Decision Support Tool

For RN and RPN Prescribing of Methadone or Slow-release Oral Morphine for Continuations, Titrations, or Restarts

November 2021

BRITISH COLUMBIA CENTRE ON SUBSTANCE USE
Networking researchers, educators & care providers

ABOUT THIS DECISION SUPPORT TOOL

Intended audience

Developed for RNs and RPNs who:

- Have completed the education and training pathway from the BC Centre on Substance Use (BCCSU) and
- Meet the requirements for methadone or SROM prescribing for continuations, titrations, or restarts.

Purpose

This DST sets out the activities that are within scope for RNs and RPNs providing care to individuals prescribed methadone or SROM for opioid use disorder, as well as the situations in which consultation or referral are required.

Using this document

- This document must be used alongside applicable BC College of Nurses and Midwives (BCCNM) Scope of Practice Standards, Limits, and Conditions for registered nurses and registered psychiatric nurses.
- Opioid use disorder care should be approached in a manner that is trauma- and violence-informed, culturally safe, patient-centred, and harm reduction-oriented.

Development

This DST was developed by the BCCSU in alignment with the provincial *Guideline for the Clinical Management of Opioid Use Disorder* and in collaboration with a committee of experts, consisting of partners from the BCCNM, Ministry of Health, Ministry of Mental Health and Addictions, and regional health authorities in BC. Consultation occurred with a number of key stakeholders, who supported the scope and definition of the work, as well as ensuring the quality of the education and clinical support tools. Reviewers included partners from First Nations Health Authority, Fraser Health, Vancouver Coastal Health, and Interior Health.

DEFINITIONS AND ABBREVIATIONS

Consult: Consultation with another provider with experience in addition medicine required (see below).

Maintenance doses: Continuing current prescription.

Missed doses: Prescribing when up to 4 consecutive days of methadone or SROM doses have been missed, with dose adjustments required for patient safety.

Restart: Restarting the previously prescribed OAT medication following 5 to 30 consecutive days of missed doses.

Refer: Care should be transferred to another provider (see below).

Take-home doses (also known as carries): Prescriptions that are filled, dispensed, and collected from the pharmacy, with ingestion not witnessed.

CONSULTING ANOTHER PROVIDER WITH EXPERIENCE IN ADDICTION MEDICINE

Throughout the DST, instances when RNs/RPNs must consult are specified. During consultation, advice will be given to the RN or RPN to inform their prescribing decision. Registered nurses and registered psychiatric nurses are also encouraged to consult if they have questions about OUD care outside of designated consultation points.

A prescriber with experience in addiction medicine can be consulted either:

- Via the 24/7 Addiction Medicine Clinician Support Line (see page 30) or
- As per health authority workflow or organizational pathways

REFERRING TO ANOTHER PROVIDER

Due to limits on scope of practice, there may be circumstances where RNs or RPNs need to refer care to another OAT provider (physician or nurse practitioner). In these circumstances, RNs and RPNs should facilitate the referral and provide any relevant support that is within the RNs or RPNs' scope of practice.

Reminder: Any consultation or referral related to the patient's care must be documented.

ABBREVIATIONS

The following abbreviations are used throughout this DST:

ALT: alanine aminotransferase; **bup/nlx:** buprenorphine/naloxone; **CNS:** central nervous system; **CYP:** cytochrome; **CYP3A4:** cytochrome P450 3A4; **DST:** decision support tool; **ECG:** electrocardiogram; **eGFR:** estimated glomerular filtration rate; **GC/CT:** Neisseria gonorrhoeae/chlamydia trachomatis; **INR:** international normalized ratio; **MAOI:** monoamine oxidase inhibitor; **OAT:** opioid agonist treatment; **OUD:** opioid use disorder; **QTc:** corrected QT; **RN:** registered nurse; **RPN:** registered psychiatric nurse; **SNRI:** serotonin-norepinephrine reuptake inhibitor; **SSRI:** selective serotonin reuptake inhibitor; **STI:** sexually transmitted infection; **SROM:** slow-release oral morphine; **UDT:** urine drug test.

SCOPE OF PRACTICE: METHADONE AND SROM

Medication	Initiation	Continuations (including missed doses)	Titrations	Restarts (up to 30 consecutive days since last dose)
Methadone	X	✓	✓	✓
Slow-release oral morphine	X	✓	✓	✓

METHADONE

High doses	Co-occurring CNS depressant use	Medications	Pregnancy	Severe hepatic dysfunction	Severe QT prolongation	Youth	
						16–18 years of age	15 years of age and younger
CONSULT if prescribed over 150mg methadone	**Prescribed** **CONSULT**: o New or ongoing CNS depressant use, as required o The patient is co-prescribed safer supply by another provider **REFER** if there is co-prescription of SROM **Non-prescribed** **CONSULT:** o New benzodiazepine, z-drug, or other sedative use o New alcohol use that exceeds *Canada's Low-risk Alcohol Drinking Guidelines* o Ongoing CNS depressant use: • That has changed significantly in terms of substance, frequency, or dose • If the patient is clinically unstable as demonstrated by sedation or further risk of overdose	**REFER** or **CONSULT** for prescription of new medications with the potential for drug–drug interactions, as appropriate	**CONSULT** in absence of evidence of a treatment plan from a (perinatal) addiction medicine specialist	**CONSULT** if GGT or ALT are over 3 times the upper limit of normal, or albumin or total bilirubin are outside of the normal ranges	**CONSULT** if QTc is over 500ms	**CONSULT**	**REFER**

