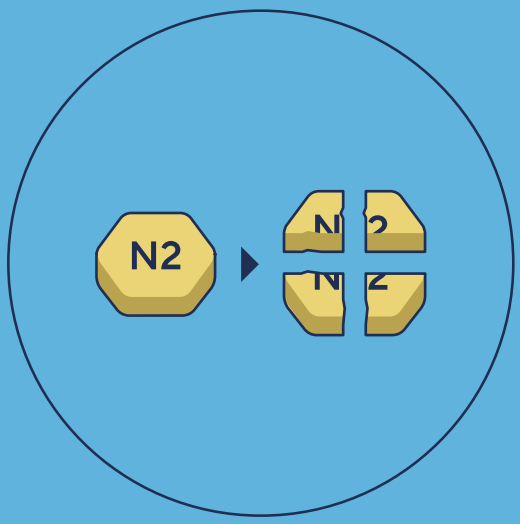
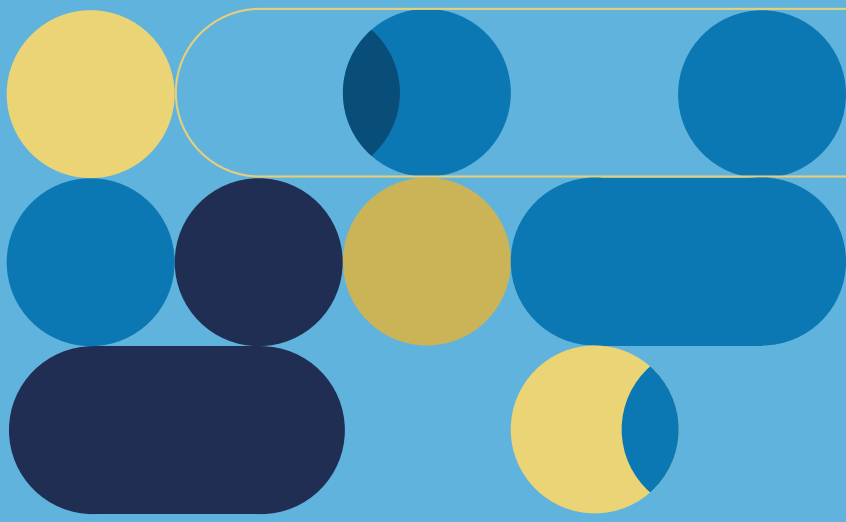
L'Équipe de soutien clinique et organisationnel en dépendance et itinérance

# Guide to Using the Buprenorphine-Naloxone (Suboxone®) Microdosing Induction Method in Opioid Agonist Therapy (OAT)

JULY 2023



Québec

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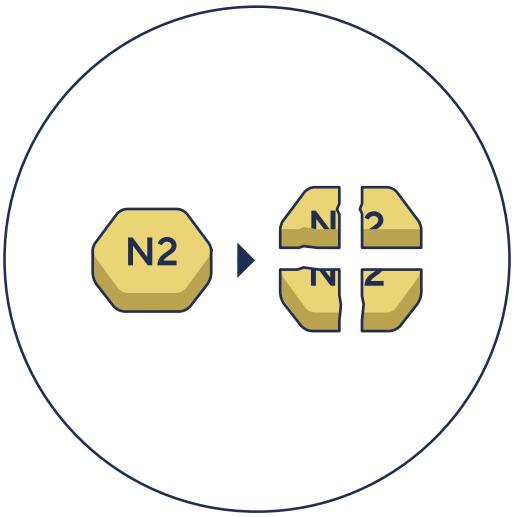


Québec

This ***Guide to Using the Buprenorphine-Naloxone (Suboxone®) Microdosing Induction Method in Opioid Agonist Therapy (OAT)*** is a publication of the Équipe de soutien clinique et organisationnel en dépendance et itinérance (ESCODI) at CIUSSS du Centre-Sud-de-l'Île-de-Montréal.

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## DISCLAIMER

The first literature to be published on the buprenorphine microdosing induction method appeared in 2016, when it was referred to as the Bernese Method.[1] At the time of writing, this method is off label and data supporting its use remain limited, but Canadian clinical guidelines suggest its use.

The content of this guide, which is based on case reports and clinical guidelines, is the result of discussions with a committee of Québec-based expert practitioners. In addition, the document was verified by competent experts to ensure that its content is as accurate as possible, in a context where there is still a paucity of quality literature on the subject.

However, it should be noted that this guide is not prescriptive in nature, and its authors cannot be held accountable for the clinical practices of professionals. Clinicians are expected to assume responsibility for being appropriately qualified and trained. They must exercise clinical judgment when providing care and services, in compliance with the professional standards and codes of ethics to which they are subject. Should there be any doubt about using this induction method, consulting an expert is recommended.

