

ASAM COVID-19 TASK FORCE RECOMMENDATIONS

CARING FOR PATIENTS DURING THE COVID-19 PANDEMIC

Addiction Treatment Medication
Formulations and Dosage Guidance



ADDICTION TREATMENT MEDICATION FORMULATIONS AND DOSAGE GUIDANCE

A guide for addiction treatment clinicians and programs working to treat patients with substance use disorders safely and effectively during the COVID-19 pandemic¹.

For additional recommendations for the Ongoing Management of the Continuum of Addiction Care during COVID-19, [please click here](#).

CONTENT DISCLAIMER

This Clinical Guidance ("Guidance") is provided for informational and educational purposes only. It is intended to provide practical clinical guidance to addiction medicine physicians and others caring for individuals with substance use disorders during the COVID-19 pandemic as it unfolds. Adherence to any recommendations included in this Guidance will not ensure successful treatment in every situation. Furthermore, the recommendations contained in this Guidance should not be interpreted as setting a standard of care or be deemed inclusive of all proper methods of care nor exclusive of other methods of care reasonably directed to obtaining the same results.

The ultimate judgment regarding the propriety of any specific therapy must be made by the physician and the patient in light of all the circumstances presented by the individual patient, and the known variability and biological behavior of the medical condition.

This Guidance and its conclusions and recommendations reflect the best available information at the time the Guidance was prepared. The results of future studies may require revisions to the recommendations in this Guidance to reflect new data.

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ADDICTION TREATMENT MEDICATION FORMULATIONS AND DOSAGE GUIDANCE

Purpose of the document

The purpose of this document is to provide guidance to outpatient addiction treatment clinicians in selecting medications and adjusting medication dose or formulation during the COVID-19 pandemic.

¹This resource was developed by a Task Force appointed by ASAM's Executive Council. To enable more rapid development and dissemination it was not developed through ASAM's normal process for clinical guidance development that is overseen by the ASAM Quality Improvement Council.

TOPICS

[1. Considerations for Opioid Use Disorder Treatment Medications \(pg.2\)](#)

- a. Medication Selection Generally
- b. Considerations for Type of Patient Visit and Medication Selection
- c. Considerations for Selection, Formulations, and Dosages of Buprenorphine
- d. Considerations for Selection, Formulations, and Dosages of Naltrexone
- e. Considerations for Selection, Dosages, and Take Home Doses of Methadone

[2. Considerations for Alcohol Withdrawal Management during COVID-19 \(pg.9\)](#)

[3. Considerations for Dosages and Formulations of Nicotine Cessation Medications \(pg.11\)](#)

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1. Considerations for Opioid Use Disorder Treatment Medications

As always, determinations regarding selection of medications, formulations, and dosages should be made based on shared decision-making with the individual patient. However, the current COVID-19 crisis has implications for the risks and benefits of different medications and formulations. This section will discuss medication selection generally, highlight some considerations related to patient visit type, and describe specific considerations for formulations and dosages for each medication approved for the treatment of opioid use disorder.

Medication Selection Generally

ASAM's released focused update to the [National Practice Guideline for the Treatment of Opioid Use Disorder](#) recommends that clinicians consider the patient's preferences, past treatment history, current state of illness, financial abilities and insurance coverage for the different medication options, and treatment setting when deciding between the use of methadone, buprenorphine, and naltrexone. During the COVID-19 crisis, clinicians should also consider how the choice of medication will impact the need for in-person appointments in combination with the individual's risks associated with COVID-19.

Considerations for Type of Patient Visit and Medication Selection

Making medication selection decisions with patients for the treatment of opioid use disorder may include some general considerations around types of patient visits. The information to consider applies to both initial and ongoing visits, regardless of medication. Considerations related to the type of patient visit that are specific to each medication are briefly reviewed by medication. For more information, see [Considerations for Formulations and Dosages of Buprenorphine](#); [Considerations for Formulations and Dosages of Naltrexone](#); and [Considerations for Dosages and Take Home of Methadone](#).