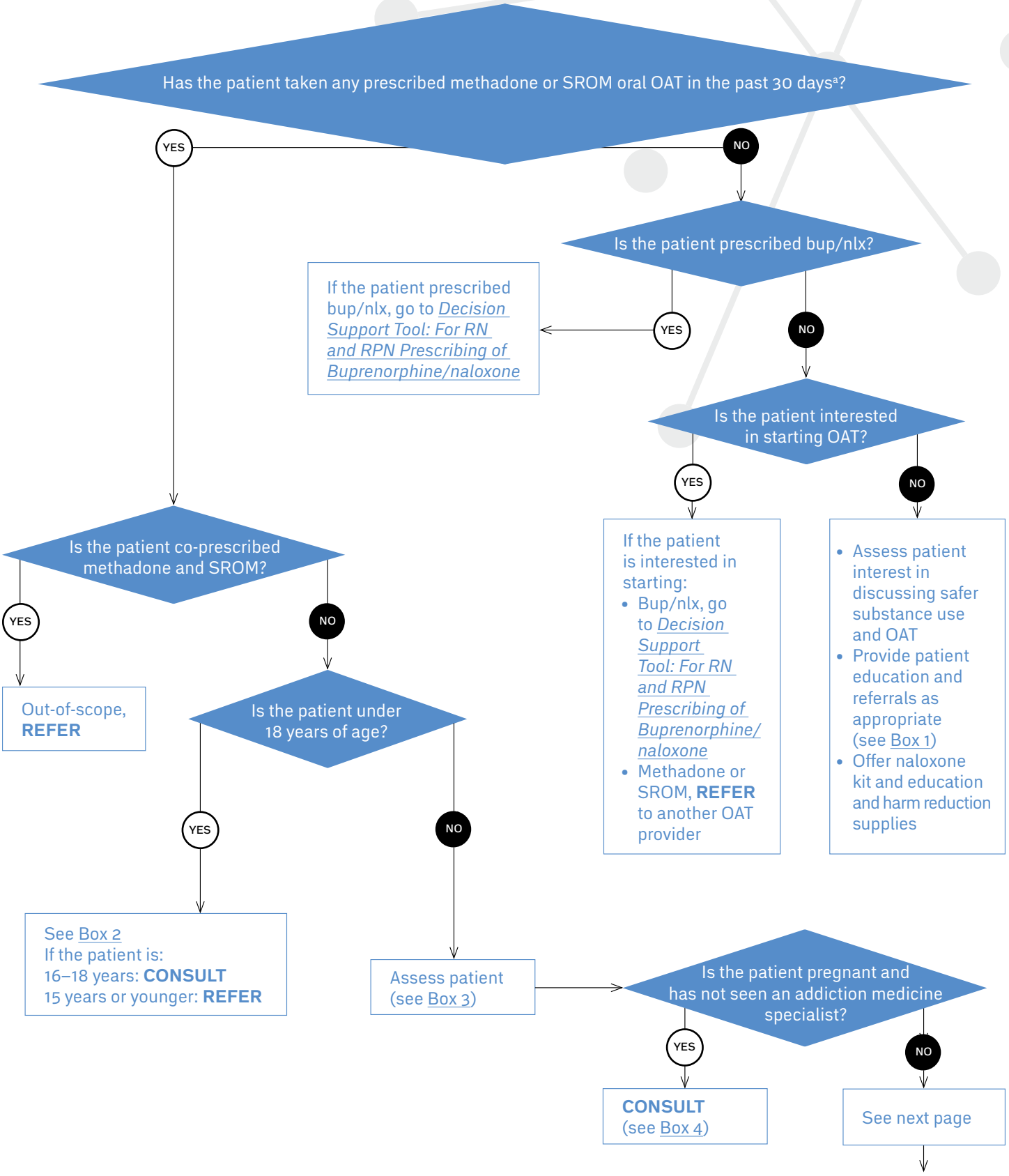
SLOW-RELEASE ORAL MORPHINE

<table>
<tr><th rowspan="2">High doses</th><th rowspan="2">Co-occurring CNS depressant use</th><th rowspan="2">Medications</th><th rowspan="2">Pregnancy</th><th rowspan="2">Severe renal dysfunction</th><th colspan="2">Youth</th></tr>
<tr><th>16–18 years of age</th><th>15 years of age and younger</th></tr>
<tr><td rowspan="2">CONSULT if prescribed over 1,500mg SROM</td><td>Prescribed
CONSULT:
o New or ongoing CNS depressant use, as required
o The patient is co-prescribed safer supply by another provider

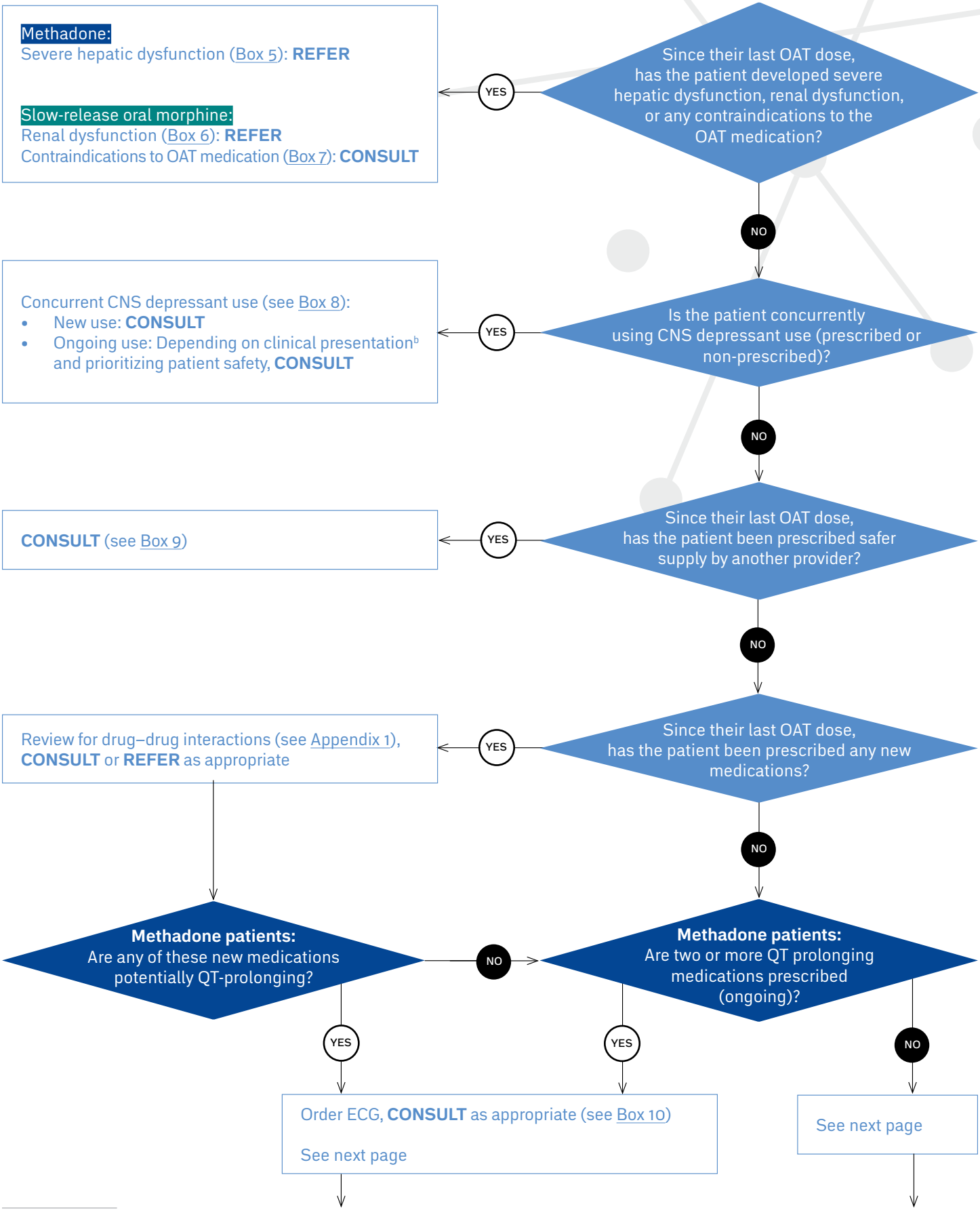
REFER if there is co-prescription of methadone</td><td rowspan="2">REFER or CONSULT for prescription of new medications with the potential for drug–drug interactions, as appropriate</td><td rowspan="2">CONSULT in absence of evidence of a treatment plan from a (perinatal) addiction medicine specialist</td><td rowspan="2">REFER if eGFR is <60mL/min/1.73m²</td><td rowspan="2">CONSULT</td><td rowspan="2">REFER</td></tr>
<tr><td>Non-prescribed
CONSULT:
o New benzodiazepine, z-drug, or other sedative use
o New alcohol use that exceeds Canada's Low-risk Alcohol Drinking Guidelines
o Ongoing CNS depressant use:
• That has changed significantly in terms of substance, frequency, or dose
• If the patient is clinically unstable as demonstrated by sedation or further risk of overdose</td></tr>
</table>

