BUPRENORPHINE/NALOXONE *SUBOXONE* GUIDE

DOSAGE FORMS

Generic: 2mg/0.5mg, 8mg/2mg
Brand: 2mg/0.5mg, 8mg/ 2mg, 12mg/3mg, 16mg/4mg (need to order; not often stocked)
✓ Can be split/ crushed to ease dosing

PMS: 2mg/0.5mg

8mg/2mg

DOSING: INDUCTION (methods for initiating someone)

Take Home: SOWS (Subjective Opioid Withdrawal Scale)
Need to ensure score ≥ 17 (moderate-severe withdrawal) prior to initiation
☺ Patient can objectively determine when appropriate to start home induction of Suboxone appropriately as they can quantify their own symptoms and use this for continuous self-monitoring
☹ Limited by understanding/ health literacy of patient - risk of precipitated withdrawal if used too early (may deter patient from continuing use)

Clinic Based: COWS (Clinical Opioid … Scale)
Need to ensure score >12 (moderate withdrawal) prior to initiation
☹ Determined based on clinician judgement - may not fully reflect patient experience
☹ May require training/ practice by clinicians for more accurate assessment

STARTING RX/ DOSE

DAY	USE	MAX DOSE
Day 1	Dissolve 4mg now and 2-4mg in >1 hr PRN	12 mg/ day
Day 2	Take day 1 dose plus additional 4mg PRN	16 mg/ day
Day 7	May reach 24 mg by this time	24mg/ day

DOSING: MAINTENANCE

The proper maintenance dose is one at which cravings and physical withdrawal are averted for at least 24 hours without causing sedation (typical doses range from 16-24 mg daily)

If withdrawal symptoms are present before the next dose, consider a dose increase (usually by 2-4mg at a time)
Max dose = 24 mg

- Suboxone has a ceiling effect at higher doses (at 16 mg, 97% of receptors are already saturated)
- **Health Canada only approved 24 mg (max)** but doses up to 32 mg have been used with effectiveness (worldwide)

WITHDRAWAL MANAGEMENT

Clonidine
- **Rationale**: anticholinergic effects help manage withdrawal related sweats and chills
- **Dosing**: 0.1-0.2 mg PO Q6-8H PRN (with dose adjusted based on symptoms)
- **S/E**: drowsiness, dizziness, hypotension, dry mouth, constipation

Analgesics (NSAIDs/Tylenol)
- **Rationale**: for myalgia/ fever/ aches
- **Dosing**: Ibuprofen: 200-400 mg PO Q4-6H PRN (max daily dose: 2400 mg) Acetaminophen: 500-1000 mg PO Q6-8H PRN (max daily dose: 4000 mg)
- **S/E**: GI upset with NSAIDs

Oxybutynin
- **Rationale**: anticholinergic activity effective for hyperhidrosis management
- **Dosing**: 2.5-5 mg PO once daily to TID PRN
- **S/E**: dizziness, drowsiness, dry mouth, constipation, urinary retention

Hydroxyzine
- **Rationale**: antihistaminic activity for managing pruritis, anxiety, and helps with sleep
- **Dosing**: 25 mg PO TID-QID (for anxiolytic activity, higher doses of 50-100 mg PO QID may be required)
- **S/E**: sedation, dry mouth

Dimenhydrinate
- **Rationale**: antihistaminic and anticholinergic effects for management of nausea, vomiting, diarrhea, itch
- **Dosing**: 50-100 mg PO Q4H PRN
- **S/E**: drowsiness, dizziness, dry mouth, potential increase in nervousness, caution potential for abuse

Loperamide
- **Rationale**: anti-diarrheal effects for managing withdrawal related diarrhea
- **Dosing**: 4 mg (2 tabs) PO initially, then 2 mg (1 tab) PO after each loose bowel movement (max daily dose: 16 mg (8 tabs))
- **S/E**: dizziness, abdominal cramps, nausea, constipation (if overuse)

MISSED DOSES (From ACP ODT Guidelines)

Table 3: Managing missed buprenorphine-naloxone doses

Number of missed consecutive days	Dose	Dose adjustment
Greater than seven days	Greater than 8 mg	Restart at 4 mg
Six to seven days	Greater than 8 mg	Restart at 8 mg
Six or more days	6 to 8 mg	4 mg (50% reduction)
Six or more days	2 to 4 mg	None

Adapted from: Handford C. et al. *Buprenorphine/naloxone for Opioid Dependence: Clinical Practice Guideline*. Centre for Addiction and Mental Health(v), 2011.