The advice given in this guide may come from case reports in the scientific literature, Canadian clinical guidelines, or Québec clinical expertise; this distinction is made in the text.

When the text refers to buprenorphine-naloxone (Suboxone®), this is understood to mean sublingual tablet and/or sublingual/buccal soluble film formulations.

Throughout this document, the buprenorphine-naloxone microdosing induction method is referred to as "microdosing" for ease of reading.

Unless otherwise indicated, the number of milligrams (mg) reported corresponds to the concentration of buprenorphine in the buprenorphine-naloxone formulation.

## NOTES

In this document, the use of the term "nurse" is consistent with the standards of the Ordre des infirmières et infirmiers du Québec (OIIQ).

# POUR NOUS JOINDRE

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# Guide to Using the Buprenorphine-Naloxone (Suboxone®) Microdosing Induction Method in Opioid Agonist Therapy (OAT)

## 1. GENERAL PRINCIPLES

- In Québec, buprenorphine-naloxone (in a sublingual tablet and/or sublingual/buccal film) is one of three oral opioid agonist (OAT) options available for treating opioid use disorder (OUD), alongside methadone and slow-release oral morphine.
- Before starting treatment with buprenorphine-naloxone, the standard induction protocol requires the individual to be in moderate to severe withdrawal. For some individuals this requirement may be difficult to meet, effectively limiting access to this drug.
  - For more information on the standard buprenorphine-naloxone (Suboxone®) induction method, see the Optimal Usage Guide: Opioid Agonist Therapy (OAT), published by the INESSS, or the product monograph.
- Buprenorphine-naloxone microdosing induction is an alternative, off-label method of induction involving repeated administration of low doses of buprenorphine-naloxone, in conjunction with the opioids used.[1] The opioids are discontinued gradually, or after 7-13 days.
  - The slow accumulation of buprenorphine at mu type (μ) opioid receptors allows for the gradual replacement of pure opioid agonists by buprenorphine without causing significant withdrawal symptoms.[1]
- The usual average duration of microdosing is 7 or 13 days, compared with 2 days for standard induction protocols.[2–5]

## 2. ELIGIBILITY

- Microdosing is suitable for use with pure opioid users, regardless of anticipated tolerance level, quantity consumed, or source of the opioids (prescribed or non-prescribed).
- Microdosing can be used to:
  - Initiate a buprenorphine-based OAT (e.g., buprenorphine-naloxone or buprenorphine sustained-release injection) in an individual taking opioids (prescribed or non-prescribed);[4,5]
  - Transfer an individual who is already on another OAT (e.g., methadone, slow-release oral morphine) to buprenorphine.

> For further information on the use of sustained-release buprenorphine injection, see A Guide to Using Extended-Release Buprenorphine (Sublocade®) in Opioid Agonist Therapy (OAT).

- Microdosing is particularly indicated for:
  - Individuals for whom the withdrawal symptoms associated with the standard induction method are unacceptable;[5–9]
  - Individuals for whom withdrawal is not recommended (e.g., CAD, induction in a pregnant person);[5]
  - Individuals whose withdrawal is not sufficient for standard induction; e.g., upon arrival at a clinic or in an emergency room.[5,10]

## 3. CONTRAINDICATIONS

- The literature does not report any contraindications to the use of microdosing.
- The usual contraindications to the use of the various buprenorphine-naloxone formulations should be taken into consideration before starting induction. Consult the product monograph for a list of contraindications.

## 4. TREATMENT PRINCIPLES

### Pre-treatment assessment

- Microdosing requires prescribers to make the same assessment as would be made before starting OAT with any drug.
  - For more information on the initial assessment required of an individual before prescribing an OAT, see the CMQ, OIIQ and OPQ guidelines (in French only).

- As microdosing is an off-label practice, the prescriber is encouraged to properly document the individual's clinical history prior to initiation of treatment, including the following:
  - Identifying the reason for choosing this induction modality,
  - Obtaining the individual's free and informed consent (consult Appendix 1).

**For Prescribers**

According to the expert clinicians consulted, it is advisable at this stage to take the time to explain to the individual that buprenorphine is a partial agonist of mu type (μ) opioid receptors, and that its effect, once a stable dose has been reached, may therefore differ from that of a pure agonist. It is therefore important to ensure that buprenorphine-naloxone is suited to the needs and preferences of the individual starting microdosing induction.