DECISION SUPPORT TOOL

FOR RN AND RPN PRESCRIBING OF METHADONE AND SLOW-RELEASE ORAL MORPHINE (LIMITED PRESCRIBING)

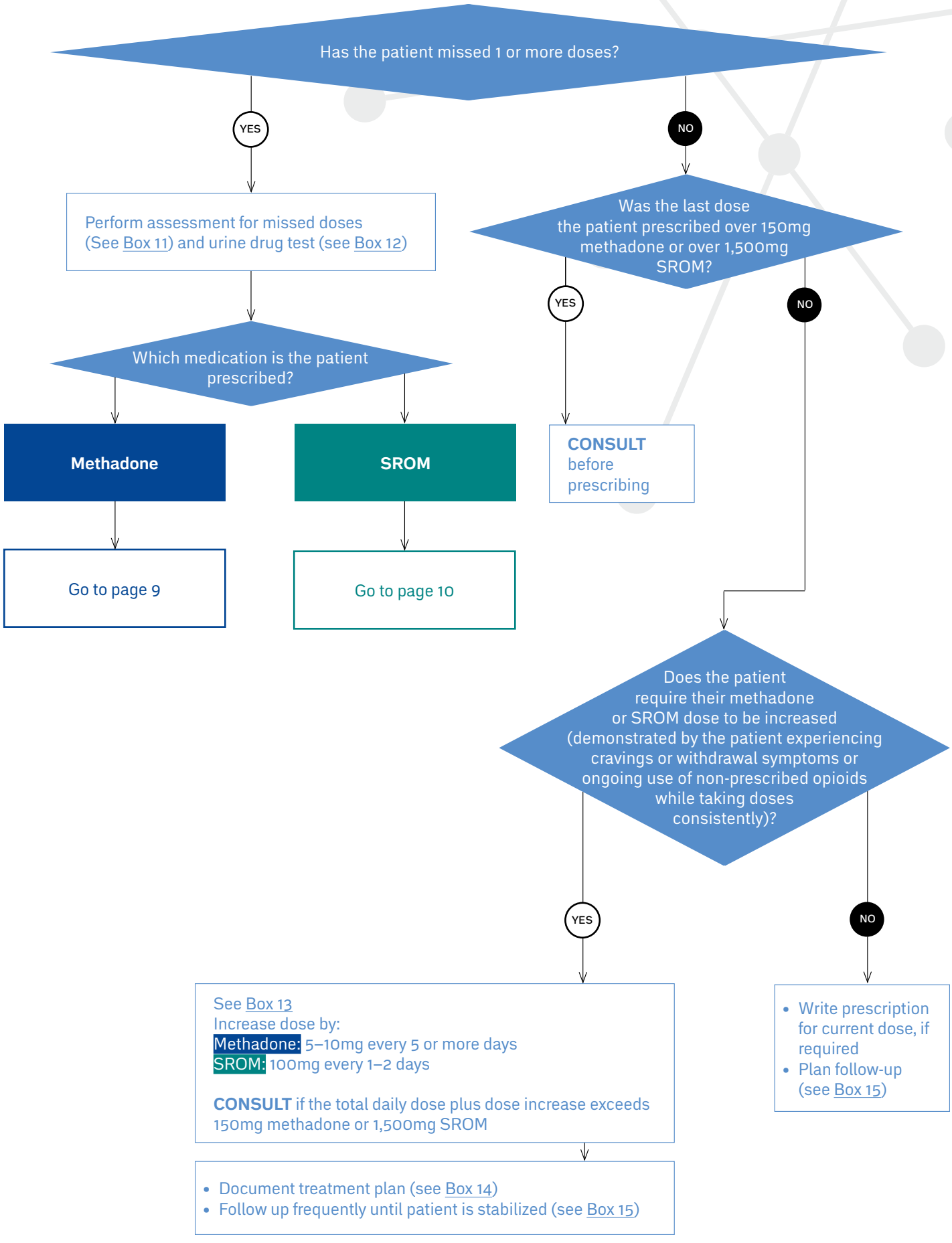


[a] As per patient report and PharmaNet review.



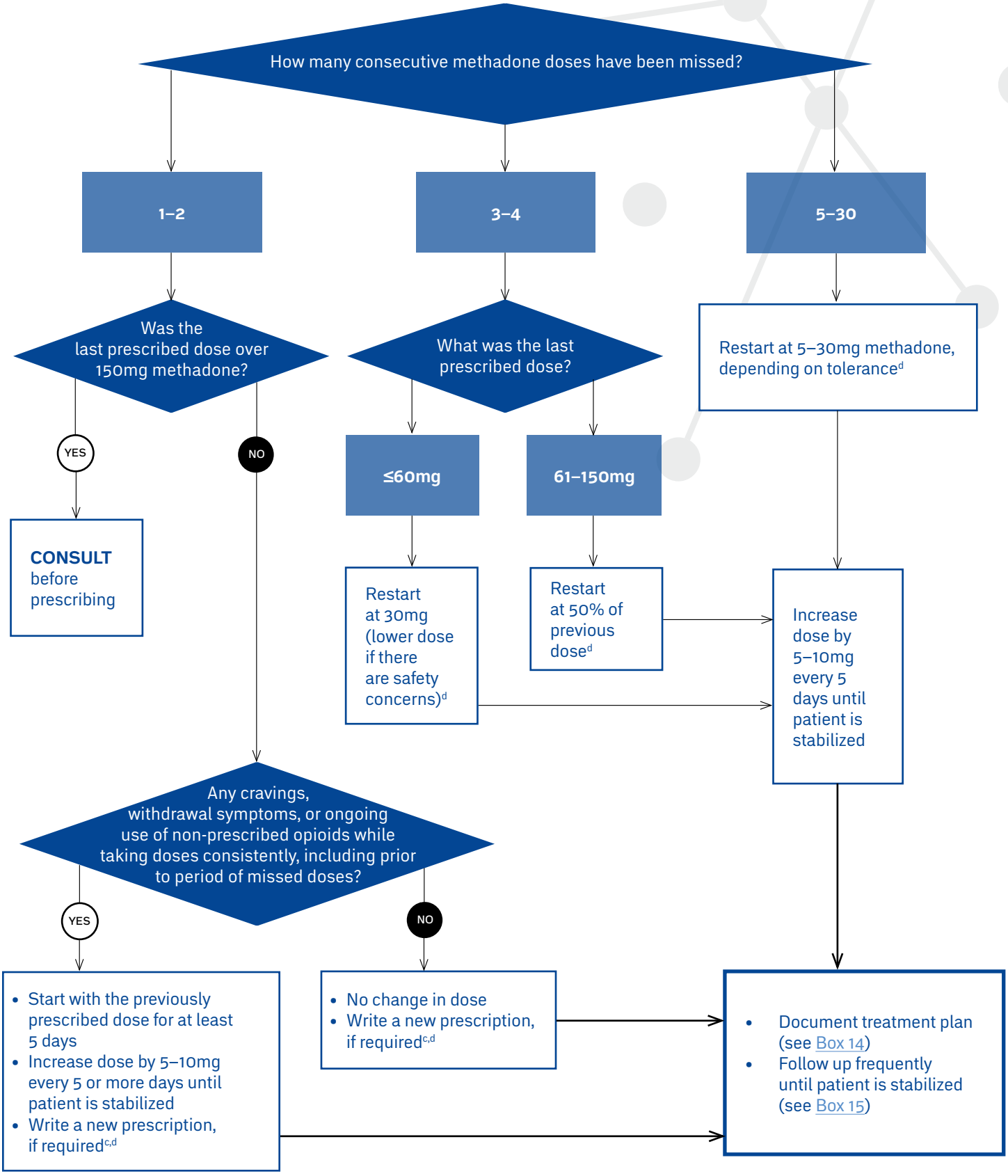
[b] For example, if the patient:

- Is clinically unstable, as demonstrated by sedation or increased risk of overdose.
- CNS depressant use has changed significantly in terms of substance, frequency, or dose.


