Guidelines for Addressing Benzodiazepine Use in Opioid Treatment Programs (OTPs)

Benzodiazepines significantly enhance the action of other Central Nervous System (CNS) depressant medications including methadone and buprenorphine. On their own, benzodiazepines have a broad safety profile but in combination with opioids in particular, the risk of sedation and respiratory depression increases significantly. Patients with a history of addiction are at much higher risk for benzodiazepine misuse and dependence; therefore, benzodiazepines are not the ideal treatment for insomnia or anxiety in most cases, in addition to causing cognitive impairment, dementia, and delirium. Tolerance to benzodiazepine-induced euphoria and sedation develops quickly, and withdrawal can be life threatening. Abuse liability of specific benzodiazepines varies depending on pharmacokinetic properties, rate of absorption, metabolism, intrinsic activity and elimination half-life. There are few clinical situations where benzodiazepines may be appropriate for short-term use in methadone or buprenorphine treated patients. Despite the known increased risks of overdose and misuse, opioid dependent patients often have access these prescriptions.

Worldwide, 18-50% of patients receiving methadone treatment are dependent on benzodiazepines. [i] Benzodiazepine use among patients in medication assisted therapy (MAT) is linked to poorer outcomes and the combination with opioid agonists poses significant risks for morbidity and mortality. There are few published articles that offer useful guidance for management of benzodiazepines in MAT. As a result, treatment protocols and clinical practice vary. In spite of the gap in the literature, care should be taken with patients admitted to MAT with either licit or illicit benzodiazepine use. Treatment of opioid use disorder with medications should not be discouraged or delayed, but the risks of ongoing benzodiazepine use should be taken seriously and interventions guided accordingly.

The purpose of this document is to offer guidance instead of restrictive procedures to assist programs in treating patients in MAT who use benzodiazepines. [ii iii iv v vi vii viii ix x xi]

- OTPs should be diligent and use caution when admitting patients taking benzodiazepines or any other sedating medications. CNS depressant use is not an absolute contraindication and such use should be addressed in treatment. Therefore, benzodiazepine using individuals should not be categorically denied admission into MAT.
- Education about the combined risks of benzodiazepine, prescribed or illicit sedatives, opioid analgesics and alcohol use should be a routine part of orientation to MAT.
- Benzodiazepines are not the treatment of choice for anxiety in patients in MAT. Benzodiazepines are associated with significant risk for patients in MAT. Treatment plans should be developed on admission, or when indicated during treatment to address benzodiazepine use. In the great majority of cases, cessation of benzodiazepines is preferred. In some cases, admission to MAT may be delayed until a taper/detox is completed, often requiring more monitoring in a higher level of care. In others, gradually tapering off a prescribed benzodiazepine or decreasing to the lowest effective dose is appropriate. A gradual taper from MAT can be therapeutic, combined with continued attempts to help the patient address benzodiazepine use, with a goal of keeping patients in treatment if possible. However, continued refusal to address benzodiazepine use on the part of the patient may be grounds for discharge from MAT.
- Patients who are prescribed or illicitly use benzodiazepines should be considered at risk for adverse reactions including overdose and death, therefore, should be routinely monitored. Prohibiting admission or creating excessive access barriers can pose even greater threats to morbidity and mortality. A balance of providing care, medications and appropriate oversight is necessary to successfully achieve desired clinical outcomes.
- The North Carolina Controlled Substance Reporting System (NCCSRS) should be checked on admission and throughout the patient's treatment.
- Informed consent is advised for patients on MAT receiving prescribed benzodiazepines

and other sedating medications for coordination of care between the OTP and prescribing clinician. Admission to MAT may be denied while referred to an appropriate alternative treatment if patients do not consent to coordination of care with outside prescribing providers.