## Induction, dosage and stabilization of treatment

- Various microdosing protocols have been published.[3–8,10–14] To date, no study has been able to determine that any particular protocol is better than another, so it is essential to tailor treatment to each individual case. However, a certain consensus appears to be emerging in the literature. The following is a summary of current practice:
  - Microdosing begins with the administration of one or more daily doses of buprenorphine-naloxone.
  - Concurrent use of other opioids may be discontinued immediately or gradually, as agreed with the individual receiving treatment.
  - The most commonly used initial dose is 0.5 mg.[3–6,12–14]
  - Daily doses are gradually increased (from 50% to 100% per day).[3–7,9–14]
  - The most common length of protocols for buprenorphine-naloxone microdosing induction is 7 days, but they can go as long as 13 days.[3–5,12]
    - A longer period is generally indicated for individuals taking long-acting opioids such as methadone, those using large quantities of opioids, and those who are fearful of discontinuing their opioid use.
      - Long-acting opioids (e.g., methadone, once-daily slow-release morphine, fentanyl patch, twice-daily (12-hour) slow-release morphine, etc.) can last 12 to 24 hours or more.

      **N.B.:** If a long-acting opioid is injected, smoked or snorted, it becomes a short-acting opioid.

    - Conversely, a short protocol is indicated for individuals taking short-acting opioids, those with low opioid tolerance, and those using small quantities of opioids.
      - Short-acting opioids are those whose effects last less than five hours (e.g., heroin, hydromorphone, oxycodone, morphine, etc.).
  - When long-acting opioids are used, some protocols recommend starting to reduce such use at 4 mg of buprenorphine-naloxone, while others stop their use completely at 12 mg, without any prior reduction.[3–5]
    - It is recommended to reach a dosage of at least 4 mg of buprenorphine-naloxone before discontinuing short-acting opioids and/or starting to gradually reduce the use of long-acting opioids.
    - In general, use of long-acting opioids is discontinued after a dosage of 12 mg of buprenorphine-naloxone, on average (range 8-16 mg), has been reached.
  - End of induction and stabilization:
    - When discontinuing other opioids, monitor the individual for withdrawal symptoms and titrate the buprenorphine-naloxone dose rapidly, if necessary.
    - At the end of the microdosing protocol, it may be useful to provide additional doses of buprenorphine-naloxone to treat the onset of withdrawal symptoms; e.g., 1 tablet of 2 mg BID PRN, to be used as required,[3,4] without exceeding a total dose of 32 mg per day.

      **N.B.:** The *Optimal Usage Guide – Opioid Agonist Therapy (OAT)* states that a "dose of 32 mg/day is commonly used and is safe in this context," although the limit established by Health Canada is 24 mg.[2]

- According to the clinical expertise, the key issues when tailoring the protocol to the individual's needs are as follows:
  - Opioid tolerance.

    **N.B.:** Individuals who are taking high doses of opioids may need to reach the maximum dose of buprenorphine-naloxone (24 or 32 mg) before discontinuing such use;
  - Feelings of attachment to concomitant opioids.
  - Susceptibility to withdrawal symptoms (e.g., a history of traumatic withdrawal).
  - The urgency of the need to intervene (e.g., hospitalization, travel, etc.).
  - Comorbidities, including chronic pain.
  - The potential benefits of BID intake with regard to displacing opioids at mu type (μ) receptors.

**Examples of buprenorphine-naloxone microdosing protocols in OAT**

| Day | Short protocol | | Long protocol | |
|---|---|---|---|---|
| | BUP dosage | Other opioid dosage | BUP dosage | Other opioid dosage |
| 1 | 0.5 mg QD | Maintenance | 0.5 mg QD | Maintenance |
| 2 | 0.5 mg BID | Maintenance | 0.5 mg QD | Maintenance |
| 3 | 1 mg BID | Maintenance | 1 mg QD | Maintenance |
| 4 | **2 mg BID** | Options:<br>➪ **Discontinuation of short-acting opioids**<br>and/or<br>➪ **Reduction of long-acting opioids** | 1.5 mg QD | Maintenance |
| 5 | 3 mg BID | Maintenance | 2 mg QD | Maintenance |
| 6 | 4 mg BID | Maintenance | 3 mg QD | Maintenance |
| 7 | 12 mg QD | Discontinuation of other opioids | **4 mg QD** | Options:<br>➪ **Discontinuation of short-acting opioids**<br>and/or<br>➪ **Reduction of long-acting opioids** |
| 8 | Adjust BUP dose until a comfort dose is reached. | | 5 mg QD | Maintenance |
| 9 | | | 6 mg QD | Maintenance |
| 10 | | | 7 mg QD | Maintenance |
| 11 | | | 8 mg QD | Maintenance |
| 12 | | | 10 mg QD | Maintenance |
| 13 | | | 12 mg QD | Discontinuation of other opioids |
| 14 | | | Adjust the BUP dose until a comfort dose is reached. | |

Tiré de : Marwah et coll.[3], Patel et coll.[4] et McHealth[5].