Has the patient missed 1 or more doses?
YES
NO
Perform assessment for missed doses (See Box 11) and urine drug test (see Box 12)
Was the last dose the patient prescribed over 150mg methadone or over 1,500mg SROM?
YES
NO
Which medication is the patient prescribed?
Methadone
SROM
CONSULT before prescribing
Go to page 9
Go to page 10
Does the patient require their methadone or SROM dose to be increased (demonstrated by the patient experiencing cravings or withdrawal symptoms or ongoing use of non-prescribed opioids while taking doses consistently)?
YES
NO
See Box 13
Increase dose by:
Methadone: 5–10mg every 5 or more days
SROM: 100mg every 1–2 days
CONSULT if the total daily dose plus dose increase exceeds 150mg methadone or 1,500mg SROM
• Write prescription for current dose, if required
• Plan follow-up (see Box 15)
• Document treatment plan (see Box 14)
• Follow up frequently until patient is stabilized (see Box 15)

Decision support tool algorithm: Missed methadone doses

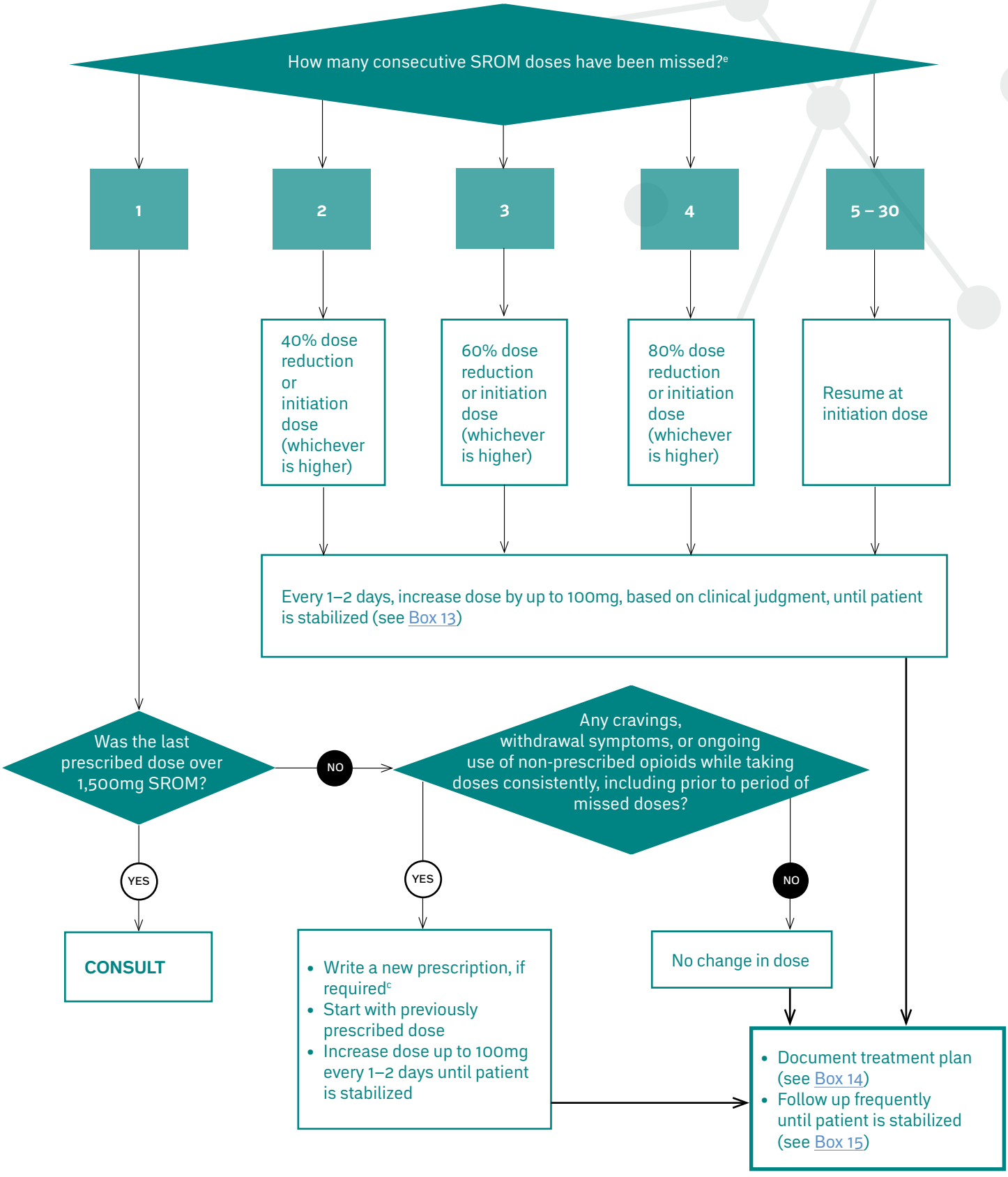
See Box 16 for the methadone missed doses protocol



[c] A new prescription may be required if the most recent prescription has expired.
[d] Methadone prescriptions are cancelled by the pharmacy after 3 consecutive missed doses. Therefore, the prescriber does not need to cancel the previous prescription prior to providing a new prescription.

Decision support tool algorithm: Missed SROM doses

See Box 17 for the SROM missed doses protocol



[c] A new prescription may be required if the most recent prescription has expired.
[e] Slow-release oral morphine prescriptions are cancelled by the pharmacy after 2 consecutive missed doses. Therefore, the prescriber does not need to cancel the previous prescription prior to providing a new prescription.

FURTHER INFORMATION BOXES

The following boxes contain further information on prescribing methadone or SROM in the case of maintenance, missed doses, or restarts. The boxes appear in the same order they appear in the decision support tool algorithm (pages 6 to 10 of this DST).

