11/21/22 mt bb

Low-threshold initiation and management of buprenorphine during pregnancy in the outpatient setting

1. Background

Buprenorphine is a type of Medication for Opioid use disorder (MOUD) that is safe and effective. Buprenorphine has unique pharmacological properties that help:

- Diminish the effects of physical dependency to opioids, such as withdrawal symptoms and cravings
- Increase safety in cases of overdose
- Lower the potential for misuse

Buprenorphine is available through the ANMC formulary. Subutex is the brand name for a buprenorphine-only product and currently available in tablets intended to be dissolved under the tongue. Suboxone is a brand-name combination product of buprenorphine and naloxone. Suboxone is available in tablet and film form. At the ANMC formulary only the film product is available. Buprenorphine-naloxone versus buprenorphine alone is the preferred medication treatment as it has a lower abuse risk. There is also an injectable form of buprenorphine, which is not discussed in these guidelines.

Only a fraction of people who need treatment with buprenorphine receive it. Many buprenorphine treatment programs have rigid requirements for entry and continuation, limiting the number of people who receive treatment. Low-threshold buprenorphine treatment should be employed at ANMC. Low-threshold is defined by the following principles: 1) Same-day treatment entry 2) Harm reduction approach 3) Flexibility, and 4) Wide availability in places where people with opioid use disorder go.

2. Candidates for at-home buprenorphine initiation

Buprenorphine products can be initiated at home in people with a history of opioid addiction and polysubstance abuse (i.e. opioids plus alcohol, cocaine, methamphetamine, benzodiazepines, etc.) with the ideal goal of abstinence from all substances. This is often a subjective decision based on conversations with the customer-owner and the care team.

To maximize the likelihood of success for the customer-owner with advanced Opioid Use Disorder (OUD), consideration of residential services may be appropriate to help support the emotional and physical challenges that can jeopardize continuation of MOUD. Southcentral Foundation's Detox unit should be offered as an alternative to outpatient initiation of MOUD for these individuals. The detox providers are available by Tiger Text and will prioritize pregnant customer-owners.

3. Cautions with buprenorphine

The only true contraindication to buprenorphine use is a hypersensitivity reaction. Customer-owners with significant liver dysfunction may need to be prescribed a mono-product (buprenorphine alone/Subutex) and at lower doses with closer monitoring of liver function.

Customer-owners undergoing opioid withdrawal are at risk of suicide, driven by the distress and fear that often accompanies opioid withdrawal and/or feelings of failure among patients unable to complete the process. Patients should be assessed for suicidality throughout supervised withdrawal.

Another significant risk associated with medically supervised withdrawal is unintentional overdose, often a result of a sequence of events:

- Customer-owner elopement during supervised withdrawal.
- Resumption of opioid use in the context of severe craving and desire to ameliorate remaining withdrawal symptoms.
- Opioid overdose of customer-owners who resumed use at their pre-withdrawal "dose."

Customer-owners should be warned of the risks associated with decreased opioid tolerance.

4. Screening and Diagnosis

Universal Screening for substance use should be part of comprehensive obstetric care and should be done at the first prenatal or transfer visit in partnership with the pregnant person. Routine screening should rely on a validated tool, such as 4Ps Plus and SBIRT (AUDIT-C). Any person with a positive screen should be offered a brief intervention and behavioral health services to identify emotionally at-risk individuals and assess for mental health concerns.

5. Steps to begin buprenorphine treatment – See provider check list (Appendix A)

5.1 An inventory of past and current substance use and past OUD treatment should be collected.

5.2 Review the dangers of using benzodiazepines when taking buprenorphine with customer-owners. Overdose deaths have occurred when buprenorphine and benzodiazepines were concomitantly abused. The customer-owner should also be informed of the risk of using alcohol and buprenorphine.

5.3 Review risk of decreased tolerance to opioids in the setting of relapse.

5.4 Review risk of Neonatal Opioid Withdrawal Syndrome (NOWS) which are lower with buprenorphine than other opioid products but carries continued risk.