**For Pharmacists**

Warning:

- 0.5 mg = ¼ of a 2 mg tablet of buprenorphine-naloxone.


- On the subject of buprenorphine-naloxone film, one study reports that cutting the film in half, rather in quarters, with a razor blade will least compromise the stability of its contents.[15] This study also reports that the concentration of a film cut in half remains stable for 7 days if stored in a plastic bag with a sealable zipper.[15]

- The provision of an opioid withdrawal symptom assessment tool, such as the Subjective Opioid Withdrawal Scale (SOWS), may be indicated to enable the individual to monitor the onset of withdrawal symptoms during induction (see Appendix 1).
- It is also recommended to prescribe a withdrawal kit to individuals commencing buprenorphine-naloxone microdosing induction.[2]

| Withdrawal kit | | |
|---|---|---|
| Symptom | Medication example | Quantity for 1 day |
| Nausea | Antiemetic (e.g., dimenhydrinate 25 mg every 6-8 hr.) | 10 tabs |
| Diarrhea | Antidiarrheal (e.g., loperamide 4 mg stat, then 2 mg after each liquid stool; max 12 mg/24 hr.) | 6 tabs |
| Anxiety, irritability, perspiration | Clonidine 0.1 mg BID-TID as needed within the first 12 hr. | 3 tabs |
| Insomnia | Diphenhydramine 25-50 mg HS **or** | 2 tabs |
| | Trazodone 50 mg HS **or** | 1 tab |
| | Quetiapine 25-50 mg HS | 2 tabs |
| Pain | NSAID (e.g., ibuprofen 200-400 mg every 6-8 hr.) **or** | 6 tabs |
| | Acetaminophen 500 mg every 4-6 hr.; max. 4 gr/24 hr. | 8 tabs |

From: Institut national d'excellence en santé et services sociaux (INESSS). Optimal Usage Guide – Opioid Agonist Therapy (OAT).

**For Prescribers**

According to clinical expertise, mild withdrawal symptoms may appear around the fourth or fifth day of the microdosing induction process. It may be worthwhile to schedule a short courtesy call with the individual to ensure that the induction is going well, and to address any needs they may have.

There is currently a risk of contamination, by benzodiazepines, of opioids that are obtained on the illicit market. According to clinical expertise, it is recommended to pay particular attention to the signs and symptoms of benzodiazepine withdrawal when opioid use is discontinued.

- In order to ensure that the induction is going well, various follow-up and support modalities can be offered to individuals who are following a microdosing induction protocol:
  - Teleconsultations,
  - Close follow-up with a community pharmacist,
  - Home visits,
  - The use of a blister pack or pill dispenser (dispill).

- At the first assessment and at each subsequent meeting, a naloxone kit should be offered, instructions should be provided on its use, and essential harm reduction materials should be distributed.


## Prescription

- For a model prescription for buprenorphine-naloxone microdosing induction, see Appendix 2.
- A fact sheet for community pharmacists is provided in Appendix 3.
- The following formulations of buprenorphine-naloxone are available in Québec for use in microdosing induction:

| Buprenorphine-naloxone formulation | Concentration | Covered by RAMQ |
|---|---|---|
| Sublingual tablets (Suboxone®) | 2 mg and 8 mg | Yes |
| Sublingual/buccal films (Suboxone®) | 2 mg, 4 mg, 8 mg and 12 mg | Yes |

## Unsupervised doses

- Whether or not to grant unsupervised doses as part of microdosing is left to the prescriber's discretion. A decision support tool for granting unsupervised dosing is available here.
- In the case of an individual who is already visiting the pharmacy daily and is prescribed buprenorphine-naloxone to be taken twice daily, the first dose is generally administered in the pharmacy and the second dose is given to the individual.[3,13]

## Missed doses

- If consecutive doses are missed for a period of more than 48 hours, the community pharmacist may reassess the individual and adjust the prescription. If necessary, the pharmacist can contact the prescriber. See: Optimisation du rôle du pharmacien communautaire (in French only).

| Missed doses | Recommended action(s) |
|---|---|
| Less than 48 hours without a dose | Take the missed dose as soon as possible. Restart the induction schedule from the missed dose. |
| More than 48 hours without a dose | Reassess the individual. If necessary, contact the prescriber. |

Inspired by: Marwah et coll.[3], Patel et coll.[4], Cho et coll.[12] et CRDQ[11].

**N.B.:** The following criteria need to be considered when determining a dosage adjustment after a missed dose: the daily dose of buprenorphine-naloxone and the concomitant opioid, the number of missed doses, the use of a pure agonist opioid (e.g., methadone), and risk of a precipitated withdrawal.