BOX 1: PATIENT EDUCATION

Following assessment of the patient's knowledge, offer as appropriate:

1. Education on safer use practices
    - Not using alone
        - Using a local supervised consumption site or overdose prevention site
        - Using with another person
        - Using the Lifeguard app
    - Using a small amount of drugs to start (i.e., a "test dose")
    - Using drug checking services, if available
    - Risks of concurrent substance use, including CNS depressant use or stimulants
2. A take-home naloxone kit and education
    - If a kit cannot be provided at the time, provide information on where to acquire
    - Offer education and training on take-home naloxone for any relevant support people (e.g., family, friends, support staff)
3. Additional education materials, where appropriate
    - e.g., *Opioids: A Survivors Guide*
    - Safer injection practices
4. Information on available community resources as required or requested
5. Provide information on relevant drug–drug interactions (see Appendix 1)

<18 BOX 2: CONSIDERATIONS FOR YOUTH

In caring for youth, RNs and RPNs must have competence related to prescribing medications and meet the applicable BCCNM standards.

- Youth aged 16–18 years: **CONSULT**
- Youth aged 15 years or younger:
    - **REFER** to another provider
    - Provide other interventions within scope
        - This includes safety planning, provision of harm reduction supplies and education, relationship building, health care connection, and provision of a safe space to discuss the patient's wellbeing
- When prescribing, RNs and RPNs should follow the *Treatment of Opioid Use Disorder Youth—Guideline Supplement*

BOX 3: PATIENT ASSESSMENT BEFORE PRESCRIBING

- Obtain informed consent to perform an assessment.
- Review PharmaNet.
  - Determine the OAT medication prescribed and when it was last prescribed.
  - Contact the care provider from the most recent OAT prescription to ensure collaboration and appropriate communication.
    - This should not delay the OAT prescription.
    - The patient's regular prescriber may want to follow up the patient at a later date.
  - Review for current prescription of safer supply.
    - **CONSULT** if the patient is currently prescribed safer supply by another provider.
  - Determine whether any new medications have been prescribed since last OAT prescription.
    - **CONSULT** or **REFER**, as appropriate (see Appendix 1).
- Assess substance use, physical health as needed, and mental health.
- If there is no documented history, take the patient's physical and mental health history.
- Assess patient's goals.
  - Including current housing, income, social support, legal support.
  - Connect with health care team or refer as appropriate.
- Offer lab tests if these have not been performed in the past 12 months (see Appendix 2).
  - Note that continuation of OAT should not be delayed while waiting for bloodwork.
- Urine drug test, when clinically indicated (see Box 12).
- Methadone: ECG, when clinically indicated (see Box 10).
- Review concurrent use of CNS depressants (see Box 8):
  - New benzodiazepine prescription since last OAT prescription.
  - Alcohol use.
- Offer pregnancy test, where appropriate (see Box 4).
- Assess for new complications, particularly:
  - Methadone: Severe hepatic dysfunction (see Box 5).
  - Slow-release oral morphine: Renal dysfunction (see Box 6).
- Review medication coverage.
- Provide education on safer substance use practices (see Box 1).
- Support around clients goals, if possible.

BOX 4: CONSIDERATIONS FOR PREGNANCY

When prescribing, RNs and RPNs should follow *Treatment of Opioid Use Disorder During Pregnancy—Guideline Supplement*.

- Offer a pregnancy test before restarting SROM or methadone, where appropriate.
  - Note that continuation of OAT should not be delayed.
- For pregnant patients prescribed methadone or SROM:
  - Ensure that there is existing documentation from a (perinatal) addiction medicine specialist that supports the prescribing plan.
  - **CONSULT** in absence of a documented plan from a specialist.

BOX 5: CONSIDERATIONS FOR PATIENTS WITH SEVERE HEPATIC DYSFUNCTION (METHADONE)

If ALT is over 3 times the upper limit of normal, or albumin or total bilirubin are outside of the normal ranges, this indicates hepatic dysfunction; however, the degree of elevation is a poor indicator of liver function.

- **CONSULT** if patient has either:
  - Severe hepatic dysfunction
  - If GGT or ALT are over 3 times the upper limit of normal, or albumin or total bilirubin are outside of the normal ranges

BOX 6: CONSIDERATIONS FOR PATIENTS WITH DECREASED RENAL FUNCTION (SROM)

An eGFR of less than 60mL/min/1.73m² indicates early stage renal dysfunction (note that eGFR below 30mL/min/1.73m² is a contraindication for SROM, see Box 7).

- **REFER** if eGFR is less than 60mL/min/1.73m²

BOX 7: CONTRAINDICATIONS TO CONTINUE OR RESTART OAT

CONSULT if any contraindications are present.

Methadone-specific contraindications

- Hypersensitivity to methadone hydrochloride
- Currently taking MAOIs or use within past 14 days
- Severe respiratory compromise or obstructive disease
- Severe liver dysfunction (see Box 5)

Slow-release oral morphine-specific contraindications

- Hypersensitivity to morphine sulfate or any component of the formulation
- Currently taking MAOIs or use within past 14 days
- Severe respiratory compromise or obstructive disease
- Known or suspected paralytic ileus
- Renal dysfunction (eGFR below 30mL/min/1.73m^2)
  - **REFER** if patient on SROM has renal dysfunction (see Box 6)

Clinical judgment may determine that patient benefit outweighs the risks associated with the following relative contraindications:

- Pregnancy or chest- or breastfeeding

BOX 8: CONCURRENT CNS DEPRESSANT USE

For example, benzodiazepines (prescribed or non-prescribed), alcohol

- New use: **CONSULT**
- New alcohol use: **CONSULT** if alcohol use exceeds *Canada's Low-risk Alcohol Drinking Guidelines*
- Ongoing use: **CONSULT** depending on clinical presentation and prioritizing patient safety:
  - If the patient is clinically unstable, as demonstrated by sedation or increased risk of overdose
  - CNS depressant use has changed significantly in terms of substance, frequency, or dose

BOX 9: SAFER SUPPLY

CONSULT if the patient is prescribed safer supply medications by another OAT provider.

BOX 10: ELECTROCARDIOGRAM (METHADONE)

Ordering an ECG, receiving ECG results, and any associated consultation **should not delay the prescription of methadone** for maintenance, missed doses, or restarts.

When to order an ECG:

New prescription of QT-prolonging medications (see Appendix 1)	Prescription of 2 or more QT-prolonging medications	Pre-existing risk of prolonged QT interval (e.g., syncope, arrythmias, history of cardiac disease, or family history of sudden cardiac death)	Prescribed 120mg methadone and above

Managing results

- **CONSULT** if QTc is 500ms or above.
  - The RN or RPN will be advised how to proceed with the methadone prescription.
- **CONSULT** if ECG is abnormal.
  - An abnormal ECG should not delay the prescription of methadone.
    - It may indicate a health concern unrelated to OAT.
  - Consultation options include the original OAT provider, primary care physician, or the provider who oversees RN or RPN prescribing in the organization.
  - A telephone consultation may not be sufficient as the provider providing guidance will require collateral information to contextualize the ECG results.

BOX 11: PATIENT ASSESSMENT FOR OAT MISSED DOSES

Prior to this assessment for missed doses, prescribers should have performed an assessment as outlined in Box 3.

1. Contact the patient's regular OAT prescriber.
    - The OAT prescription should not be delayed if unable to get hold of the OAT prescriber.
2. Discuss whether the current treatment continues to be the best option for the patient.
    - If the patient would like to start buprenorphine/naloxone, go to *Decision Support Tool: For RN and RPN Prescribing of Buprenorphine/naloxone*.
    - **REFER** to another prescriber if the patient is interested in transitioning to another full agonist.
3. Ask patient if they have missed OAT doses.
    - If the patient reports missed doses, discuss the reason and number of missed doses.
    - Explore with the patient the reasons for missed doses and ask what they think could help support retention in care.
4. Communicate with original OAT prescriber.
5. Discuss missed-doses protocol.
6. Perform missed-doses protocol (see Box 16 and Box 17).
7. Follow up frequently until patient is stabilized.