5.5 A query of the Alaska Prescription Drug Monitoring Program to assess prescription opioid use is recommended.

5.6 A physical examination should be completed, with attention to potential sequelae of substance use.

5.7 The following laboratory tests should be obtained, either with routine pregnancy labs or adjunct to: Complete Blood Count, Complete Metabolic Profile, hepatitis B surface antigen, hepatitis C antibody, HIV, Syphilis, Gonorrhea, Chlamydia, Trichomonas, Urine Drug Screen POC and the Millennium Confirmatory Drug Tox Panel – High Risk.

5.8 Anyone with a substance use disorder or living with someone with a substance use disorder should be prescribed naloxone in case of overdose.

5.9 Arrange for collaboration with Behavioral Health Consultant and Community Resource Specialist.

5.10 Develop a follow up plan for 2-3 days either in-person or by phone.

5.11 Begin discussion on long term planning for buprenorphine care.

6. Management of OUD with at home micro-dosing buprenorphine products

6.1 Fentanyl products are frequently found in illicit opioid products. Although one-time/short-term use of fentanyl clears relatively quickly, long-term/chronic use of fentanyl gets stored in the fat (lipophilic) and can be released more slowly. Customers can go into precipitated withdrawal, even when waiting up to 72 hours post-use and even when having a relatively high Clinical Opiate Withdrawal Scale (COWS) score. Repetitive small buprenorphine doses with sufficient dosing intervals should not precipitate withdrawal. Because of the long binding time to the receptor, buprenorphine will slowly accumulate at the opioid receptor. Over time, the full mu-agonist will be replaced by the buprenorphine at the opioid receptor

6.2 Initially, customer-owners should be seen in person or by phone frequently while induction is being completed, from daily to every 2-3 days. Then weekly visits until they are well stabilized. Once well stabilized, frequency will be determined by the provider and customer-owner.

6.3 Provide instructions on starting Buprenorphine-Naloxone micro-dosing (Appendix B). The graph below provides micro dosing instructions of buprenorphine.

	Dose		**Stop opioid Day**
	AM	**PM**	
Day 1	0.5 mg		
Day 2	0.5 mg	0.5 mg	
Day 3	1 mg	1 mg	
Day 4	2 mg	2 mg	
Day 5	3 mg	3 mg	
Day 6	4 mg	4 mg	
Day 7	8 mg	?	No use today
Day 8	Day 7 total dose		No use today

The customer-owner will continue opioid use as needed through day 7 of the initiation plan. On Day 7 of initiation the 8 mg dose should be taken in the morning and in the evening a second dose of buprenorphine can be taken as needed at a dose as needed. On day 8 the total dose taken on day 7 would be taken in the morning. Some flexibility with this plan will be needed to address individual differences between patients due to the amount and type of illicit opioid that they have been using. Once patients have been taking at least a total of 4mg for the day (on Day 4), typically

the buprenorphine dose can more rapidly be increased as needed for patient comfort without eliciting precipitated withdrawal.

6.4 Due to the increased metabolic rate in pregnancy, twice a day dosing or "split-dosing" can sometimes be more effective than once a day dosing in pregnant customer-owners, especially in the third trimester. Use caution to avoid the customer-owner from getting a positive response instead of the desired elimination of withdrawal symptoms. Customer-owner should be cautioned about taking buprenorphine-naloxone on an as-needed basis which reinforces addiction behavior.

7. Management of OUD with at-home standard Buprenorphine-Naloxone

Certain clinical situations may warrant a standard induction plan. These may be people who have used buprenorphine in the past and are familiar with initiation of the product, are sure their opioid products are not fentanyl-contaminated through checking their products or urine with fentanyl test strips or are in the inpatient setting. The standard induction plan is included in Appendix C.