## 5. PRECAUTIONS

- The literature on microdosing reports few adverse reactions.
- It is recommended to consult the product monograph of the chosen formulation for information on adverse effects and potential drug interactions.
- It is not uncommon for individuals to report mild to moderate withdrawal symptoms during induction.[9] It is recommended practice to prescribe a withdrawal kit at the same time as the induction.
    - If severe withdrawal symptoms appear, the individual should be reassessed to determine whether the microdosing should be continued or discontinued.

**L'Équipe de soutien clinique et organisationnel** en dépendance et itinérance

## Contact us

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# APPENDICES

**Appendix 1**
Buprenorphine-Naloxone (Suboxone®) Microdosing Induction – Frequently Asked Questions

**Appendix 2**
Model Prescription

**Appendix 3**
Buprenorphine-Naloxone (Suboxone®) Microdosing Induction – Information for the Pharmacist

APPENDIX 1

# BUPRENORPHINE-NALOXONE (SUBOXONE®) MICRODOSING INDUCTION

## Frequently Asked Questions

### What is buprenorphine-naloxone microdosing?

It is a treatment initiation method for opioid dependence, or for switching treatment (e.g., from methadone to buprenorphine-naloxone), through the use of very small doses of buprenorphine-naloxone and without the person having to stop consumption of opioids or discontinue their usual treatment (e.g., methadone). Opioid use or treatment will be discontinued during the process.

### Why is this method used?

Following this method does not require stopping the use of other opioids, and the individual being followed can be spared significant withdrawal symptoms. This can benefit individuals whose withdrawal symptoms are intolerable or unacceptable, as well as those for whom withdrawal is not recommended.

### How does it work?

Low doses of buprenorphine-naloxone are taken orally every day and are gradually increased over a period of several days until a sufficient dose is reached, i.e., one that enables the individual to stop consuming opioids without experiencing significant withdrawal symptoms.

It is essential not to take the doses listed in the induction schedule any faster than suggested, as this could trigger withdrawal symptoms.

### How long does the microdosing last?

The treatment usually lasts 7 or 13 days. However, the individual and prescriber may agree on a schedule tailored to the individual's needs.

Once the opioids have been discontinued, the dose of buprenorphine-naloxone can continue to be increased until a comfortable daily dose is reached.

### Are there any conditions for following this method?

Yes, the individual must want to treat their opioid dependence with buprenorphine, understand its effects, and aim to stop using opioids. Buprenorphine is a drug that does not produce a "soothing" effect like other opioids, such as methadone and morphine.

In addition, the individual must be prepared to take this drug according to a schedule. Depending on the situation, two doses a day may be indicated. It is also possible that at least one of these doses will be administered in a pharmacy.

### What should I do if I miss a dose?

It is important to follow the established schedule to limit the onset of withdrawal symptoms.

| Missed doses | Recommended action(s) |
|---|---|
| Less than 48 hours (2 days) without a dose | Take the missed dose as soon as possible. Continue with the next dose according to the schedule, starting from the missed dose. It is important not to speed up the schedule to "make up" for missed days. |
| More than 48 hours (2 days) without a dose | See the prescriber or the pharmacist, who will readjust the protocol if necessary. |

### What should I do if I experience withdrawal symptoms?

Mild withdrawal symptoms may occur during microdosing. A withdrawal symptom self-assessment tool is available on the following page to help judge their intensity. If these symptoms are too severe, a withdrawal kit is prescribed. The kit contains various drugs that will relieve symptoms. The pharmacist can provide support on how to use it properly.

## Who should I contact for help or if I have questions?

For questions about the microdosing method, side effects, abnormal withdrawal symptoms and cravings, contact a member of the partner care team. The community pharmacist, who is a member of the care team, is also able to quickly provide advice.

***Document inspired by the CHUM Addiction Medicine Department***
We would like to thank to Marie-Christine Grégoire and Jonathan Ménard for their contribution.

# Subjective Opioid Withdrawal Scale (SOWS)[1]

The SOWS is used to evaluate the intensity of one's opioid withdrawal symptoms on a 5-point scale ranging from 0 (not at all) to 4 (extremely).

