Pharmacy & Therapeutics Committee
Request for Addition of Buprenorphine/ Naloxone to Drug Formulary

Submitted/Prepared by: _____Designation/Title:_____Contact ext.: _____

Drug for Addition to Drug Formulary (e.g., generic name, proprietary name, therapeutic classification, dosage form):
Buprenorphine/naloxone (Suboxone®). Opioid (partial opioid/opioid antagonist). Tablets for sublingual use 2/0.5 mg and 8/2 mg

BACKGROUND AND RATIONALE

Opioid agonist therapy (OAT) is the recommended first-line treatment for opioid use disorder (OUD) and a core component of a multi-pronged response to the current opioid crisis. There is strong evidence that OAT with methadone or buprenorphine is significantly more effective than non-pharmacologic treatments at retaining people who inject opioids in treatment, reducing morbidity and mortality from ongoing opioid use. Initiation of OAT with buprenorphine is recommended as first-line treatment whenever feasible because of its reduced risk of toxicity, relative accessibility, and more flexible dosing schedule compared with methadone.

Buprenorphine is a partial opioid agonist with high affinity for the opioid receptor, long duration of activity, and a ceiling effect. These properties combine to make buprenorphine an effective treatment for opioid withdrawal symptoms and for opioid use disorder. The Health Quality Ontario (HQO) Quality Standard for OUD specifically recommends that opioid withdrawal be treated with buprenorphine within two hours of presentation.

Patients attending the emergency department (ED) with opioid overdose or other conditions associated with opioid use present an opportunity to initiate treatment for opioid use disorder and initiate a life-saving intervention. Due to its safety profile, buprenorphine does not require additional certification or authorization for use as methadone does.

Patients who receive their first doses of buprenorphine in the ED are more likely to follow up with addiction treatment than those who are offered referral to addiction services. Trials in both Canada and the United States have demonstrated that initiating buprenorphine in the ED is associated with reductions in subsequent ED visits.

There is good evidence that initiating buprenorphine treatment in the ED is feasible and can be completed in a timely manner. Clinical algorithms, order sets, template prescriptions, and patient handouts will all be available to facilitate treatment initiation and plan for continuation of care.

COSTS

Ontario Drug Benefits (ODB) pays $1.34 for a 2 mg tablet of buprenorphine/naloxone and $2.37 for an 8 mg tablet. The usual maximum initial dose of buprenorphine dispensed in the ED would be would be 16 mg as 8 x 2 mg tablets, for a total cost of $10.72. Buprenorphine/naloxone tablets are more expensive than clonidine or IR morphine ($0.17 each), but the direct costs of bup/nx treatment will be far outweighed by its indirect savings, i.e., fewer ED visits and hospitalizations for opioid use disorder and its complications.

RECOMMENDED DOSE AND ADMINISTRATION (approved indications)

Initial doses range from 2–16 mg of buprenorphine. Patients who are on full-dose therapy may be on doses of up to 32 mg.

Protocols will be in place and advise:

- Initial dose of 4 mg SL when the patient has a score of 13 or above on the Clinical Opioid Withdrawal Scale (COWS) and appropriate time since their last opioid use.
- Initial dose of 2 mg for people at risk of respiratory depression such as those with heavy alcohol or benzodiazepine use, or at risk of medical complications from precipitated withdrawal such as elderly and medically complex patients.
- Reassessment at one to two hours and repeat dosing if the patient is still in withdrawal and not sedated.

We suggest having 2/0.5 mg and 8/2 mg tablets on formulary.

ADVERSE EFFECTS

Opioid treatment can be associated with respiratory depression, especially in patients with heavy alcohol or benzodiazepine use or elderly patients with complex co-morbidities. However, buprenorphine is safer than other opioids.

Patients treated with opioids are monitored for respiratory suppression and level of consciousness.

Administration of buprenorphine/naloxone incorrectly can result in precipitated withdrawal, a condition associated with severe opioid withdrawal symptoms. This can require treatment with opioid agonist and non-opioid treatments.

COMPARISON

Drug formulary alternatives include opioids (e.g., morphine, methadone) and non-opioid treatments such as clonidine, acetaminophen, and non-steroidal anti-inflammatories.

Morphine and other short-acting opioids are effective at relieving withdrawal symptoms acutely but do not reduce the patient's risk of resuming opioid use/overdose after discharge; they are effectively contraindicated for the treatment of opioid withdrawal in the ED.

Clonidine and other non-agonist therapies are modestly effective at treating opioid withdrawal symptoms; buprenorphine has been found to be more effective at relieving opioid withdrawal and at retaining people in treatment for opioid use disorder.

Relative to other medications used for OAT (methadone and slow-release oral morphine), buprenorphine has lower rates of overdose and toxicity.

Clinicians do not require specific certification to prescribe buprenorphine.

Buprenorphine may be less effective than methadone with people who use high-potency opioids frequently, such as patients who inject fentanyl on a daily or near-daily basis.

CONCLUSIONS

Buprenorphine/naloxone tablets should be added to the hospital formulary so that patients presenting with a complication of opioid use/opioid use disorder can initiate treatment without delay.

CONFLICT OF INTEREST DISCLOSURE

QUESTIONS TO ADDRESS

- Cost
- How many capsules to stock at a given time
- Time to expiry
- Adding buprenorphine to the ED opioid counts

RECOMMENDATIONS

We recommend holding the following doses of buprenorphine/naloxone in the ED:

- 8/2 mg x 8 tablets
- 2/0.5 mg x 20 tablets

RELEVANT LITERATURE

Bruneau J, Ahamed K, Gover M, Poulin G et al. Management of opioid use disorders: a national clinical practice guideline. *CMAJ* 2018 Mar 5; 190(9): E247–E257

Health Quality Ontario. Quality Standards: Opioid Use Disorder. Toronto 2017.

D'Onofrio G, O'Connor PG, Pantalon MV, Chawarski MC, Busch SH, Owens PH, et al. Emergency department-initiated buprenorphine/naloxone treatment for opioid dependence: a randomized clinical trial. *JAMA*. 2015;313(16):1636-44.

Srivastava A, Kahan M, Njoroge I, Sommer L. Buprenorphine in the emergency department: Randomized clinical controlled trial of clonidine versus buprenorphine for the treatment of opioid withdrawal. *Can Fam Physician* 2019 May 65 (5): e214-e220.

Hu T, Snider-Adler M, Nijmeh L, Pyle A. Buprenorphine/naloxone induction in a Canadian emergency department with rapid access to community-based addictions providers. *CJEM* 2019 Jul; 21 (4): 492-498.

Klaiman,M, Bahinski K, Costello L, Dell E, McGowan M, Medcalf K…Cheng,A. (2018). L027:Improving emergency department management of acute opioid withdrawal. *CJEM*, 20(S1), S16-S16. doi:10.1017.cem,2018.89.

Bruneau J, Ahamed K, Gover M, Poulin G et al. Management of opioid use disorders: a national clinical practice guideline. *CMAJ* 2018 Mar 5; 190(9): E247–E257

Health Quality Ontario. Quality Standards: Opioid Use Disorder. Toronto 2017.

STAKEHOLDER SIGNATURES

Program:

Clinical Manager:

	Print Name	Signature	Date
_____	_____	_____	_____

Clinical Director:

	Print Name	Signature	Date
_____	_____	_____	_____

Vice President of Patient Care:

	Print Name	Signature	Date
_____	_____	_____	_____

Program:

Medical Director:

	Print Name	Signature	Date
_____	_____	_____	_____

Director of Pharmacy:

	Print Name	Signature	Date
	_____	_____	_____