8. Supportive pharmacological methods

Supportive pharmacological methods can be prescribed in pregnancy to help with some symptoms associated with withdrawal and MOUD. The use of these medications concurrently can help the customer-owner achieve maintenance on the lowest dose possible. These medications include:

- Anxiety/Irritability/Restlessness: Hydroxyzine 25-100 mg po q 6-8 hours prn (maximum 400 mg daily)
- Diarrhea: Loperamide 4 mg po then 2 mg po every each loose stool (maximum 16 mg daily)
- Nausea/Vomiting: Ondansetron 4-8 mg po or IV every 12 hours as needed (maximum 16 mg daily)
- Muscle Aches/Joint Pain/Headache: Acetaminophen 650-1000 mg po q 4-6 hours prn (maximum 4000 mg daily)
- Muscle Spasm/Restless Legs: Cyclobenzaprine 5-10 mg po q 8 hours prn (maximum 30 mg daily)

6. Maintenance of Medications for Opioid Use Disorder during Pregnancy

6.1 Most customer-owners can be stabilized on a dose between 8 mg and 16 mg/24 hours (in QD or BID dosing). If the customer-owner requires a dose higher than 24 mg daily, consider residential treatment or treatment with outpatient methadone. The Addiction Medicine Physician with Four Directions may be consulted with OB providers over the phone as well as accept a referral for continued MOUD care.

6.2 The prescribing provider, BHC, and customer-owner will agree on frequency of visits to monitor MOUD. Initially, the customer-owner should be seen either in person or by phone every 2-3 days for the first two weeks, then weekly, and eventually monthly.

6.3 At each visit, effective dosing should be assessed and monitored.

6.4 Doses should be titrated according to regular review of the following clinical signs/symptoms:

6.4.1 Intoxication, withdrawal, and cravings over the past 24 hours

6.4.2 Additional drug use and the customer-owner's reason for use of illicit street drugs or prescription opioids

6.4.3 Side effects or other adverse events

6.4.4 Adherence to dosing regimen

6.4.5 Customer-owner's expressed satisfaction

7. Intrapartum and Postpartum Medication for Opioid Use Disorder

7.1 MOUD should be continued during antepartum, intrapartum, and postpartum care.

7.2 Be aware of the customer-owner's usual dose and schedule and try to maintain. (However, withdrawal is unlikely if the customer-owner is receiving opioids for pain control.)

7.3 Fentanyl may be used for analgesia, but higher and more frequent dosing may be required.

7.4 Epidurals and nitrous oxide are preferred for pain management.

7.5 Stadol (Butorphanol) should be avoided. It is a partial narcotic antagonist which may precipitate withdrawal.

7.6 Expect decreased Fetal Heart Rate variability and fewer accelerations.

7.7 Naloxone (Narcan) may be used as a life-saving measure in the mother. Opioid withdrawal seizures may occur if used during infant resuscitation.

7.8 Maximize multi-modal non-opioid options such as non-steroidal anti-inflammatories (NSAIDS), acetaminophen, local anesthetics, etc.

Use 0.5-4mg buprenorphine q4-8hr for pain, total daily dosing not to exceed 32mg in a 24-hour period. Conversion equivalent is 30mg PO morphine to 1mg SL buprenorphine, (ie: 60mg PO morphine equates to 2mg SL buprenorphine).

7.9 For customers-owners having cesarean delivery or who have greater pain management needs:

- Follow Enhanced Recovery after Surgery (ERAS) guidelines.
- Inject the cesarean incision with local anesthetic before starting the procedure or consider use of Transversus Abdominis Plane (TAP) Block.
- Use scheduled NSAIDs and acetaminophen .
- Gabapentin may be used for acute pain management in postpartum people and is safe in breastfeeding.
- Use opioids like hydrocodone and oxycodone PRN. Doses of hydrocodone or oxycodone may need to be greater than normally prescribed, or with increased frequency, to be effective in a patient who is on buprenorphine. Providers are encouraged to use the smallest amount of opioids upon discharge and arrange daily follow up contact either in clinic or by phone.

7.9 Breastfeeding should be encouraged in individuals who are stable on their opioid agonists, without recent use of illicit substances. If they are stable with their treatment without recent

return to use, the recommendation for breastfeeding should be made on a case-by-case basis factoring in their likelihood for relapse onto illicit drug use. The amount of buprenorphine in human milk is small and unlikely to have short-term negative effects on the developing infant. Breastfed infants have less severe NAS and are less likely to require pharmacological intervention than the formula-fed infants. Customers should be counseled about the need to suspend breastfeeding in the event of a relapse.

7.10 The neonate may need to stay at least 72 hours or longer. During the time from the mother's discharge to the baby's discharge, the Customer-owner should have their own buprenorphine or methadone to take. Rooming-in with newborn is encouraged.