**Instructions :** Please circle the answer that best describes how you feel now. Add up your points to obtain your final score.

| | | 0 = Not at all; 1 = A little; 2 = Moderately; 3 = Quite a bit; 4 = Extremely | | | | |
|---|---|---|---|---|---|---|
| **Symptom** | Date | | | | | |
| | Time | | | | | |
| I feel anxious. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| I feel like yawning. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| I am perspiring. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| My eyes are teary. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| My nose is running. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| I have goosebumps. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| I am shaking. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| I have hot flushes. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| I have cold flushes. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| My bones and muscles ache. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| I feel restless. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| I feel nauseous. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| I feel like vomiting. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| My muscles twitch. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| I have stomach cramps. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| I feel like using now. | | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 | 0 1 2 3 4 |
| **Total score** | | | | | | |

**Mild withdrawal: 1-10** **Moderate withdrawal: 11-20** **Severe withdrawal: 21-30**

1 Handelsman L, Cochrane KJ, Aronson MJ, Ness R, Rubinstein KJ, Kanof PD. Two New Rating Scales for Opiate Withdrawal. 1987. *American Journal of Alcohol Abuse* 13, 293-308.

# APPENDIX 2
# Model Prescription

[ Patient's contact information ]

**PHARMACEUTICAL PRESCRIPTION FOR BUPRENORPHINE-NALOXONE (SUBOXONE®) MICRODOSING INDUCTION**

**Hospital** ☐ **Recovery Housing** ☐ **Rehabilitation** ☐ **Frontline** ☐

Allergy/Allergies: _____ No known allergies: ☐ Adverse reactions to medications: _____

**PRESCRIPTION FOR BUPRENORPHINE-NALOXONE (SUBOXONE®) MICRODOSING INDUCTION**

**The principle of microdosing involves gradually inducing microdoses of buprenorphine-naloxone in order to minimize symptoms of withdrawal from the other opioid, which is taken at the same time and discontinued once the therapeutic dose of buprenorphine-naloxone has been reached. See the indication.**

***** By convention, the number of milligrams indicated in the dosages corresponds to mg of buprenorphine. *****

**INDICATION**

QHR notice: **Substitution treatment for opioid use disorder (opioid agonist therapy)**

Period: _____ / _____ / _____ TO _____ / _____ / _____
DD MM YYYY DD MM YYYY

| Microdosing Protocol | | |
|---|---|---|
| Day | Buprenorphine-naloxone dosage | Dosage of the other opioid: _____ |
| 1 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 2 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 3 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 4 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 5 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 6 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 7 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 8 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 9 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 10 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 11 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 12 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 13 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |
| 14 | _____mg ☐ QD ☐ BID ☐ Other:_____ | ☐ Maintenance ☐ Discontinuation |

- Number of doses taken in front of the pharmacist (specify number of doses observed per day or week): _____
- The patient can never take more than _____ doses at home between the dates on which he or she must take the medication in front of the pharmacist.

☐ Serve the microdosing protocol in a dispill.

**Total quantity of buprenorphine-naloxone** for the duration of the prescription: _____ mg

**Discontinue all other prescribed opioids (including previous OAT) on day _____ , if more than one opioid, follow these guidelines:**

_____

Adjustment to the buprenorphine-naloxone dose at the end of the protocol:

- Starting on day _____ (end of the protocol), continue with _____ mg of buprenorphine-naloxone QD.
- Allow _____ buprenorphine-naloxone tablets/films of _____ mg _____ PRN, to be used as needed but not exceeding a total dose of 32 mg per day.
- Do not dispense if the patient is visibly under the influence of alcohol or intoxicated by medication or drugs.
- Protocol for a missed dose:

| **Missed doses** | **Recommended action(s)** |
|---|---|
| Less than 48 hours without a dose | Take the missed dose as soon as possible.<br>Restart the induction schedule from the missed dose. |
| More than 48 hours without a dose | Reassess the individual.<br>If necessary, contact the prescriber. |

Check the following as needed:

☐ Please give the naloxone kit and explain how to use it.

☐ Give the following withdrawal kit:

| **Symptom** | **Drug** | **Quantity** |
|---|---|---|
| Nausea | Dimenhydriante : _____ mg | _____ tab |
| Diarrhea | Loperamide : _____ mg | _____ tab |
| Anxiety, irritability, perspiration | Clonidine : _____ mg | _____ tab |
| Insomnia | Diphenhydramine : _____ mg | _____ tab |
| | Trazodone : _____ mg | _____ tab |
| | Quetiapine : _____ mg | _____ tab |
| Pain | Ibuprofen : _____ mg | _____ tab |
| | Acetaminophen : _____ mg | _____ tab |

**OTHER MEDICATIONS**

**Daily dosage of the other opioid:** _____ _____ **mg** QD (total quantity for the duration of the prescription: _____ mg) given in addition to buprenorphine-naloxone. Discontinue as per the above microdosing protocol.

Period: _____ / _____ / _____ TO _____ /_____ /_____
DD MM YYYY DD MM YYYY

- Number of doses taken in front of the pharmacist (specify number of doses observed per day or week): _____
- The patient can never take more than _____ doses at home between the dates on which he or she must take the medication in front of the pharmacist.