In-person visits

- Is the patient experiencing any symptoms consistent with COVID or have they had any potential exposures?

- Is the patient at high risk for severe COVID-19 illness?
- Is the patient living with or caring for someone at high risk?
- Is the patient living in a high-risk environment for COVID-19 transmission?
- Would the patient need to take mass transit or ride with another person to the visit?
- What is the patient's level of anxiety around coming to an in-person visit?
- What is the availability of appropriate personal protective equipment (PPE) for both healthcare workers in the facility and the patient?

Telehealth

- Is the patient at high risk of adverse events related to their OUD (e.g., overdose, suicide)?
- Can the patient engage in phone or audio-visual [telehealth](#) visits?
- Is the patient at high risk for disengaging from treatment?
- Can the patient appropriately and safely manage take home medications?
- Is the patient likely to divert or misuse their medication?
- Can [drug testing](#) be safely delayed?

Buprenorphine-specific visit considerations

For new patients

- An in-person medical exam is not required under federal regulations before initiation of buprenorphine. The initial medical examination may occur through phone or audio-visual telehealth visits (see [SAMHSA's FAQ's on Provision of methadone and buprenorphine for the treatment of Opioid Use Disorder in the COVID-19 emergency](#)).
- Medication initiation and follow-up visits can be safely accomplished through phone or audio-visual telehealth.

For existing patients

- Clinicians should check in with patients more regularly through telehealth (including telephone-based check-ins) to assess the patient's response to medication and any signs that the patient's medication or treatment plan may need to be modified.
- For patients started on buprenorphine, clinicians should be alert to signs that patients may be misusing or diverting their medications, such as patients returning early for additional medication. Programs and clinicians should consider how to manage these situations in the context of the COVID-19 crisis.
 - When to request having the patient come in for an in-person appointment.
 - How to address suspected diversion (including to friends or family who lost access to their medication during this crisis).
 - Moving to a shorter duration prescription with refills to limit the number of films a patient receives while minimizing the frequency of visits to obtain a prescription.
 - Ensuring refills have "do not fill before" dates.
 - Consider enhanced methods for monitoring medication adherence including the use of apps or audio-visual visits for observed dosing.
 - Consider transition to a formulation that allows for monitoring of empty unique serial-number labeled packaging either at in-person visits or by audio-visual means.
 - Enhanced use of the state prescription drug monitoring program.

- Enhanced urine drug testing for a period of time, as long as precautions related to COVID transmission and exposure are followed ([See Adjusting Drug Testing Protocols](#)).

Naltrexone-specific visit considerations

For new patients

- Starting a patient on XR-NTX requires a period of opioid abstinence of 7-10 days. Is the patient likely to be able to sustain this at home or in an unmonitored setting? How willing is the patient to access residential treatment services as a setting to start XR-NTX? If the patient is willing to engage in residential treatment, are these services available?

For existing patients

- XR-NTX requires an intramuscular injection every 3-4 weeks. Is the practice set up to accommodate this during the COVID-19 pandemic? Is the patient willing to attend an in-person visit for the injection?
- If the XR-NTX injection has to be delayed due to the clinician being unavailable, is there an alternative place in the community that can provide these injections?

Methadone-specific visit considerations

For new patients

- An in-person medical exam is required under federal regulations before initiation of methadone. (See [Ensuring Access to Care in Opioid Treatment Programs](#) Guidance)

For existing patients

- The patient can engage in phone or audio-visual [telehealth](#) visits for follow-up as required.
- Some in-person visits will still be needed for patients to pick-up take-home medication doses, unless an alternative medication delivery system is established.

Considerations for Selection, Formulations, and Dosages of Buprenorphine

Buprenorphine can be used in patients with a higher risk for overdose. As a partial agonist, it has less risk of respiratory depression compared to full agonists, may be less likely to be misused, and titration to a stable dose can be achieved quickly. Regardless, all patients with opioid use disorder treated with buprenorphine should also receive at least a prescription for the overdose reversal medication naloxone, if not the actual naloxone medication.