BOX 12: URINE DRUG TESTING

When performing UDT, RNs and RPNs should follow *Urine Drug Testing in Patients Prescribed Opioid Agonist Treatment—Breakout Resource*. Urine drug testing should not be used punitively.

When to perform UDT (methadone or SROM):

Treatment stage	Urine drug testing schedule
Induction and stabilization	• Monthly or more or less frequently • When clinically indicated
Maintenance	When clinically indicated
Take-home doses	At least 6–8 per year, or more frequently if there are any safety concerns (e.g., return to use or diversion)

Reminder (SROM-specific): A positive hydromorphone UDT result does not necessarily indicate that hydromorphone has been taken.

- Morphine is metabolized to hydromorphone and codeine by a minor pathway.
- With low doses of morphine, the amount of hydromorphone may not be detectable.
- Patients who are prescribed SROM for OUD are prescribed relatively high doses, which can lead to concentrations of hydromorphone well above the cut-off being detected in their urine.

Missed doses

- A UDT negative for prescribed medication indicates that the patient has missed doses.

BOX 13: DOSE ESCALATIONS

- A dose escalation may be required if the patient is experiencing cravings, withdrawal symptoms, or ongoing use of non-prescribed opioids while taking OAT doses consistently.
- If the patient has missed doses: The dose may need to be decreased (see Box 16 and Box 17). The dose will then need to be increased until the patient is stabilized.

Methadone

- Prior to dose increases, the patient must be assessed (either in-person or virtually).
- Patients can be re-titrated by 5–10mg methadone every 5 or more days, based on whether the patient:
  - Tolerated the previous dose, as demonstrated by no drowsiness post-dose.
  - Requires a dose increase, as demonstrated by the patient experiencing:
    - Cravings,
    - Withdrawal symptoms, or
    - Ongoing non-prescribed opioid use.
- Monitor patient frequently until stable.

CONSULT if the total daily dose plus dose increase exceeds 150mg methadone.

Individuals at high risk of opioid toxicity

- A slower dose escalation is recommended for patients who may be at high risk of opioid toxicity, including individuals:
  - Using a small amount of illicit opioids daily.
  - With recent loss of tolerance.
    - For example, recent discharge from hospital, withdrawal management, residential treatment, or correctional facilities where they did not receive OAT.
  - Severe respiratory illness or decompensated liver disease.
  - Using alcohol, benzodiazepines, sedatives, or prescribed medications that affect methadone metabolism.
    - i.e., CYP inhibitors and inducers.
  - Older adults.
    - i.e., over 55 years of age.

Slow-release oral morphine

- Prior to dose increases, the patient must be assessed.
- Patients can be re-titrated by 100mg SROM every 1–2 days, based on whether the patient:
  - Tolerated the previous dose, as demonstrated by no drowsiness post-dose.
  - Requires a dose increase, as demonstrated by the patient experiencing:
    - Cravings,
    - Withdrawal symptoms, or
    - Ongoing non-prescribed opioid use.
- Monitor patient frequently until stable.

CONSULT if the total daily dose plus dose increase exceeds 1,500mg SROM.

BOX 14: DOCUMENTATION

When documenting care relating to OUD, include:

Subjective

- Patient report
  - Substance use and treatment history
  - Reasons for missed dose
- Collateral information from team or family
- Consultation related to the patient's care (e.g., via the 24/7 Addiction Medicine Clinician Support Line)

Objective

- PharmaNet review
- Test results
- Urine drug test, medication counts, vitals
- Physical symptoms, mood, mental status

Assessment

- Diagnosis
- Any assessment performed
- Take-home doses: monitoring (e.g., medication counts, UDT)

Plan

- Treatment plan
  - Medication prescribed, dose, indication, length of prescription
  - Treatment plan for resuming medication after missed doses
  - Take-home doses: rationale to initiate take-home doses, confirmation the patient criteria have been met
  - Any referrals
- Patient education
- Follow-up plan

BOX 15: FOLLOW UP

Clinical follow-up appointments

- Continue to assess the patient every 1–2 weeks once the patient is stabilized on methadone or SROM
  - Consider decreasing follow-up visits to every 2–4 weeks and then monthly as increased clinical stability is achieved
- Follow-up assessments should include:
  - Adequacy of dosage (e.g., patient report of withdrawal symptoms or cravings)
  - Adverse effects
  - Review of drug–drug interactions (see Appendix 1)
  - Substance use (via patient report and, when indicated, UDT)
  - Patient goals and support for these goals
  - Physical and mental health
  - Psychosocial domains, as clinically indicated
    - Including housing, relationships, and finances
  - Education about harm reduction and safer injection practices, as clinically indicated
  - Offering referrals to appropriate services
  - Health promotion

BOX 16: SAMPLE MISSED-DOSES PROTOCOL (METHADONE)

Missed methadone (consecutive days)	Methadone dose prior to missed doses	Suggested dose adjustment
1–2	Any dose	Same dose (no change)
3–4	30mg	Same dose (no change)
	≤60mg	Restart at 30mg (lower dose if safety concerns)
	>60–150mg	Restart at 50% of previous dose
5–30	Any dose	Restart at 5–30mg (depending on tolerance)

Dose escalation

- See Box 13

BOX 17: SAMPLE MISSED-DOSES PROTOCOL (SROM)

Missed SROM (consecutive days)	How to adjust dose	Example of dose adjustment for a stabilization dose of 800mg
1	No change in dose	800mg
2	Reduce dose by 40% of current dose or restart at initiation dose, whichever is higher	480mg (40% reduction)
3	Reduce dose by 60% of current dose or restart at initiation dose, whichever is higher	320mg (60% reduction)
4	Reduce dose by 80% of current dose or restart at initiation dose, whichever is higher	200mg (initiation dose)
5–30	Restart—Resume at initiation dose	Resume at initiation dose (i.e., 100–200mg)

Initiation dose

- Individuals with known tolerance who are currently using opioids: A starting dose of up to 200mg may be used.
- Individuals with unknown tolerance: A lower dose should be used (e.g., 100mg).

