



Prescribing Guidelines for Pennsylvania



USE OF ADDICTION TREATMENT MEDICATIONS IN THE TREATMENT OF PREGNANT PATIENTS WITH OPIOID USE DISORDER

The misuse of opioids has increased significantly over the past decade. Pregnant women are represented in this problem. The 2014 National Survey on Drug Use and Health found that 0.2 percent of pregnant women report using heroin, and 1.1 percent report the illicit use of opioid pain medications.

This guideline addresses treatment for opioid use disorders during pregnancy and is intended to help health care providers improve patient outcomes when caring for these patients. The guideline is intended to supplement and not replace the individual provider's clinical judgement. All treatment should be determined

©2016 Brought to you by the Commonwealth of Pennsylvania

by the provider and the patient on an individual basis based on needs of the patient.

It is recommended that providers review associated Pennsylvania state guidelines related to the use of opioids in different patient populations, including 1) the use of opioids to treat chronic pain, 2) the use of opioids to treat pain in the emergency department, 3) the use of opioids in dental practice, and 4) the use of opioids in obstetric and gynecologic care, which all may provide insight into treatment options for this population.



These guidelines address stabilization, treatment and recovery management for opioid use disorder (OUD) during pregnancy. The guidelines are based on recent directives from the American Society of Addiction Medicine, The American College of Obstetricians and Gynecologists, Federal Guidelines for Opioid Treatment and other professional organizations involved in engaging this special high-risk population.

Patients should be co-managed through their pregnancy by an obstetrician and substance use disorder (SUD) specialist with critical need for collaboration. Patients may also be referred to a perinatologist for assessment.

BACKGROUND - Medication assisted treatment (MAT) is the use of FDA-approved medications in combination with evidence-based behavioral health therapies to treat substance use disorders. Currently, the only two FDA-approved medications indicated for the treatment of SUD during pregnancy are methadone and buprenorphine. Naltrexone is also used for opioid use disorders but is not recommended during pregnancy.

During pregnancy, medication assisted treatment (MAT) is the recommended standard of care for women with opioid use disorders. While any opioid use during pregnancy, including MAT medications, can increase the risk of neonatal abstinence syndrome, the use of medications improve maternal and infant outcomes and are now the standard of care in this patient population. MAT prevents erratic maternal opioid levels; protects the fetus from repeated episodes of withdrawal; is associated with improved obstetrical care and reduced fetal and neonatal morbidity and mortality; and supports and sustains the mother's recovery. Additionally, MAT for pregnant patients can also reduce the risk of other self-injurious drug and alcohol use.

Methadone has been used for the treatment of pregnant opioid-dependent women for over 50 years. In 1997, a National Institute of Health Consensus Panel recommended its use for the treatment of SUD during pregnancy. Buprenorphine was approved by the FDA in 2002 for treatment of opioid use disorders. In

2012, the American College of Obstetrics and Gynecology and the American Society of Addiction Medicine issued a Joint Committee Opinion recommending the use methadone or buprenorphine for the treatment of opioid use disorders during pregnancy.

Medication Assisted Treatment vs. Medical Withdrawal

It is not recommend to conduct medically supervised withdrawal from opioids for pregnant patients with opioid use disorders because it is associated with high relapse rates. This treatment recommendation has been endorsed by several organizations, including the World Health Organization (WHO), the American College of Obstetricians and Gynecologists, the American Society of Addiction Medicine and the U.S. Department of Health and Human Services.

THE GUIDELINES

1 The Use of Methadone for the Treatment of Opioid Use Disorder in Women Who Are Pregnant

Methadone is classified as a Schedule II drug, and its use for the treatment of opioid use disorders is highly regulated under 42CFR 8.12. Methadone may only be prescribed for MAT within a licensed and accredited opioid treatment program (OTP), except when the patient is hospitalized for a medical condition. Non-pregnant patients must have documented opioid dependence for a minimum of one year in order to receive methadone; pregnant women are exempt from this requirement, but their pregnancy must be certified. The pregnant patient must either be currently opioid dependent or have a documented history of opioid dependence and be at high risk for relapse.

OTP's are required to provide medical, counseling, vocational, educational, and other assessment and treatment services in addition to the treatment medication. Prenatal care and other gender-specific services must be provided to pregnant women by the OTP or by referral to appropriate health care providers.