Buprenorphine is currently available in multiple formulations including sublingual films and tablets, a monthly extended-release injection, and a subcutaneous implant (6 months). The COVID-19 crisis may impact considerations for the selection and formulation of buprenorphine for a given patient.

Considerations for the selection of buprenorphine

- Assess the patient's ability to afford and obtain the medication. Many people have lost their employer-based health insurance during the COVID-19 pandemic and may have limited income available to pay for the medication.

Considerations for daily formulations vs. injectable

There are several factors a clinician needs to weigh when deciding to either continue the current formulation (daily or injectable) or switch between formulations with different delivery methods.

- The need for in person visits should be assessed for all patients and is an important factor in determining an appropriate formulation.
- Patients who are experiencing any symptoms consistent with COVID-19 or has had any known exposure to an individual who has tested positive for, is awaiting a COVID-test result, or is suspected of having COVID should avoid in-person visits until their quarantine or isolation period has been ended by a knowledgeable medical clinician.
- Patients who are unable to come to in-person visits may need to transition from injectable buprenorphine to films or tablets that can be delivered or retrieved by the patient, or another responsible family member or other adult.
 - Is the patient living with or caring for someone at high risk of severe illness, such that they should not come to clinic for injection?
- Are there any anticipated risks to the patient associated with switching formulations?
 - How stable is the patient on their current medication?
 - Are they likely to be adherent with daily medication?
- How will the choice of formulation impact the anticipated frequency of in-person appointments?
 - Can the patient be safely managed through telehealth alone if taking daily buprenorphine?
 - If the patient requires in-person visits, how frequently would they need to be seen for daily buprenorphine vs monthly visits for the injectable formulation, given that there is little data on this question for guidance?
- Assess the need for drug testing, and if so, the anticipated required frequency. See [Adjusting Drug Testing Protocols](#) Guidance.
- Which formulation does the patient prefer, given the anticipated requirements for in-person appointments for each formulation?
- What is the availability of injectable buprenorphine?
 - Does the patient have insurance that will cover this formulation?
 - Does the patient have access to a site where the injection can be provided?
 - Is the treating provider able to obtain, deliver, and bill for the injections?
- Evaluate patient at high risk for misusing or diverting their sublingual buprenorphine

Considerations for Transitioning Patients Between Formulations

- Only transition patients between formulations after assessing the patients desire, as well as their willingness and ability to tolerate any destabilizing effects that may occur.
- Patients should not be forced to change medications or formulations arbitrarily or without their input.
- Transitioning between formulations may require dose adjustments and titration over time, and thus increase the need for in-person visits.
- The goal is to minimize in-person encounters while safely treating the patient's OUD (see [Access to Buprenorphine in Office Based Settings](#) Guidance). Clinicians should consider the length of any prescription and availability of refills to minimize the chances that the patient will run out of medication and minimize COVID exposure at pharmacies while balancing the risk of misuse and diversion.

Considerations for Selection, Formulations, and Dosages of Naltrexone

Naltrexone is available in an extended release injectable formulation (XR-NTR) and as an oral tablet. However, only the extended release formulation has been proven effective for the prevention of relapse to OUD. XR-NTR requires in-person visits for an injection every 3-4 weeks (the standard dosing is every 4 weeks but some patients who metabolize naltrexone more rapidly benefit from dosing every 3 weeks. All patients with opioid use disorder treated with naltrexone should also receive at least a prescription for the overdose reversal medication naloxone, if not the actual naloxone medication. (See [ASAM's National Practice Guideline for the Treatment of OUD](#)).

Considerations for the selection of naltrexone

In determining whether naltrexone is the right medication for a given patient during the COVID-19 crisis there are several factors a clinician needs to weigh:

- Starting a patient on naltrexone, including XR-NTX, requires a period of opioid abstinence of 7-10 days. Is the patient likely to be able to sustain this at home or in an unmonitored setting? How willing is the patient to access residential treatment services as a setting to start XR-NTX?