MECHANISM OF ACTION/ SAFETY PROFILE

Buprenorphine:
- Partial agonist at μ opioid receptor to limit euphoria/ side effects due to ceiling effect → limits respiratory depression/ increasing safety when titrating
- High affinity for μ receptor → ability to compete with other opioid agonists and displaces them and has long acting effect (24 hrs) so only require once daily dosing

Naloxone:
- Pure opioid receptor antagonist
- Rationale → deterrent to prevent diversion as SL/PO intake has no activity (due to first pass metabolism) but if tampered to be injected, naloxone is bioavailable and will block other opioids, thereby causing withdrawal

USE IN PREGNANCY & BREASTFEEDING

- Use in pregnancy, no longer contraindicated [Health Canada]
- Monotherapy buprenorphine has more studies available to recommend use (unknown safety of naloxone in pregnancy). It is available via the Special Access Program.
- Compared to methadone, buprenorphine has less severe NOWS (Neonatal Opioid Withdrawal Symptoms) and potentially lower risk of preterm labour, larger head circumference, greater birthweight
- Use with caution in breastfeeding as buprenorphine and metabolite is found in breast milk and infant urine
- Potential for infant to experience opioid adverse effects if breastfed (monitor for drowsiness and difficulty breathing in infant)

USE IN PAIN MANAGEMENT

- Due to the long onset and duration of action of buprenorphine, NOT appropriate for acute pain management
- Only used for moderate-severe chronic pain (may require multiple daily doses vs once daily dose for ODT) when patient is stabilized
- Prefer to use non-opioid alternatives (e.g. non-pharmacological; NSAIDs, acetaminophen, or combination of both; etc.) for acute pain management over traditional opioids when concurrently initiating Suboxone for chronic pain use (due to risk of inducing precipitated withdrawal associated with high affinity of buprenorphine displacing other opioids at opioid receptors)

OVERDOSE MANAGEMENT

- Relatively uncommon due to ceiling dose effect
- Risk increases with concurrent use of sedating drugs (ex. benzos, ETOH)
- Overdose management may require higher quantity/ dose of naloxone to be used than normal (due to high affinity of buprenorphine)

DIVERSION

- Tampering with SL formulation for IV injection will induce opioid withdrawal (due to activation of naloxone)
- If sold to others and used inappropriately (swallowed instead of SL), buprenorphine undergoes first pass metabolism in liver and opioid effects are limited/ ineffective – would be insufficient to induce euphoria
- If diverted, risks are lower compared to other opioids due to formulation

When/ Why to Allow Carries:

- May consider daily dispense upon induction if concerns of diversion
- But carries may quickly be provided once reach stabilized dose and patient able to demonstrate adherence/ lack of concerns on diversion/ stable living environment (considering safety profile)
- Take home inductions can be provided as long as follow up can be ensured
- Carries may increase adherence (compared to daily witness), reduce stigma, improve outcomes, and enable more "normal" life (e.g. jobs)
- Patients may benefit from going to dose at pharmacy a few times per week (gets them out, gives them a purpose, increasing social interactions)
- Dispensing: witness 2x per week, carry rest - ensures monitoring
- May authorize additional carries depending on UDT results, progress, relationship with practitioners, level of trust etc.

COLLABORATION WITH PHARMACY

- **MAR** – generic template for dosing (name, DOB, date, monitoring, misses)
- **Notification template** for missed doses/other issues (vomited doses (witnessed or not), diversion attempts (details) etc.
- **Opioid Treatment Agreements/ Contract** between patient, pharmacy, and/or physician → pending pharmacy preference

SIDE EFFECTS AND MANAGEMENT

Headache (usually transient in 1st week)
→ use analgesics (NSAIDs/ Tylenol – see above)
Constipation (may persist/need long-term treatment)
→ routine bowel regimen (PEG 3350 17 g PO daily, sennakot 8.6 - 17.2 mg PO daily); maintaining adequate hydration/ fibre intake
Nausea (usually occurs early on)
→ dimenhydrinate prior to Suboxone dose and PRN in between doses; use ginger to alleviate sensation
Dry mouth
→ staying well hydrated (especially prior to dose); use of artificial saliva (ex. Biotene)
Somnolence
→ may require dose decrease if possible; question other drugs being used (Rx or street)
Insomnia
→ sleep hygiene; assess for untreated anxiety/ depression
→ question if dose too low (causing withdrawal at night?) or if other drugs being used (stimulants?)
Dizziness (occurs more commonly at higher doses)
→ staying hydrated to prevent hypotension (check BP), consider dose decrease if possible
Sweating (may persist/need long-term treatment)
→ pharmacologic management with clonidine, oxybutynin (see above)

Note: At correct dose, Suboxone does not impair motor skills, mental capacity, or ability to operate cars/ machinery

MONITORING & FOLLOW UP

- **On induction:** follow up for withdrawal symptoms ideally within same day to determine if sufficient dose provided
- **During titration:** follow up daily or every 2-3 days to determine effectiveness/ for craving control/ adverse effects
- **Once stabilized:** follow up every 2 weeks (initially) then can be extended to monthly (case by case basis)

Urine Drug Tests (UDT)

- At baseline to confirm substances used (reported/ non-reported)
- Random UDT within 2 months of initiation
- Once stabilized, may randomly test at least 4 times a year for maintenance of carries (frequency dependent on case by case basis)