OTPs must conduct a minimum of eight random drug tests per year. Initially, patients must attend the clinic daily to receive their methadone. There are specific criteria that, in addition to no illicit drug use, include a number of other behavioral indices to qualify for take-home medication. The allowance of take-home medication follows a rigid progressive timetable from three months in treatment for a one-day take-home to two years in continuous treatment to be eligible for a 30-day supply of take-home medication. State regulations may be more restrictive, e.g., in Pennsylvania the maximum take-home dose after two years in treatment is 13 days.

The admission process to an OTP is also highly regulated by both federal and state regulations in terms of requiring a full medical exam, psychosocial assessment (including family history, financial, educational, vocational and legal histories), the development of a treatment plan and timelines for completion.

A. Methadone Induction

Induction may take place either within an outpatient setting or an inpatient hospital setting. An inpatient setting is optimal, as it allows for a comprehensive approach with continuous medical monitoring. However, it requires a relationship with an OTP(s) so that the woman may be admitted immediately upon discharge from the hospital in order to be medicated on the following day. As such, outpatient induction is often a practical necessity.

Federal regulations specify that the initial dose of methadone must not be greater than 30mg. It is common to start with 10-20mg, depending on the patient's history and clinical presentation. If withdrawal symptoms persist after two to four hours, the initial dose may be supplemented with an additional 5-10mg. The maximum dose for the first day is 40mg, unless documented by the physician that the dose was insufficient to control withdrawal. Supplemental dose increases are given as needed until the patient is stable on a dose for 24 hours.

B. Maintenance

Methadone doses for pregnant women should be based on the same criteria as those for women who are not pregnant. The dose must be adequate to be therapeutic for the individual. No maximum dose of methadone should be set during pregnancy. The daily methadone dose should be adequate for the individual to prevent withdrawal phenomena and to promote participation in recovery-focused counseling and prenatal support activities.

Pregnant women may develop symptoms of withdrawal as pregnancy progresses and may require dose increases in order to maintain the same plasma level, due to physiological expansion in maternal blood volume. In some cases, splitdosing may be necessary to maintain a steady state for 24 hours. Additionally, a maternal dose should not be reduced during pregnancy to minimize neonatal abstinence syndrome (NAS). There is no compelling evidence that the reduction of a maternal dose will reduce NAS, and a non-therapeutic maternal dose may promote supplemental drug use and increase risk to the fetus.

Patients should be tested weekly by urine drug screen to confirm continued adherence to medication regimen and that the patient is not taking illicit drugs.

C. Intrapartum Dosing

Patients should continue with their regular methadone-dosing schedule, i.e., dose, timing and frequency during the intrapartum period. The patient should be reassured that she may request pain medication.

D. Intrapartum and Postpartum Pain Management

Patients receiving methadone who are undergoing labor and delivery can benefit from the same pain therapy offered to women not receiving methadone.

- I. Epidural or spinal anesthesia should be offered where appropriate.
- II. Opioid agonist-antagonist drugs such as buprenorphine, nalbuphine and pentazocine,



MUST be avoided, as they may precipitate acute withdrawal.

- III. Buprenorphine should NOT be administered to a patient who takes methadone, as it may precipitate withdrawal.
- IV. It is important to note that the daily methadone dose should be confirmed, then continued. While methadone for MAT is most often administered via a single daily dose, the total daily methadone dose can be divided and administered on an every six- or every eight-hour schedule during hospitalization, which may improve pain control.

Vaginal birth

- V. Acetaminophen and NSAID agents should be used for mild to moderate pain.
- VI. A short-acting opioid analgesic may be available on PRN basis as needed.
- VII. No opioid pain medication should be needed following discharge from the hospital.

Cesarean delivery

- VIII. Acetaminophen and NSAID agents should be used for mild to moderate pain.
- IX. Patients may require as much as a 70 percent increase in short-acting opioid requirements.
- X. Intravenous patient-controlled analgesia with morphine or hydromorphone may be used for the first 24 hours. Again, the patient's daily dose of methadone should be continued throughout the hospitalization.
- XI. Short-acting opioids may be needed in decreasing amounts for five to seven days to supplement breakthrough pain from regularly administered NSAIDs.

E. Postpartum Dosing

Women should continue on their established methadone dose postpartum. Dose adjustments may be necessary, especially if there were dose increases in the third trimester, as maternal blood volume returns to pre-pregnancy levels. Patients require monitoring for over-sedation at all times while on methadone protocol. In general, methadone dose adjustments should be managed by the physician responsible for MAT.