7.11 Access to adequate postpartum psychosocial support services, including substance use disorder treatment and relapse prevention programs, should be made available.

7.12 Contraceptive counseling and access to contraceptive services should be a routine part of substance use disorder treatment among people of reproductive age to minimize the risk of unplanned pregnancy.

References

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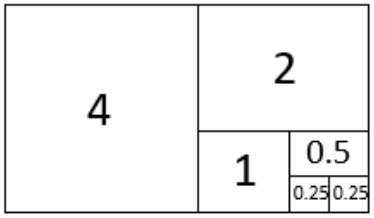
Appendix A

Buprenorphine initiation checklist

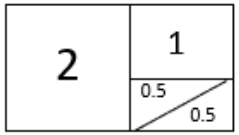
- ☐ An inventory of past and current substance use and past OUD treatment should be collected.
- ☐ Review dangers of concurrent benzodiazepine and/or alcohol use
- ☐ Review decreased tolerance to opioids in the setting of relapse
- ☐ Review risk of Neonatal Opioid Withdrawal Syndrome (NOWS)
- ☐ A query of the Alaska Prescription Drug Monitoring Program to assess prescription opioid use is required.
- ☐ A physical examination should be completed, with attention to potential sequelae of substance use.
- ☐ Obtain lab work as needed:
    - ☐ Complete Blood Count
    - ☐ Complete Metabolic Profile
    - ☐ Hepatitis B surface antigen
    - ☐ Hepatitis C antibody
    - ☐ HIV
    - ☐ Syphilis
    - ☐ Gonorrhea, Chlamydia and Trichomonas
    - ☐ Urine Drug Screen POC and Millennium Confirmatory Drug Tox Panel – High Risk
- ☐ Prescribe naloxone
- ☐ Review Micro-dosing instruction and handout with customer. Paying special attention to dose you are prescribing and instructions for cutting strips (Appendix B)
- ☐ Set up a follow up appointment for the next 2-3 days (phone appointments are acceptable)
- ☐ Begin discussion on long term planning for buprenorphine care

Appendix B

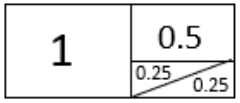
Micro-dosing is a way to start Buprenorphine without getting sick



Strip: 8 mg



Strip: 4 mg



Strip: 2 mg

Carefully check for which dosing strip you are using.

Standard Plan	Dose	Stop Heroin/Opioid Day
Day 1	0.5	
Day 2	0.5 + 0.5	
Day 3	1 + 1	
Day 4	2 + 2	
Day 5	3 + 3	
Day 6	4 + 4	
Day 7	8 + ?	No use today
Day 8	AM	No use

Personal Plan	Dose	Stop Heroin/Opioid Day	Notes
Day ____			
Day ____			
Day ____			
Day ____			
Day ____			
Day ____			
Day ____			
Day ____			
Day ____			
Day ____			
Day ____			