Dose escalation

- See Box 13

APPENDIX 1

DRUG–DRUG INTERACTIONS (METHADONE)

Common drug–drug interaction		Comment	Action for RN/RPN
Category	Examples		
Alcohol	Medications containing alcohol	The additive depressant effect increases the risk of respiratory depression, profound sedation, coma, and death.	• New use (since last methadone prescription): **CONSULT** • Ongoing use: **CONSULT** if the patient is clinically unstable, if CNS depressant use has changed significantly in terms of substance, frequency, or dose and prioritizing patient safety
Central nervous system depressants	Anti-depressants Anti-emetics Anti-histamines Anti-psychotics Anxiolytics Muscle relaxants Neuroleptics Other opioids Phenothiazines Sedatives/hypnotics Benzodiazepines Z-drugs Tranquilizers	The additive depressant effect increases the risk of respiratory depression, profound sedation, coma, and death.	• New use (since last methadone prescription): **CONSULT** if medication is used regularly • Ongoing use: Depending on clinical presentation (e.g., if the patient is clinically unstable, if CNS depressant use has changed significantly in terms of substance, frequency, or dose) and prioritizing patient safety, **CONSULT**
Diuretics	Acetazolamide Amiloride Bumetanide Chlorthalidone Ethacyrnate Furosemide Indapamide Hydrochlorothiazide Metolazone Spironolactone Triamterene		• **CONSULT** if uncertain or patient is experiencing urine retention.
Opioid antagonists	Naltrexone	Contraindicated. Blocks the pharmacological effects of methadone, which can lead to precipitated withdrawal.	• **CONSULT** original prescriber of naltrexone

Common drug–drug interaction		Comment	Action for RN/RPN
Category	Examples		
Mixed agonist/ antagonist, and partial agonists	Buprenorphine	Contraindicated. Blocks the pharmacological effects of methadone, which can lead to precipitated withdrawal.	• Discuss treatment plan with patient • **CONSULT** original prescriber of medication **Micro-dosing buprenorphine/naloxone induction** • This is the only circumstance where methadone and buprenorphine/ naloxone may be co-prescribed • Otherwise, methadone and buprenorphine must not be co-prescribed
Monoamine oxidase inhibitors	Isocarboxazid Phenelzine Tranylcypromine	May increase the risk of serotonin syndrome.	• This is a contraindication • Do not prescribe methadone for individuals who have received MAOI in previous 14 days • **CONSULT** another provider with addiction medicine experience
CYP3A4 inhibitors	Macrolide antibiotics Azole antifungals Protease inhibitors (antiretroviral therapy)	May require methadone dose reduction or a change in antibiotic, antifungal, or protease inhibitor.	• **CONSULT** prior to prescribing in absence of a documented plan for the methadone prescription • Closely monitor patient • Contact antibiotic or antifungal prescriber if change required
CYP3A4 inducers	Carbamazepine Phenytoin Rifampicin/rifampin	May result in under treatment of opioid use disorder. May require dose adjustment of CYP3A4 inducer or methadone.	• Closely monitor patient • Consult pharmacy or other resources prior to prescribing if uncertain **Discontinuation of CYP3A4-inducer medication** • If the medication is discontinued, it can lead to abrupt increases in serum levels and possible toxicity **Change in medication** • Contact the prescriber if change in CYP3A4-inducer medication required

Common drug–drug interaction		Comment	Action for RN/RPN
Category	Examples		
Serotonergic medications	**SSRIs** Citalopram Escitalopram Fluoxetine Fluvoxamine Paroxetine Sertraline Vilazodone **SNRIs** Desvenlafaxine Duloxetine Levomilnacipran	May increase the risk of serotonin syndrome.	• Be aware of the symptoms of serotonin syndrome • Follow up with patient after the first methadone dose adjustment. Perform an assessment for: o Mood alteration o Agitation, anxiety, disorientation, excitement, or restlessness o Neuromuscular excitation o Tremors, clonus , hyper-reflexia, muscle rigidity, bilateral Babinski signs, and akathisia o Autonomic dysfunction o Diaphoresis, flushed skin, hyperactive bowel sounds • **CONSULT** if any symptoms arise or if uncertain
Potentially arrhythmogenic agents	Class I and III anti-arrhythmics Some antipsychotics Some tricyclic anti-depressants Some calcium channel blockers Diuretics and laxatives (due to potential electrolyte disturbance Some antibiotics	These medications have the potential to prolong the QT interval.	• **CONSULT** if QTc is over 500ms • **CONSULT** if ECG is abnormal (reminder: A telephone consultation may not be sufficient as the provider providing guidance will require collateral information to contextualize the ECG results)
Diuretics	Acetazolamide Amiloride Bumetanide Chlorthalidone Ethacyrnate Furosemide Indapamide Hydrochlorothiazide Metolazone Spironolactone Triamterene		• **CONSULT** if uncertain or patient is experiencing urine retention.

DRUG–DRUG INTERACTIONS (SROM)

Common drug–drug interaction		Comment	Action for RN/RPN
Category	Examples		
Alcohol	Medications containing alcohol	The additive depressant effect increases the risk of respiratory depression, profound sedation, coma, and death.	• New use (since last SROM prescription): **CONSULT** • Ongoing use: **CONSULT** if the patient is clinically unstable, if CNS depressant use has changed significantly in terms of substance, frequency, or dose and prioritizing patient safety

Central nervous system depressants	Anti-depressants
	Anti-emetics
	Anti-histamines
	Anti-psychotics
	Anxiolytics
	Muscle relaxants
	Neuroleptics
	Other opioids
	Phenothiazines
	Sedatives/hypnotics
	  Benzodiazepines
	  Z-drugs
	Tranquilizers
		The additive depressant effect increases the risk of respiratory depression, profound sedation, coma, and death.	• New use (since last SROM prescription): **CONSULT** if medication is used regularly
			• Ongoing use: Depending on clinical presentation (e.g., if the patient is clinically unstable, if CNS depressant use has changed significantly in terms of substance, frequency, or dose) and prioritizing patient safety, **CONSULT**

Diuretics	Acetazolamide Amiloride Bumetanide Chlorthalidone Ethacyrnate Furosemide Indapamide Hydrochlorothiazide Metolazone Spironolactone Triamterene	Morphine reduces the efficacy of diuretics by inducing the release of antidiuretic hormone. Morphine may also lead to acute retention of urine by causing spasm of the sphincter of the bladder, particularly in men with prostatism.	• **CONSULT** if uncertain or patient is experiencing urine retention.

Common drug–drug interaction		Comment	Action for RN/RPN
Category	Examples		
Opioid antagonists	Naltrexone	Contraindicated. Blocks the pharmacological effects of SROM, which can lead to precipitated withdrawal.	• **CONSULT** original prescriber of naltrexone
Mixed agonist/ antagonist, and partial agonists	Buprenorphine	Contraindicated. Blocks the pharmacological effects of SROM, which can lead to precipitated withdrawal.	• **CONSULT** original prescriber of medication • During a micro-dosing buprenorphine/naloxone induction, SROM and buprenorphine/naloxone may be co-prescribed • Otherwise, SROM and buprenorphine must not be co-prescribed
Monoamine oxidase inhibitors	Isocarboxazid Phenelzine Tranylcypromine	Contraindicated. May increase the risk of serotonin syndrome.	• Do not prescribe SROM for individuals who have received MAOI in previous 14 days. • **CONSULT** another provider with addiction medicine experience

Serotonergic medications	**SSRIs**
	Citalopram
	Escitalopram
	Fluoxetine
	Fluvoxamine
	Paroxetine
	Sertraline
	Vilazodone
	SNRIs
	Desvenlafaxine
	Duloxetine
	Levomilnacipran
	Milnacipran
	Venlafaxine
		Theoretical increase in the risk of serotonin syndrome.	• Be aware of the symptoms of serotonin syndrome
			• Follow up with patient after the first SROM dose adjustment. Perform an assessment for:
			  • Mood alteration
			  • Agitation, anxiety, disorientation, excitement, or restlessness
			  • Neuromuscular excitation
			  • Tremors, clonus , hyper-reflexia, muscle rigidity, bilateral Babinski signs, and akathisia
			  • Autonomic dysfunction
			  • Diaphoresis, flushed skin, hyperactive bowel sounds
			• **CONSULT** if any symptoms arise or if uncertain