Patients may be at increased risk of an opioid overdose during this postpartum interval, and it is strongly recommended that the patient or family, spouses, and/or significant others that are connected with the individual have at-hand naloxone and receive training on this rescue medication to quickly intervene in the event of an overdose event.

It is best practice that patients continue methadone treatment and psycho-social treatment, including case management, throughout the postpartum period.

2 The Use of Buprenorphine for the Office-based Treatment of Opioid Use Disorder in Women Who Are Pregnant

Buprenorphine is a schedule III medication approved by the FDA for the treatment of opioid use disorders and, as such, may be prescribed by qualifying physicians in medical offices outside the OTP system. Patients who receive buprenorphine treatment from an office-based physician are given a prescription for buprenorphine to be filled at a local pharmacy. Although recommended, there are no requirements for behavioral therapies. However, if buprenorphine is provided within an OTP, all of the same treatment services are required as for methadone patients.

Buprenorphine is a partial opioid agonist and, as such, has a ceiling effect, i.e., a point at which effects do not increase even if the dose is increased. The maximum dose that can be prescribed is 32mg a day, but there does not appear to be much of a clinical advantage with doses greater than 24mg daily. Buprenorphine is



available both as a mono-therapy and in a combination form of buprenorphine and naloxone. The mono product is available only in a sublingual tablet, whereas the combination product is available both as tablet and a filmstrip. The combination product was developed specifically to decrease the potential for abuse and is the preferred medication for MAT, except for pregnant patients, because there is insufficient data on the safety of sublingual naloxone during pregnancy.

Office-based buprenorphine treatment is not appropriate for patients who use alcohol and/or benzodiazepines due to increased risk of respiratory depression.

Patient assessment prior to administration of buprenorphine for MAT should include the use of a screening tool to identify an opioid use problem, with further assessment to determine the scope of an opioid use disorder. If MAT is indicated, attention should be given to the appropriate treatment approach, setting and level of intensity based on needs of the individual patient.

A. Buprenorphine Induction

Induction to buprenorphine must take into account the type of opioid -- i.e., short-acting opioids or long-acting opioids -- that a patient is using. Because buprenorphine can precipitate withdrawal, patients should not have any residual effect from opioids before receiving an initial dose of buprenorphine.

If a patient is using short-acting opioids, there should be a minimum of 12-24 hours between opioid use and buprenorphine administration, and, as a result, the patient should be exhibiting mild to moderate withdrawal symptoms.

If the patient has been maintained on methadone, she must taper the methadone dose to a maximum daily dose of 30mg for at least one week, have received the last dose of methadone 24 hours before receiving buprenorphine, and, as a result, be exhibiting withdrawal symptoms before buprenorphine administration. For this reason, pregnant women

maintained on methadone should not be transitioned to buprenorphine.

The Clinical Opiate Withdrawal Scale (COWS) is a widely used tool to assess withdrawal in this setting.

Induction can take place in one day or over a week. A typical induction takes place over a three-day to one-week period. The following are general recommendations based on clinical experience and limited research. Providers should consider a patient's recent drug history when determining a therapeutic dose. Most patients can stay in outpatient status through induction.

Initial dose may begin with 2mg or 4mg, then be monitored for two to four hours. If withdrawal symptoms are not relieved, then an additional buprenorphine dose can be administered, followed by continued monitoring. If withdrawal symptoms persist, manage symptomatically with a maximum first day dose of 8 mg. Patients who require an initial dose greater than 8mg should be under direct observation. If a patient is still exhibiting withdrawal on subsequent days, follow the same procedure with a first dose equal to the total amount administered on the previous day plus 4mg until the patient has no withdrawal symptoms since last dose. Typical recommendations are a maximum of 12-16 mg on day 2 and 16-32 until withdrawal no longer occurs. The target dose for most patients is 12-16 mg by the end of the first week.

It is expected and recommended best practice that individuals be referred and escorted (if possible) to a licensed treatment site for screening and comprehensive assessment to determine the most clinically appropriate intensity and type-of-psychosocial service needed to supplement the medication regimen.

B. Maintenance

The dose of buprenorphine must be adequate to be therapeutic for the individual.

Pregnant women may develop symptoms of withdrawal as pregnancy progresses and may require



dose increases in order to maintain the same plasma level. Additionally, the maternal dose should not be reduced during pregnancy to minimize neonatal abstinence syndrome (NAS). Buprenorphine dose reduction during pregnancy does not improve fetal outcomes and may increase the risk of recurrent substance use disorder in the mother.

Patients should be tested weekly by urine drug screen to confirm continued adherence to the medication regimen and that the patient is not taking illicit drugs.