Considerations for formulation of naltrexone

- If the patient is willing to engage in residential treatment to start XR-NTX, are these services available? Are community settings available and identified to continue XR-NTX injections once they have been started?
- If the XR-NTX injection has to be delayed due to the clinician being unavailable, is there an alternative place in the community that can provide these injections? What is the patient's risk for return to substance use if their medication has to be delayed or discontinued?
- Is the patient a candidate for oral naltrexone?
 - Oral naltrexone has not been proven to be effective for the treatment of OUD, primarily because of issues with patient adherence. This formulation is not recommended except under limited circumstances. For example, for highly motivated patients who can be closely supervised in taking the medication.
 - Is the patient likely to be adherent with the oral medication?
- Is the patient a candidate for buprenorphine if they are unable to continue XR-NTX?
 - What is the patient's risk for relapse if XR-NTR is discontinued?
 - Is the patient likely to be adherent with daily buprenorphine?
 - Does the patient have any contraindications to buprenorphine?
- What is the risk to the patient from an in-person visit?
 - Is the patient at high risk for severe COVID-19 illness?
 - Is the patient living with or caring for someone at high risk of severe illness?
 - Would the patient need to take mass transit to the visit?
 - What is the patient's level of anxiety around coming to an in-person visit?
- Does your facility have sufficient staff and PPE to provide injections?
 - Is there an alternate location where the patient can safely receive an injection?

- Which formulation is the patient willing to take, given the need for in-person appointments every 3-4 weeks for injections for XR-NTR?

Considerations for Selection, Dosages, and Take-Home Doses of Methadone

SAMHSA and the DEA have relaxed regulations on Opioid Treatment Programs (OTPs) to enable increased telehealth and take-home doses during this public health emergency. However, clinicians need to weigh the risks for each individual patient associated with both OUD and COVID-19. Many aspects of this crisis may increase the risk for relapse. Patients are experiencing high levels of stress and anxiety related to the pandemic, many have or will lose their jobs, and social isolation is exacerbating mental health and addiction related symptoms. Treatment with methadone continues to be an effective and safe option for patients with moderate to severe opioid use disorder. Clinicians need to balance multiple risks in determining the number of take-home doses of methadone for any given patient. All patients with opioid use disorder treated with methadone should also receive at least a prescription for the overdose reversal medication naloxone, if not the actual naloxone medication.

Considerations for the selection of methadone

- The physician needs to determine the number of in-person visits expected during the initial dose titration period and the number of take-home medication doses the patient can safely manage during induction and stabilization.
- The number of take-home doses should be based upon individual patient risk and need.
- Strategies to minimize the risk associated with take-home doses:
 - lock boxes designed to release a single dose of methadone at a pre-set time.
 - increased frequency of phone or audio-visual check-ins with the patient may be helpful.
 - Identify a chain-of-custody for take-home doses with a responsible family member or other adult.
- The patient can engage in phone or audio-visual [telehealth](#) visits for follow-up as required.

Considerations for Methadone Formulation

If dispensing larger numbers of take-home doses, consider 40mg dispersible tablets instead of the liquid formulation. This formulation can only be dispensed in an OTP setting. It can be easier to secure and store, and safer with which to travel.

Considerations for Methadone Dosing

Opioid Treatment Programs (OTPs) should consider promoting physical distancing through the use of telehealth and increased take-home doses, when safe and appropriate (See [Ensuring Access to Care in Opioid Treatment Programs](#) Guidance). Programs should also make changes to how patients flow through their facility to ensure patients and staff can maintain 6+ feet of distance.

The stress, anxiety, and social isolation associated with the COVID-19 pandemic may exacerbate a patient's addiction and mental health symptoms. Clinicians should check in with patients more regularly through telehealth (including telephone-based check-ins) to assess the patient's response to medication and any signs that the patient's medication or treatment plan may need to be modified.

