [Prescriber and Pharmacist Procedures for Prescribed Safer Supply](#), below), so that pharmacists or other practitioners are able to provide appropriate and informed care and record the prescription in different information systems. More information will be forthcoming from the Province on how to correctly record prescriptions in appropriate data systems.
2. As the provincial evaluation is initiated, prescribers will be invited to engage in additional types of evaluation as appropriate.

See the provincial [Prescribed Safer Supply](#) policy for more information on evaluation.

Prescriber and Pharmacist Procedures for Prescribed Harm Reduction Drugs: Risk Mitigation or Prescribed Safer Supply

The safety and sustainability of the prescribed harm reduction drug options outlined in the *Risk Mitigation Interim Clinical Guidance*, the *Opioid Use Disorder Practice Update*, and the *Prescribed Safer Supply Policy* are predicated on ongoing fulsome monitoring and evaluation to inform program effectiveness and identify any unintended risks or harms. Accurately capturing these prescriptions in PharmaNet is essential to enable comprehensive and rigorous evaluation.

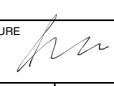
Most of the drugs prescribed as alternatives to support people to reduce their reliance on the toxic illicit drug supply, both for risk mitigation and as a safer supply alternative, are used for additional

indications; therefore, prescriptions for harm reduction and safer supply must be distinguished from other indications (e.g., pain). Prescribers and pharmacists are therefore being asked to assist as follows:

Instructions for Prescribers:

Any prescription written for a drug to be used as an alternative to the toxic street supply including prescriptions written for risk mitigation during the dual public health emergencies or as a safer supply option should clearly include “SA” in the Directions for Use section of the form, **BELOW** the instructions written on the form. This code is not part of the official instructions but indicates to the dispensing pharmacist that the prescription is to be tagged with the non-public facing code that will allow the prescription to be identified in the PharmaNet database. An example follows.

-----BC CONTROLLED PRESCRIPTION FORM-----

| | | | |
|---|--------------------------|--|--|
| PERSONAL HEALTH NO. 1234 567 890 | | PRESCRIBING DATE 01 08 21 <small>DAY MONTH YEAR</small> | |
| PATIENT NAME | FIRST (GIVEN) Generic | MIDDLE / INITIAL A | LAST (SURNAME) Name |
| PATIENT ADDRESS STREET 123 Main Street | | | |
| CITY Victoria | | PROVINCE BC | DATE OF BIRTH 16 12 76 <small>DAY MONTH YEAR</small> |
| Rx: DRUG NAME AND STRENGTH Hydromorphone 8mg | | | |
| ONLY ONE DRUG PER FORM | | | |
| VOID IF ALTERED | | | |
| QUANTITY (IN UNITS) | | | |
| 784mg <small>NUMERIC</small> | | Seven hundred and eighty-four milligrams <small>ALPHA</small> | |
| THIS AREA MUST BE COMPLETED IN FULL FOR OPIOID AGONIST TREATMENT (OAT) | | | |
| START DATE: 01 08 21 <small>DAY MONTH YEAR</small> | | END DATE: 14 08 21 <small>DAY MONTH YEAR</small> | |
| TOTAL DAILY DOSE 112 One hundred twelve mg/day <small>NUMERIC ALPHA</small> | | NUMBER OF DAYS PER WEEK OF DAILY WITNESSED INGESTION Nil Nil <small>NUMERIC ALPHA</small> | |
| <input type="checkbox"/> NOT AUTHORIZED FOR DELIVERY | | | |
| DIRECTION FOR USE, INDICATION FOR THERAPY, OR SPECIAL INSTRUCTIONS Hydromorphone 8mg tablets 1-3 tablets per hour as needed Maximim 14 tablets per day Dispensed daily, no witness Prescribed safer supply SA | | | |
| NO REFILLS PERMITTED | | PRESCRIBER'S SIGNATURE  | |
| VOID AFTER 5 DAYS <small>UNLESS PRESCRIPTION IS FOR OAT</small> | | | |
| PRESCRIBER'S CONTACT INFORMATION Generic Prescriber 123 Health Street Victoria BC V8Z 4H4 | | Tel: 250-999-9911 Fax: 250-999-9119 | 91-09898 PRESCRIBER ID 0000000005 FOLIO |
| PHARMACY USE ONLY | | | |
| RECEIVED BY: PATIENT OR AGENT SIGNATURE | | SIGNATURE OF DISPENSING PHARMACIST | |
| PHARMACY COPY - PRESS HARD YOU ARE MAKING 2 COPIES PRINTED IN BRITISH COLUMBIA | | | |