**Be sure to list all other opioids prescribed concurrently here.**

**CONFIDENTIAL TRANSMISSION BY FAX**

Pharmacy: _____

Fax number: _____ Date/Time: _____

[ Identification of the prescriber's location of practice ]

**Prescriber's name** (block letters): _____ **Permit n°:** _____

**Prescriber's signature:** _____ **Date and time:** _____

## PHARMACEUTICAL PRESCRIPTION FOR BUPRENORPHINE-NALOXONE (SUBOXONE®) MICRODOSING INDUCTION

APPENDIX 3

# BUPRENORPHINE-NALOXONE (SUBOXONE®) MICRODOSING INDUCTION

## Information for the Pharmacist

### What is buprenorphine-naloxone microdosing?

- In the context of opioid agonist therapy (OAT), buprenorphine-naloxone microdosing induction is an alternative method to the standard, off-label induction method, which relies on the repeated administration of low doses of buprenorphine-naloxone, concomitantly with the other opioids used.[1] Consumption of the other opioids will be discontinued gradually, or after 7-13 days.
  - The slow accumulation of buprenorphine at mu type (μ) opioid receptors allows for the gradual replacement of pure opioid agonists by buprenorphine without causing significant withdrawal symptoms.[1]
- The usual average microdosing period is 7 or 13 days, compared with 2 days for standard induction protocols.[2-5] See the prescription.

### Why use this induction technique?

- Microdosing can be used to:
  - Initiate buprenorphine-based OAT in an individual taking opioids (whether prescribed or not);[4,5]
  - Transfer an individual who is already on another OAT (e.g., methadone, slow-release oral morphine) to buprenorphine.
- Microdosing is particularly indicated for:
  - Individuals for whom the withdrawal symptoms associated with the standard induction method are unacceptable;[5-9]
  - Individuals for whom withdrawal is not recommended (e.g., CAD, induction of a pregnant person);[5]
  - Individuals whose withdrawal is not sufficient for standard induction upon arrival at a clinic or in an emergency room.[5,10]

### What support should be provided to individuals who are following a buprenorphine-naloxone microdosing induction protocol?

- When it is deemed safe to serve all the doses of buprenorphine-naloxone required, the offer can be made to use of a blister pack or dispill.
- In cases where the individual is already taking buprenorphine-naloxone on a daily basis and is prescribed a twice-daily dose, the first dose is generally administered in the pharmacy, and the second dose is given to the individual.[3,11]
- The individual will also receive a fact sheet detailing the induction schedule, the steps to be followed to ensure that the induction goes well, and some advice, including the following:
  - It is not necessary to observe a strict interval between doses of buprenorphine-naloxone. They can be taken a few hours before or a few hours after the scheduled time.
  - Buprenorphine-naloxone can be taken at the same time as other opioids. It is not necessary to take these drugs at different times.
  - Withdrawal symptoms may be experienced during the process. A withdrawal kit will also be prescribed, and can be used as needed.
- If consecutive doses are missed over a period exceeding 48 hours, the community pharmacist may reassess the individual and adjust the prescription. If necessary, the pharmacist can contact the prescriber. See: Optimisation du rôle du pharmacien communautaire (in French only).

| Missed doses | Recommended action(s) |
|---|---|
| Less than 48 hours without a dose | Take the missed dose as soon as possible.<br>Restart the induction schedule from the missed dose. |
| More than 48 hours without a dose | Reassess the individual.<br>If necessary, contact the prescriber. |

Inspired by: Marwah et coll.[3], Patel et coll.[4], Cho et coll.[12] et CRDQ[13].

For a complete guide to using the buprenorphine-naloxone microdosing induction method, consult the Dépendence section at https://dependanceitinerance.ca (the site includes many documents in English).

***Document inspired by work carried out by the Centre de réadaptation en dépendance du CIUSSS de la Capitale-Nationale.***