OTPs should be aware of the safety risks associated with increased take-home doses of methadone, and the need for increased patient monitoring. Clinicians should be alert to signs that patients may be misusing or diverting their medications, such as patients returning early for additional medication. Programs and clinicians should consider how to manage these situations in the context of the COVID-19 crisis. For example,

- When to require an in-person appointment with the patient
- How to address suspected diversion (including to friends or family who lost access to their medication during this crisis)
- Moving to smaller number of take-home doses
- Enhanced urine drug testing (see [Adjusting Drug Testing Protocols](#) Guidance)

Programs should also explore methods for minimizing patient risks related to take-home methadone. For example:

- Consider enhanced methods for monitoring medication adherence
 - Specially designed lock boxes with controlled release, enabling one dose to be released once per day at a specific time.
 - If these tools are too expensive for the program to cover, the program could consider exploring funding options with the State Opioid Treatment Authority as there may be opportunities for using SOR or CARES funding for this purpose.
 - For select, extremely complex patients, consider using telehealth to monitor their daily dosing, including ensuring that remaining doses are all accounted for.
 - Engaging the patient's family or support system to manage and monitor dosing, if the patient has a reliable support system that could play this role
 - Increased telephonic check-ins

The COVID-19 crisis will force clinicians to make some very challenging clinical decisions as they try to balance the risks associated with OUD versus those associated with the COVID-19 Pandemic. Programs and clinicians should also consider data you have access to that can help you assess the impact of the changes you or your program is implementing. While you may have limited access to local and state level data during the crisis, consider data you can collect in your own practice or program. For example:

- Early returns/early refills
- Suspected misuse or diversion (among patients considered to be stable vs. less stable)
- Patient hospitalizations such as for overdose or withdrawal
- Unexpected drug screen results (if these are being done)

Resources

- ASAM's National Practice Guideline for the Treatment of Opioid Use Disorder: Focused Update 2020. <https://www.asam.org/Quality-Science/quality/2020-national-practice-guideline>

ASAM's COVID-19 Resources: <https://www.asam.org/Quality-Science/covid-19-coronavirus>

- Guidance for Buprenorphine Treatment Clinicians: <https://www.asam.org/Quality-Science/covid-19-coronavirus/access-to-buprenorphine>
- Guidance for OTPs: <https://www.asam.org/Quality-Science/covid-19-coronavirus/access-to-care-in-opioid-treatment-program>
- Guidance on Adjusting Drug Testing Protocols: <https://www.asam.org/Quality-Science/covid-19-coronavirus/adjusting-drug-testing-protocols>
- SAMHSA's COVID-19 Resources: <https://www.samhsa.gov/coronavirus>
- AATOD's Guidance for OTPs: http://www.aatod.org/advocacy/policy-statements/covid-19-aatods-guidance-for-otps/?utm_source=COVID-19&utm_campaign=medicaid+webinar6&utm_medium=email

2. Considerations for Alcohol Withdrawal Management During COVID-19

During the COVID-19 pandemic, access to alcohol may be reduced in some areas, which may increase the risk for the development of alcohol withdrawal. At its most severe, alcohol withdrawal can cause seizures, delirium, and even death. ASAM has released [Clinical Practice Guidelines for Alcohol Withdrawal Management](#). These guidelines provide recommendations for determining the appropriate level of care for a given patient. However, the risks and medical issues associated with COVID-19 may influence this determination.

Clinicians should consider

- Can the patient be safely monitored in an ambulatory care setting, or at home?
 - Does the patient have safe housing?
 - Does the patient have support at home?
 - Can the patient maintain the necessary telephone-based contact?
 - Can the patient follow the necessary medication instructions?
- Does the patient need inpatient care?
 - Are they at risk of severe or complicated withdrawal?
 - Does the patient have a history of withdrawal seizures or delirium tremens?
 - Does the patient have medical comorbidities likely to complicate their withdrawal or its treatment?
- Is the patient experiencing any clinical effects consistent with COVID-19 or have they had any potential exposures?
 - How severe are their clinical effects? How is this likely to impact their alcohol withdrawal symptoms?
 - Does your facility have the capacity to provide remote monitoring and services for patients with alcohol withdrawal syndrome?
 - If providing residential or inpatient services, does your facility have the capacity to manage patients with, or suspected of having, COVID-19?
- What is the risk to the specific patient associated with inpatient care?
 - Are they at high risk for severe COVID-19 illness?
 - Are they living with or caring for someone at high risk of severe illness?
 - What is the patient's level of anxiety around inpatient care?