- Program medical providers should collaborate with the prescribers so they are aware of the patient's admission to MAT, the concerns of concurrent use of benzodiazepines, and to plan for coordination of care. Prescriber should be advised to decrease benzodiazepine dose to the lowest effective dose for the safety of the patient, and to strongly encourage the prescriber to consider alternative medications and non-pharmacologic treatments to address anxiety or insomnia.
- Taking steps towards further integration of opioid treatment with mental health treatment either in specialty or primary care is essential for managing OTP patients' chronic health conditions. Patients admitted to MAT who are prescribed benzodiazepines should be considered for a psychiatric evaluation to verify diagnosis and determine the best course of treatment for their condition.
- If unable to integrate those services in-house, then more emphasis needs to be placed on partnerships/collaborations for providing the mental health care.
- If a patient is sedated, holding or decreasing the methadone or buprenorphine dose is appropriate until further evaluation is completed.
- Diversion of prescribed medications is a risk for any patient with a substance use disorder. Care should be taken to ensure that patients are taking the medications prescribed and not diverting or supplementing with illicit drugs.
- Toxicology screening should test for prescribed and illicit benzodiazepines.

There is little literature to support regulating ceiling doses of methadone or buprenorphine as a strategy to address benzodiazepine use in MAT patients but may be reasonable to reduce confusion and improve consistency. The OTP physician and prescribing clinician should be able to make exceptions to the rule and individually determine the appropriate dose for the patient and not be held to arbitrary dose limits. Not having a ceiling has a tendency to create chaos.

61% of NC OTP medical directors responding to a survey in April 2017 on the use of ceiling doses of methadone on admission when patients are using Benzos ranged from 20-80 mg. Six medical directors responded that they do not prescribe methadone but use buprenorphine when patients are using Benzos on admission.

55% of NC OTP medical directors have a ceiling dose that they taper patients down to after relapsing on Benzos. The ceiling dose ranges from 0-40 mg with dose reductions ranging from 2-10% a day, 1 mg QOD, or 5-10 mg a week.

There is no question that the use of benzodiazepines and other sedating medications combined with methadone or buprenorphine pose safety risks. Careful evaluation of undiagnosed or misdiagnosed co-occurring psychiatric disorders, and determining the most effective and lowest risk medications, should be the goal for understanding and addressing benzodiazepine use in MAT patients. Careful monitoring and coordination of care that is respectful but not capricious or punitive offers the best chance of ensuring access to safe, effective and individualized care for patients in MAT.

[i] Williams, J. *Management of Benzodiazepines in Medication-Assisted Treatment. The creation and dissemination of new practice guidelines*. ATTC Messenger. April 2014.

[ii] IRETA, *Management of Benzodiazepines in Medication-Assisted Treatment.* Report to Philadelphia Department of behavioral health and Disability Services. November 2013.

[iii] Baltimore Substance Abuse Systems, Inc. *Clinical Guidelines for the Use of benzodiazepines Among Patients Receiving Medication-Assisted Treatment for Opioid Dependence*. May 2013.

[iv] 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 Services Administration, 2005, reprinted 2006 and 2008.

[v] Center for Substance Abuse Treatment. *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction.* Treatment Improvement Protocol (TIP) Series 40. DHHS Publication No. (SMA) 07-3939. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2004.

[vi] Renner, JA**.** *Management of psychiatric medications in patients receiving buprenorphine/naloxone.* PCSS-B Training. April 17, 2006. Available at: http://pcssb.org/wp-content/uploads/2010/09/PCSS-BManagement- of- psychiatric-medications-in-patients-receiving-buprenorphine-naloxone.pdf. Last accessed 3/9/13.

[vii] Kenneth Minkoff, M.D., Developing Standards of Care for Individuals With Co-occurring Psychiatric and Substance Use Disorders,' Psychiatric Services. May 2001 Vol. 52 No. 5. http://ps.psychiatryonline.org/doi/pdf/10.1176/appi.ps.52.5.597

[viii] Methadone Safety: A Clinical Practice Guideline: the American Pain Society and College on Problems of Drug Dependence, in Collaboration With the Heart Rhythm Society. The Journal of Pain: official journal of the Pain Society 15(4):321–337 · March 2014.

[ix] 'Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders', SAMSHA: 2012 www.ncbi.nlm.nih.gov/books/NBK92048

[x] Clinical Guidelines for the Use of Benzodiazepines Among Patients Receiving Medication-Assisted Treatment for Opioid Dependence - Behavioral Health System Baltimore, May, 2013.

[xi] Paulozzi, L. J. et al., (2012). Vital signs: Risk for overdose from methadone used for pain relief-united states, 1999- 2010. Morbidity and Mortality Weekly Report, Atlanta: U.S. Center for Disease Control.