C. Intrapartum Dosing

Patients should continue with their regular buprenorphine-dosing schedule, i.e., dose, timing and frequency during the Intrapartum period. The patient should be reassured that she may request pain medication.

D. Intrapartum and Postpartum Pain Management

Patients receiving buprenorphine who are undergoing labor and delivery can benefit from similar pain therapy offered to women not receiving buprenorphine.

- I. Epidural or spinal anesthesia should be offered where appropriate.
- II. While opioid analgesics may be used in combination with buprenorphine, they may not be effective in some patients. Medications such as butorphanol, nalbuphine and pentazocine, should be avoided, as they may precipitate acute withdrawal.
- III. The daily buprenorphine dose should be confirmed and continued.

Vaginal birth.

- IV. Acetaminophen and NSAID agents should be used for mild to moderate pain.
- V. A short-acting opioid analgesic may be available on PRN basis as needed.

- VI. No opioid pain medication should be needed post discharge.

Cesarean delivery

- VII. The patient's pain may be able to be managed with a combination of NSAID, acetaminophen and short-acting opioids for at least the first five days postoperatively.
- VIII. Patients may require as much as a 47 percent increase in short-acting opioid requirements.
- IX. PCA with morphine or hydromorphone may be used for the first 24 hours.
- X. Short-acting opioids may be needed in decreasing amounts for five to seven days to treat breakthrough pain not responding to basal NSAID therapy.
 - a. If a patient requires more than one to two days of opioid pain medication, buprenorphine may be discontinued, with pain treated with frequent administration of short-acting opioids. When pain has decreased, buprenorphine may be restarted using an induction protocol. However, decision making with regard to rotation from buprenorphine to other opioids should be made via careful coordination of care with an addiction specialist.

E. Postpartum Dosing

Women should continue on their established buprenorphine dose postpartum eight hours after their last opioid use. Dose adjustments may be necessary, especially if there were dose increases in the third trimester. It is not necessary to introduce another induction.

Patients may be at an increased risk of an overdose during the postpartum period. Therefore, patients should be co-prescribed the medication naloxone.



It is best practice that patients continue psycho-social treatment, including case management, through the postpartum period.

Guidelines for Breastfeeding in Mothers Receiving Methadone or Buprenorphine

Breastfeeding should be encouraged in mothers maintained on methadone or buprenorphine with the following exceptions: urine drug screens positive for illicit drugs, HIV-positive status, and the existence of medical and/or psychiatric contraindications. Illicit drugs include both illegal drugs and prescription medications that are misused. The American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, the Academy of Breastfeeding Medicine and the American Society of Addiction Medicine support these recommendations.

A number of studies have found that concentrations of methadone or buprenorphine in breast milk are minimal regardless of maternal dose. In addition to all of the known benefits of breastfeeding for both mother and child, there appears to be an important benefit for infants experiencing neonatal abstinence syndrome (NAS) as a result of prenatal exposure to methadone or buprenorphine.

Conclusion

There are no empirical criteria for determining whether a pregnant woman with an opioid use disorder should be treated with methadone or buprenorphine. Each woman's medical, psychiatric, bio-psychosocial and substance use history must be considered in any treatment decision. However, some general guidelines have been established related to pregnancy: 1) a woman with an opioid use disorder who is naïve to methadone treatment may be a good candidate for buprenorphine, in that, if she does not respond well to buprenorphine, she can easily be transferred to methadone; and 2) women stabilized on buprenorphine or methadone who become pregnant should remain on their current medication. Whichever medication is used, comprehensive treatment and social support are important for successful outcomes,

and best practice standards indicate the need for engagement in psychosocial treatment. Attempts to criminalize OUD in pregnancy should be avoided, as this may deter that patient from obtaining adequate prenatal care for herself and the fetus.

Resources

Academy of Breastfeeding Medicine, clinical Protocol #21 (2015). Guidelines for breastfeeding and substance use or substance use disorder. *Breastfeeding Medicine*, 10(3), 135-141.

ACOG Committee on Health Care for Underserved Women: American Society of Addiction Medicine, ACOG Committee Opinion No. 524 (2012). Opioid Abuse, Dependence and Addiction in Pregnancy. *Obstetrics and Gynecology*, 119, 1070-1076.

American Academy of Pediatrics Policy statement (2012). Breastfeeding and the use of human milk. *Pediatrics*, 129, e872-e841.