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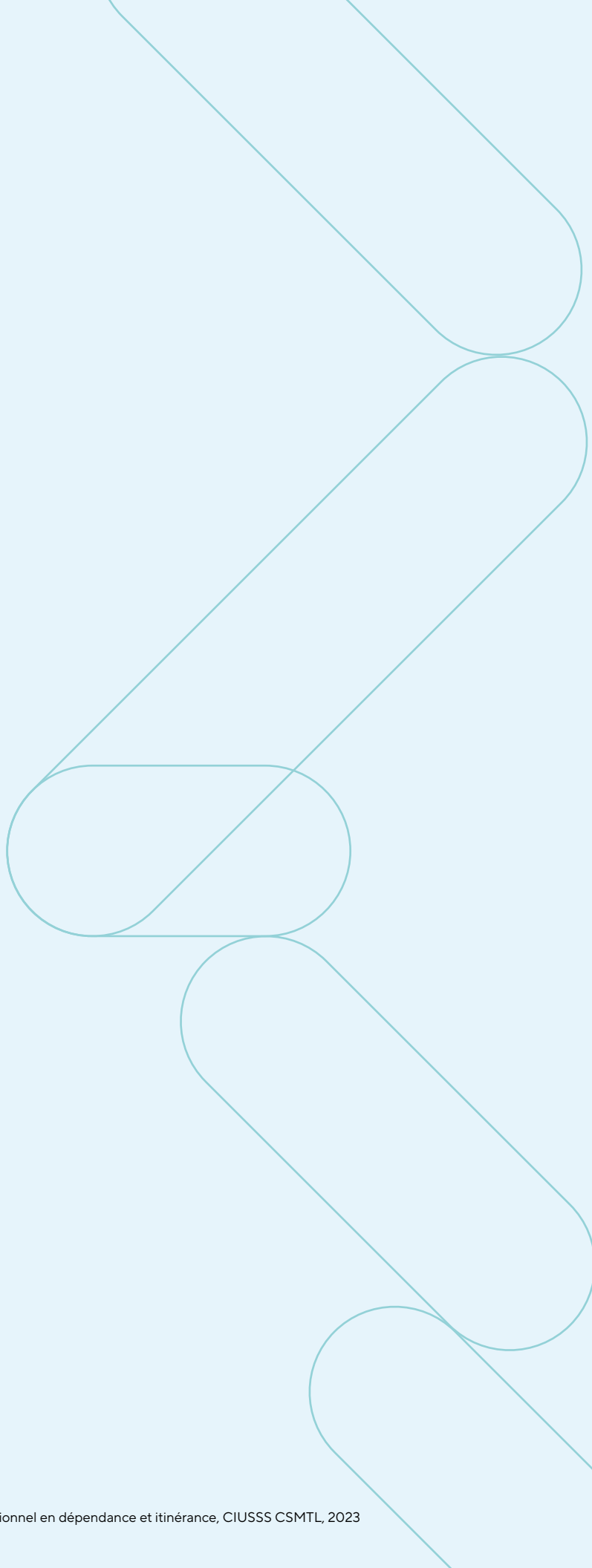

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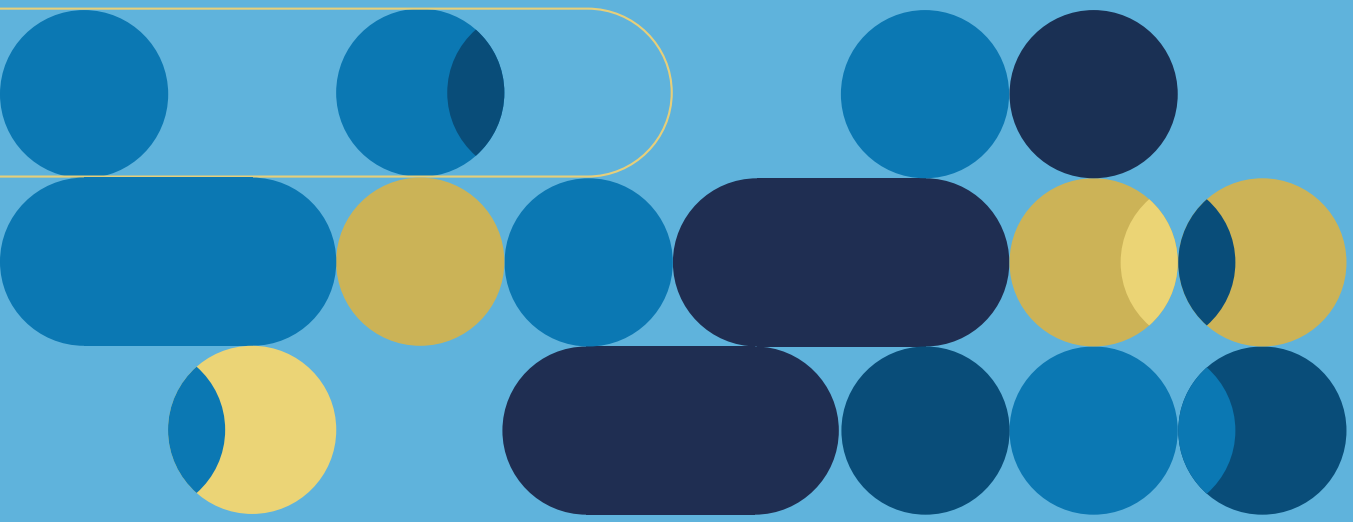

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