APPENDIX 2

LABORATORY TESTS

Laboratory test	Follow-up for RNs and RPNs
Tests to be offered every 12 months These tests should not be a barrier to resuming prescriptions	
Blood Complete blood count Creatinine—serum/plasma Albumin Total bilirubin Prothrombin time/INR	**CONSULT** if outside the normal ranges
Liver function Albumin Alanine aminotransferase Bilirubin	**Methadone** **CONSULT** before prescribing methadone if albumin, ALT, or bilirubin are over 3 times the upper limit of normal
Renal function eGFR	**Slow-release oral morphine** **REFER** if less than 60mL/min/1.73m²
Tests to be offered as clinically indicated	
ECG (methadone patients only)	**CONSULT** if QTc is 500ms or above **CONSULT** if ECG is abnormal
Pregnancy	**CONSULT** in absence of a documented plan from a (perinatal) addiction medicine specialist
Tests for health promotion, to be offered as clinically indicated These tests should not be a barrier to resuming prescriptions	
Hepatitis A, B, and C serology	**Interpretation** • Review BC Centre for Disease Control (BCCDC) resources for interpretation of chronic or active infection. • For support with interpretation, call the BCCDC line. • Those who have completed the Immunization Competency Course from the BCCDC can: • Use Hep A and B serology to determine patient immunity • Recommend vaccination where appropriate **Treatment** **REFER** to another provider
HIV test	Follow up as per organizational pathways for care referrals
Sexually transmitted infections	**Gonorrhea and chlamydia (GC/CT urine or swab)** • STI-certified RNs: can diagnose and treat within the STI-certified practice DSTs • Those without certified practice (RPNs): **REFER** to an STI-certified RN, an NP, or physician for positive test results **Syphilis serology** • For support with interpretation, call the BCCDC line • **REFER** to another provider for diagnosis and management that requires treatment

SUPPLEMENTARY MATERIAL

Considerations for take-home doses

- When prescribing take-home methadone or SROM doses, RNs and RPNs should follow the provincial *Guideline for the Clinical Management of Opioid Use Disorder*.

Methadone

- Should generally be prescribed as daily-witnessed ingestion until patients demonstrate a persistent, high degree of stability.

Slow-release oral morphine

- The standard should be indefinite daily witnessed ingestion.
- In exceptional cases where patients:
  - Have demonstrated high clinical stability and
  - When daily-witnessed dosing schedules are a significant barrier to treatment (e.g., employment, school, childcare).
- In these exceptional cases, graduated take-home dosing can be considered on a case-by-case basis as per the best judgment of the treating clinician, and with appropriate monitoring and follow-up.

Patient criteria (methadone and SROM)

- Prior to provision of take-home methadone or SROM doses, the following patient criteria should be met:
  - Appropriate urine drug tests for a minimum of 12 weeks.
    - For example, no evidence of cocaine, amphetamine, or illicit opioid use.
  - Social, cognitive, and emotional stability.
    - Confirmed by attending all scheduled appointments, no record of missed doses, improved social relationships, or returning to work or school.
  - Ability to safely store medication at home.
    - i.e., secure, locked containers, or cabinets.

Considerations for initiating taper

Evidence on successful OAT tapers, including ideal candidates and speed is lacking. Due to the high likelihood of return to illicit opioid use, OAT tapers are not generally recommended. However, if the patient requests a taper, then a gradual tapering regimen over months to years is recommended.

If a patient requests an OAT taper,:

- **CONSULT** another prescriber
- Provide education
  - Counsel the patient on the risks of return to substance use and overdose
  - Offer information on harm reduction strategies including access to take-home naloxone
- Offer support and referrals to appropriate services

Medication shortages (SROM)

In the past, there have been temporary shortages of specific strengths of SROM—brand name Kadian (24-hour formulation). For reports about current drug shortages, visit Drug Shortages Canada. In the event this happens in the future, the BCCSU will provide guidance through release of a bulletin. General management steps include:

- Contact the patient, determine treatment plan, and document in the patient's medical record.
- The usual course of action is to switch to sustained-release oral morphine (12-hour formulation; M-Eslon) **in the short term**.
- Discuss with the patient that conversion to M-Eslon is temporary and that they will be transitioned back to Kadian once the shortage resolves.

Converting patients to M-Eslon

1. Cancel existing SROM prescription.
2. Write a prescription for M-Eslon.
    - Note that M-Eslon is the same therapeutic dosage of Kadian, but will be divided into 2 doses.
    - For example, 1,000mg Kadian per day is equivalent to 500mg M-Eslon twice daily.
3. The first dose will generally be daily-witnessed ingestion, while the second dose may be a carry.
    - Prescribers can consider witnessing of the second dose and indicate this on the prescription; however, take into consideration the hours of the pharmacy and logistics for the patient.
4. Transition the patient back to Kadian once the medication shortage has resolved.

FURTHER GUIDANCE AND ADDITIONAL RESOURCES

24/7 Addiction Medicine Clinician Support Line

To speak to an addiction medicine specialist, call 778-945-7619.

Provides telephone consultation from an addiction medicine specialist to physicians, nurse practitioners, registered nurses, registered psychiatric nurses, midwives, and pharmacists who are involved in addiction and substance use care and treatment. Consultation can include support in screening, assessment, treatment, and management of substance use and substance use disorder(s).

Further Guidance

Guideline for the Clinical Management of Opioid Use Disorder: Provincial guideline for the management of OUD in BC.
Opioid Use Disorder Practice Update: Provides updates on the provision of OAT in line with planned updates to the forthcoming provincial *OUD Guideline*.
Urine Drug Testing in Patients Prescribed Opioid Agonist Treatment—Breakout Resource: A stand-alone resource that replaces UDT-specific guidance in the provincial guideline.
Treatment of Opioid Use Disorder During Pregnancy—Guideline Supplement: Supplement to the provincial guideline focused on management of OUD during pregnancy.
Treatment of Opioid Use Disorder for Youth—Guideline Supplement: Supplement to the provincial guideline focused on the management of OUD for youth (age 12–25).
Clinical Bulletin: Benzodiazepines and Opioids: Guidance on providing care to individuals exposed to benzodiazepine-adulterated drugs in the street opioid supply.

Additional Resources

Provincial Opioid Addiction Treatment Support Program: Mandatory online training program offered by the BCCSU and UBC CPD for prescribing OAT in BC.
Clinics accepting new OAT patients: Contact information for OAT clinics across BC currently accepting new OAT patients.
Toward the Heart: Current listing of harm reduction services in BC that provide needles, syringes, and other injection supplies, overdose prevention training, and take-home naloxone kits.
Lifeguard Digital Health: App that alerts emergency services to a potential overdose, if individual does not respond to app within set time.
Drug Shortages Canada: Provides information about drug shortages.
Canada's Low-risk Alcohol Drinking Guidelines: Defines a standard alcoholic drink and outlines safer drinking limits.