Instructions for the Pharmacist:

When a prescription for any drug that is identified as a safer alternative is processed (new or refill/part-fill prescription), it should be entered per usual prescription entry standards with the addition of an “SA” intervention code in the customary intervention code section of the software, not the Directions for Use (“sig”) section. This code goes in the intervention code field and is simply a tag on the prescription that can be captured when monitoring and evaluating these harm reduction prescriptions for program evaluation. Entry of the intervention code with each prescription fill is the only action required on the pharmacist’s part and has no monetary reimbursement attached.

Drugs to be Included

Any drug prescribed for risk mitigation to support self-isolation or quarantine due to COVID-19 or drugs prescribed for safer supply should be identified on the prescription and tagged with the “SA” intervention code upon entry into PharmaNet. The list below identifies the medications included in this practice update, but all drugs prescribed for prescribed safer supply should be identified as per above:

OPIOIDS

All those prescribed for risk mitigation or prescribed safer supply, which include:

- Hydromorphone tablets
- Sustained-release oral morphine (M-Eslon)

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 continued engagement with both substance use disorder treatment and prescribing to reduce reliance on the illicit drug supply. 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)
- Accompanying patients to appointments, if requested
- Facilitating access to treatment and recovery services, harm reduction, primary care services (e.g., vaccination), and social services
- Helping patients to navigate challenges accessing treatments or interventions
- Providing insight and expertise related to the patient experience to prescribers and other health care team members

Several key resources may inform engagement with and employment of peer navigators, including:

- [Best Practice Manual For Supporting Peers/Experiential Workers in Overdose Response Settings](#)
- [Community Research Report: Peer Work](#)
- [There is No Authority But Yourself: A Reader Guide to Drug User Self-determination and Organizing](#)
- [Meaningful Engagement](#)
- [Meaningful Results: Engagement and Consultation Road Map from the Provincial Peer-training Project](#)

Patient Education and Informed Consent

The informed consent process should include a discussion and documentation of the potential risks and benefits of hydromorphone or M-Eslon prescribing as a safer supply option, as well as a discussion of continuing care and harm reduction education. 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. See [Assessment of Benefit and Continuing Care](#) for more information on clinical and psychosocial parameters indicating benefit and [Appendix 1: Informed Consent](#) for more information on the informed consent process.

When counselling patients 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 1: 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](#) and The Canadian Nurses Protective Society's [Consent to Treatment: The Role of the Nurse](#). In addition, nurse practitioners must meet the BC College of Nurses and Midwives' [Consent Practice Standard](#). 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.

Note: Prescribers prescribing hydromorphone as a harm reduction measure must participate in the provincial evaluation; a discussion of the evaluation and use of patient data should be included in the consent process

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 OAT, 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 is capable giving informed consent. If patient is temporarily unable to provide informed consent (e.g., due to impairment), the conversation should be revisited when the patient is capable of providing informed consent.

7. Document consent or refusal of care.

APPENDIX 2: AUTHORSHIP LIST

Development Process

This practice update was developed by the authorship committee listed below. As part of the development process, broad consultation was sought from key stakeholders, including health systems partners, OAT prescribers in BC, and people with lived and living experience.

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