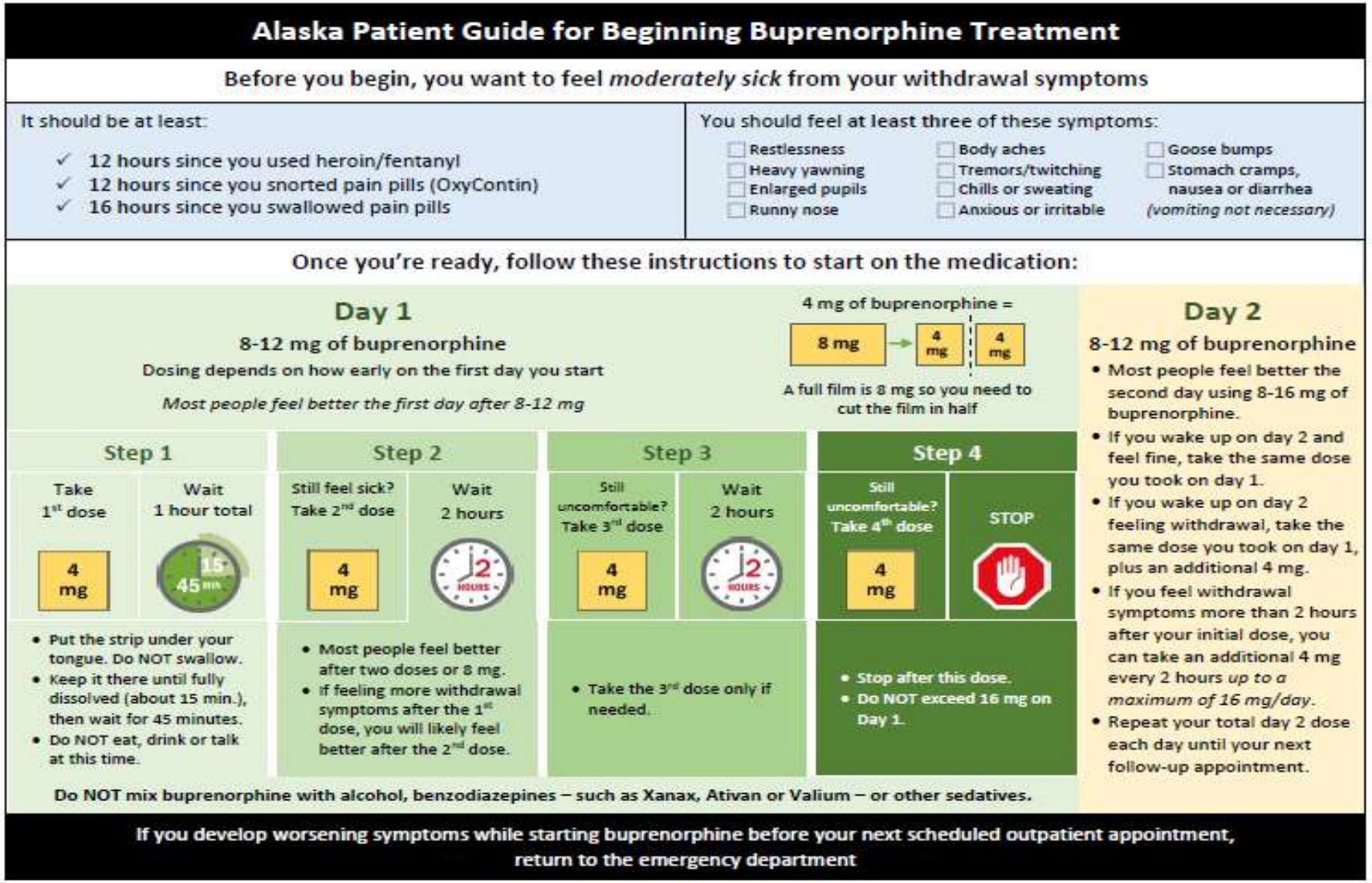
How does micro-dosing work?

- You can start buprenorphine without having to stop the heroin/opioid first.
- Micro-dosing starts buprenorphine slowly so that your body doesn't feel it.
- You don't have to be sick (in withdrawal) to start. You can keep using the heroin/opioid while you're getting to the right dose.
- Once you get to 8 mg of buprenorphine you will feel the heroin/opioid less. Then stop using and increase the buprenorphine until you feel comfortable up to 16 mg.
- Continue on this same dose that you were comfortable on, taking the total amount once daily in the morning starting the morning after you quit using.
- Follow your doctor's instructions for any dose increases beyond the 16mg.

Other medications. ***Take only the ones your doctor prescribes.***

- HYDROXYZINE: Take one to two tabs up to 4 times a day if you feel anxious. ☐ 25 mg ☐ 50 mg
- CYCLOBENZAPRINE: Take half to 1 tab up to 3 times a day for leg cramps/restlessness. ☐ 10 mg
- ONDANSETRON: Take one to two tabs up to 3 times a day for nausea/vomiting. ☐ 4 mg
- LOPERAMIDE (IMODIUM): Take one tab up to 4 times a day for diarrhea. ☐ 2 mg
- ACETAMINOPHEN (Tylenol): Take one to two tabs for body aches and headaches ☐ 500 mg

APPENDIX C - Standard Induction Plan



Developed by the Alaska Department of Health and Social Services with assistance from Dr. Mark Simon; based on materials from the National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services. *11/19/2019*