Abdel-Latif ME, Piner J, Clews S, Cooke ZF, Lui K, Oei J. (2006). Effects of breast milk on the severity and outcome of neonatal abstinence syndrome among infants of drug dependent mothers. *Pediatrics*, 117(6): e1163-1169.

Center for Behavioral Health Statistics and Quality (2015). *Behavioral health trends in the United States: Results From the 2014 National Survey on Drug Use and Health*. (HHS Publication No.SMA 15-4927, NSDUH Series H-50) Retrieved from <http://www.samhsa.gov/data>

Center for Substance Abuse Treatment. *Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs*. Treatment Improvement protocol (TIP) Series 43. DHHS Publication No.(SMA) 08-4214. Rockville, MD: Substance Abuse and Mental Health Service Administration, 2005, reprinted 2006 and 2008.

Debelak K, Morrone WR, O'Grady KE, Jones HE. (2013). Buprenorphine + naloxone in the treatment of opioid dependence during pregnancy-initial patient care and outcome data, *American Journal of Addiction*, 22(3): 252-254.

Jones HE, Johnson RE, Miiio, L. (2006). Post-cesarean pain management of patients maintained on methadone or buprenorphine. *The American Journal on Addictions*, 15(3):258-259.

Jones HE, O'Grady K, Dahne J, Johnson R, Lemoine L, Milio L, Ordean A, Selby P. (2009). Management of acute postpartum pain in patients maintained on methadone or buprenorphine during pregnancy. *Am J Drug Alcohol Abuse*. 35(3):151-6.

Jones HJ, Finnegan LP, Kaltenbach K. (2012). Methadone and buprenorphine for the management of opioid dependence in pregnancy. *Drugs*, 72(6):747-757.

Jones HJ, Deppen K, Hudak ML, Leffert L, McClelland C, Sahin L, Starer J, Terplan, M Thorp JM, Walsh J, Greanga AA. (2014). Clinical care for opioid-using pregnant and postpartum women: the role of obstetrics



providers. *American Journal of Obstetrics and Gynecology*, 210(40):302-310.

Lund IO, Fischer G, Welle-Strand GK, O'Grady KE, Debelak K, Morrone WR, Jones HE. (2013). A comparison of buprenorphine + naloxone to buprenorphine and methadone in the treatment of opioid dependence during pregnancy: maternal and neonatal outcomes. *Substance Abuse Research and Treatments* 7: 61-74.

Meyer M, Wagner K, Benvenuto A, Plante D, Howard D. (2007). Intrapartum and postpartum analgesia for women maintained on methadone during pregnancy. *Obstetrics and Gynecology*, Aug;110(2 Pt 1):261-6.

Marjorie Meyer M, Paranya G, Norris AK, Howard D. (2010). Intrapartum and postpartum analgesia for women maintained on buprenorphine during pregnancy. *European Journal of Pain*, 14: 993-943.

Pritham UA, Paul JA, Hayes MJ. (2012). Opioid dependency in pregnancy and length of stay for neonatal abstinence syndrome. *J Obstetrics and Gynecology Neonatal Nursing*, 41(20): 180-190.

Weigand SI, Stringer EM, Stuebe AM, Jones HE, Seashore C, Thorp J. (2015). Buprenorphine and naloxone compared with methadone treatment in pregnancy. *Obstetrics and Gynecology*, 125(2):363-368.

Welle-Strand GK, Skurtveit S, Jansson LM, Bakstad B, Bjarko L, Ravndal E. (2013). Breastfeeding reduces the need for withdrawal treatment in opioid-exposed infants. *Acta Paediatr*, 102(11): 1060-1066.

World Health Organization (2014). Guidelines for identification and management of substance use and substance use disorders in pregnancy. WHO Press.

Available at:
http://www.who.int/substance_abuse/publications/pregnancy_guidelines/en/

Department of Drug and Alcohol Programs – Methadone Treatment Program locator:

<https://apps.ddap.pa.gov/gethelpnow/CountyServices.aspx>

Buprenorphine Physician and Treatment Program Locator:

<http://www.samhsa.gov/medication-assisted-treatment/physician-program-data/treatment-physician-locator>

Find a Pa. addiction treatment provider:

<https://apps.ddap.pa.gov/gethelpnow/CareProvider.aspx>

McCarthy, J.J., Leamon, M.H., Willits, N.H. & Salo, R. (2015). The Effect of Methadone Dose Regimen on Neonatal Abstinence Syndrome. *J.Addict Med*, ;00: 1-6.

The ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use, May 27, 2015