SLOW-RELEASE ORAL MORPHINE AS OPIOID AGONIST THERAPY

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INTRODUCTION

Methadone and buprenorphine (brand name Suboxone) have been the most common medications for opioid agonist therapy (OAT) in Canada for a long time. Slow-release oral morphine (or SROM, also known by the brand name Kadian) is a long-acting form of morphine that has also been used as an OAT medication. It has been considered as a "third-line" OAT option, which means that it's usually only prescribed to people who have already tried both buprenorphine and methadone. One reason for this is that there's not a lot of research showing the benefits of SROM, and there's a lot of guidance and research available about methadone and buprenorphine. However, the risks of the unregulated opioid supply make it very important that people who want to be on OAT have access to as many OAT choices as possible. For this reason, we think that buprenorphine, methadone, and SROM should all be available as options for people who want OAT.

WHO ARE WE?

- 7 people: 5 people with clinical expertise of SROM (3 doctors, 1 nurse practitioner, and 1 pharmacist) and 2 with lived and living expertise of SROM.
- We spent a long time talking about what research has shown about using SROM as OAT, our personal and clinical experiences of SROM, what we know about its benefits and risks, and what we think prescribers, pharmacists, and people taking OAT need to know about SROM.

WHAT'S OUR GOAL?

Our goal is to give heath care providers updated information about SROM and how to prescribe it. We hope that this will make SROM more available, so that people who want to take OAT have as many choices as possible. This document is a summary of our **recommendations**, and it's for people taking OAT (or interested in taking it) who want to know more about SROM.

RECOMMENDATIONS

CHOOSING AN OAT MEDICATION

There are lots of things to consider when deciding on an OAT medication, like past experiences with OAT, goals, current substance use, and other health conditions. **We recommend that the health care provider and the person starting OAT have a conversation about these things and decide together which medication to try, and that SROM should be an option whether or not buprenorphine or methadone have been tried before**. Using a decision aid tool can be helpful when going through all the information and talking about making a choice. Every situation is different, but here are some situations that might make SROM a good choice for someone:

- High opioid tolerance.
- Side effects like nausea with other types of OAT.
- Other types of OAT didn't help withdrawal and cravings enough.
- Health conditions like irregular heart rhythms that make methadone riskier.

There are some situations where SROM might not be the best choice:

- People should not take SROM if they have serious kidney, liver, or lung conditions.
- People should not take SROM if they have taken MAOIs (like Nardil, Parnate, or Manerix) in the last 14 days.
- SROM has a stronger sedating effect in people who use alcohol, people who take sedating medications like benzos, and people who are older, which makes it riskier.

STARTING AND INCREASING SROM DOSES[1]

The right starting dose of SROM, and how quickly to increase it, depends on the tolerance of the person starting OAT, their health conditions, and their other medications. We recommend a starting dose of 200–400 mg for people who have been using fentanyl regularly and have very high opioid tolerance. People who haven't been using opioids as much or as often, or people who might have other risk factors for toxicity like drinking alcohol or taking benzodiazepines, might start at a dose of 100–150 mg. Lower starting doses (30–50 mg) would be appropriate for people who have been using opioids in lower doses or less regularly, or who need to be very careful with SROM because of other health factors.

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[1] These doses are for people who are starting SROM in a clinic rather than people who are in the hospital.

Doses are usually increased every 2 days, but there are protocols for increasing daily in the first week. The increases should slow down once the dose is more than 800 mg per day. There's no maximum dose of SROM – the right dose is a dose that controls cravings and withdrawal symptoms for a full day without causing sleepiness.

OPIOID TOLERANCE	STARTING DOSE	DOSE INCREASES
Low tolerance or high risk for toxicity	30–50 mg	50 mg every 2 days
Moderate tolerance	100–150 mg	50–100 mg every 2 days
High tolerance	200–400 mg	100 mg daily OR 200 mg every 2 days to 800 mg, then 50–200 mg every 2 days

People will probably have check-ins at least once a week while the dose is being increased, and then less frequently once the dose is stable.

SROM can also be used with methadone. Because methadone needs to be increased very slowly, it can take a long time for someone to get to a dose where they feel comfortable. In these cases, people can take SROM along with methadone to help control their withdrawal as their methadone dose gets increased. People are usually started on 30 mg of methadone and 100–200 mg of SROM, and the SROM dose can be increased by 100 mg every 2 days.

SWITCHING OAT MEDICATIONS

When people stop one OAT medication and start another, the dose of the new medication has to be lower at first, since tolerance can be different with different opioids. To make the switch between medications less sudden, it's possible to do a gradual transition from one medication to the other, where you lower the dose of the old medication while raising the dose of the new medication. Here's an example showing how someone might gradually switch from methadone to SROM over 5 days:

	METHADONE	SROM
Day 0	100 mg	
Day 1	50 mg	150 mg
Day 2	30 mg	300 mg
Day 3	20 mg	400 mg
Day 4	0 mg	500 mg
Day 5		600 mg

A gradual switch like this can be done faster or slower, depending on the medications, the doses, and how the person is feeling.

OTHER THINGS TO KNOW ABOUT SROM

OAT medications can be dangerous, especially if they're not taken as prescribed or are taken by people they are not prescribed for. Here are some things people should know about starting OAT with SROM:

- Because morphine tolerance is lost quickly, people who miss 4 SROM doses in a row will need to cut their dose in half, and people who miss 5 doses in a row will need to go back to a starting dose. Health care providers will also consider other things like the person's tolerance and drug use to decide whether the dose should be adjusted differently.
- Because of the danger of chewing, crushing, or injecting morphine pellets, health care providers usually don't provide take-home doses of SROM until they're confident that the person will be safe. People usually don't get take-home doses for the first 4 weeks of taking SROM. After 4 weeks, people may start receiving up to 3 take-home doses per week if they have a safe place to keep their medication and haven't been using substances in high-risk ways in the past month (like blackouts or overdoses). After about 3 months, people might start getting 4–6 take-home doses if they're doing well and haven't had any blackouts or overdoses in 3 months. There hasn't been any research yet about the risks or benefits of more than 6 take-home doses of SROM at a time, so we're recommending a maximum of 6 doses for now.
- Urine drug testing is a regular part of OAT. The urine results should match what the person is prescribed and says they're taking. People usually need to provide a urine sample every time they see their health care provider. This will be more frequent (maybe once a week) early in treatment as the dose gets adjusted but may get less frequent (maybe once or twice a month) as time goes on.