When treating in an outpatient setting with home monitoring, consider a higher dosing protocol. In the context of COVID-19, the community has diminished access to monitored environments where clinician-administered assessments of withdrawal are feasible. While there is an elevated risk of adverse effects (typically sedation) from withdrawal medications, these may be outweighed by the risk of under-treated alcohol withdrawal syndrome.

- Consider using the short alcohol withdrawal scale (SAWS) which can be self-administered.
- Connect with community resources that may have or would consider launching an “on-call” line for urgent SUD and withdrawal management services where patients can be triaged to determine if they need inpatient care.
- Consider developing standard protocols for specific settings where alcohol withdrawal management may be needed. For example:
 - Protocols for management of low acuity alcohol withdrawal in emergency shelters for people experiencing homelessness
 - Protocols for COVID-19 quarantine sites staffed by nurses that may be able to handle more moderately acute patients.

See sample protocols, courtesy of Dr. Brian Hurley MD, MBA, DFASAM ([see the content disclaimer](#)):

- [Management of OUD, AUD, and withdrawal in Low Acuity Settings](#)
- [Management of OUD, AUD, and withdrawal in quarantine sites](#)

When patients are treated for alcohol withdrawal the clinician should work to engage the patient in treatment for alcohol use disorder.

FDA-approved Medications for Alcohol Use Disorder (MAUD)

- Naltrexone 25-50 mg oral once daily (must ensure opioid abstinence for at least 7 to 10 days prior to administration)
- Naltrexone ER 380 mg IM once every 28 days intramuscular (gluteal) injection (must ensure opioid abstinence for at least 7 to 10 days prior to administration)
- Acamprosate 333-666 mg oral TID
- Disulfiram 250-500 mg oral once daily

For additional information, see [Supporting Access to Alcohol Use Disorder and Alcohol Withdrawal Treatment](#).

Resources

ASAM’s Clinical Practice Guideline for Alcohol Withdrawal Management: <https://www.asam.org/Quality-Science/quality/guideline-on-alcohol-withdrawal-management>

APA’s Practice Guideline for the Pharmacological treatment of Patients with Alcohol Use Disorder: <https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9781615371969>

3. Considerations for Dosages and Formulations of Nicotine Cessation Medications

Early research suggests that smoking is associated with increased risk for severe COVID-19 illness.² In addition, the COVID-19 response, including quarantine and physical distancing measures can limit access to nicotine-containing products (cigarettes, chew, tobacco, vape) and/or limit opportunities to smoke. Finally, this period of stress, anxiety and isolation can lead to relapse among former smokers.

Clinicians should continue to screen patients for nicotine use and support individuals interested in nicotine cessation. It is important for patients to continue to have access to nicotine replacement therapy (NRT) and other medications and support services. Clinicians should continue to recommend online and telephone-based support for nicotine cessation including quit lines and apps. Smokefree.gov provides helpful resources for patients. Clinicians should continue to offer medications to support nicotine cessation. FDA-approved medications include:

- Varenicline 0.5 mg PO daily x 3 days, then 0.5mg PO BID x 4 days, then 1mg PO BID
- Bupropion 150 mg PO daily x 3 days, then 150mg PO BID
- Nicotine replacement therapies including patches, gum, lozenges, nasal spray and inhalers
 - 21 mg patch for >10 cigarettes/day
 - 14 mg patch for <10 cigarettes/day
 - 7 mg patch used for tapering

Resources

- 2018 ACC Expert Consensus Decision Pathway on Tobacco Cessation Treatment: <http://www.onlinejacc.org/content/72/25/3332>

²<https://www.ncbi.nlm.nih.gov/pubmed/32293753>; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7083240/>