Interpretation of results

- Need to specifically order for buprenorphine on lab requisition
- Detected as norbuprenorphine in analysis
- Buprenorphine can be detected for 7-10 days at typical doses (varies on each individual's metabolism)
- Provide no more than 24 hours notice to complete random urinalysis
- If buprenorphine not detected, question diversion

COVERAGE & COST

NIHB: Covers generic and brand name in full
AB Blue Cross (AISH, AB Works): Covers generic in full and brand name with copay
Indivior Compassionate: For brand name in exceptional, short term circumstances
Note: Programs available for multi-use coverage covering up to 50% of BRAND name Rx.
e.g. Innovicares (may lead to overall higher cost to public payor)

→ NOTE: emergency coverage is also available (with varying degrees provincially)

COST (per tab):

- Brand: 2/0.5mg → $2.73
  8/2mg → $4.83
- Generic: 2/0.5mg → $0.67
  8/2mg → $1.18
- Street value: $30

→ high profit in jail ($100)

PRESCRIBING RESTRICTIONS

- Prescribing restrictions for prescriptions and Triplicate Programs vary provincially (see below) - confirm with local guidelines
- Physicians and Nurse Practitioners do NOT require Health Canada exemptions or special training to prescribe Suboxone → may help improve patient access
  →NOTE: Although, provincial regulatory bodies may require select specifications/ approval (depending on indication and route of buprenorphine) and/or highly encourage additional training/ completion of courses before prescribing - confirm with local legislation for prescriber requirements

British Columbia	**Alberta**	**Saskatchewan**	**Manitoba**	**Ontario**
• ALL buprenorphine products are REQUIRED to be written on a duplicate prescription pad as per Controlled Prescription Program (CPP) • Prescribing patterns are monitored under the Prescription Review Program	• Buprenorphine/naloxone combination products do NOT require a triplicate prescription (new as of July 15, 2019) but prescribing patterns remain to be monitored by program • Single entity buprenorphine and all buprenorphine products for veterinary use remain to REQUIRE prescriber personalized triplicate prescriptions	• ALL buprenorphine products are monitored under the Prescription Review Program (PRP) • Specific "triplicate/ duplicate" prescriptions are not used in SK	• ALL buprenorphine products are REQUIRED to be written on a M3P prescription as per the Manitoba Prescribing Practices Program (M3P)	• ALL buprenorphine products are monitored under the Ontario Narcotic Monitoring System for prescribing, dispensing, and use patterns • Specific "triplicate/ duplicate" prescriptions are not used in ON
New Brunswick	**Nova Scotia**	**Newfoundland & Labrador**	**Yukon**	**PROVINCES/ TERRITORIES WITHOUT ANY MONITORING/ PRESCRIBING PROGRAMS FOR NARCOTICS:**
• ALL buprenorphine products are monitored under the New Brunswick Prescription Monitoring Program (established from the Nova Scotia program) for prescribing and dispensing patterns via their e-health system • Specific "triplicate/ duplicate" prescriptions are not used in NB	• ALL buprenorphine products are monitored under the Nova Scotia Prescription Monitoring Program for prescribing and dispensing patterns • Specific "triplicate/ duplicate" prescriptions are not used in NS	• ALL buprenorphine products are REQUIRED to be written on a prescriber personalized Tamper Resistant Drug Pad (a prescription with security features to prevent forgeries but this is NOT a monitoring program)	• Follows triplicate prescription program administered by Alberta – see Alberta for prescribing details	• Quebec • Prince Edward Island (does have Drug Information System monitoring dispensing history but not narcotic specific) • Northwest Territories • Nunavut

References: Alberta College of Pharmacy ODT Guidelines 2014, Alberta Interactive Drug Benefit List, BCCSU Guidelines for Clinical Management of OUD 2017, BCCSU Treatment of OUD in Pregnancy 2018, Canadian Association of Schools of Nursing - Prescription Monitoring Programs Across Canada, College of Surgeons and Physicians of Alberta - Triplicate Prescription Program College of Physicians and Surgeons of British Columbia - CPP, College of Physicians and Surgeons of Manitoba - M3P, College of Physicians and Surgeons of Saskatchewan - PRP, Controlled Drugs and Substances Act, Dynamed Plus, Innovicares Suboxone Benefit Changes Fax Information Update, Lexicomp, National Clinical Guidelines and Procedures for the use of Buprenorphine, NIHB 2019 Report - Drug Benefit List, New Brunswick Prescription Monitoring Program, Nova Scotia Prescription Monitoring Program, Ontario Narcotic Strategy, RxTx, Tamper Resistant Drug Pad Program, US Drug Test Centers

Abbreviations: S/E = side effects, UDT=urinary drug testing

September, 2019

Created By: Brittany Wong (PharmD) Reviewed By: Amy Semaka (BScPharm, PharmD) - Alberta - April 2019; Updated September 2019
Reviewed in collaboration with RxFiles and posted online at, www.RxFiles.ca