HIV CLINICAL RESOURCE ¼-FOLDED GUIDE

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TREATMENT OF OPIOID USE DISORDER

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE FEBRUARY 2024

ALL RECOMMENDATIONS P.1

Overdose Prevention

- Clinicians should provide overdose prevention counseling (A3); prescribe, dispense, or offer resources for NLX (A2); and dispense or offer resources for fentanyl and xylazine test strips (if available) (A3) as part of OUD treatment evaluation. For full recommendations on overdose prevention, see NYSDOH AI guideline Substance Use Harm Reduction in Medical Care > Implementing Substance Use Harm Reduction.

Who to Treat

- Clinicians should offer pharmacologic treatment to adult patients with OUD (A1), including those who are not actively using opioids but are at risk of returning to use or overdose. (B3)
- Clinicians should *not* exclude patients from pharmacologic OUD treatment because of:
  - Previous OUD treatment failure, which is defined as the inability to adhere to medications for OUD or achieve treatment goals. (A3)
  - Lack of participation in structured psychosocial treatment, such as counseling, cognitive behavioral therapy, or contingency management. (A1)
    Note: If a patient is court-ordered to participate in psychosocial therapy, the clinician's primary responsibility is to maintain the therapeutic alliance and partner with the patient to address legal mandates.
  - Co-occurring substance use or SUD. (A2)
- Before discharging a patient treated for an opioid-related overdose or complication, and as medically indicated, clinicians in an ED or other acute care setting should initiate or recommend pharmacologic OUD treatment. (A1)

Treatment Options

- Clinicians should obtain complete histories of patients' previous OUD treatment, including tolerance of and success with medication initiation, experience with long-term treatment, adherence challenges, adverse effects, treatment duration, and reasons for stopping treatment. (A2)
- BUP/NLX and methadone are the preferred treatments for OUD. Clinicians should inform patients with OUD about all available pharmacologic options (BUP, methadone, and XR naltrexone) and all formulations. (A3)
- Because OUD is a chronic condition, clinicians should recommend long-term pharmacologic treatment rather than withdrawal management alone. (A1)

ALL RECOMMENDATIONS *continued* P.2

Treatment Options *continued*

- In choosing the best option for OUD treatment, clinicians should engage patients in shared decision-making that accounts for the patient's opioid tolerance and preferences, available and accessible options, and comorbidities. (A3)

BUP/NLX: Preferred Treatment

- Clinicians should recommend coformulated BUP/NLX as a preferred treatment for individuals with OUD. (A1)

BUP/NLX Initiation

- **Initiation setting:** Because both home-based (unobserved) initiation and office-based (observed) initiation are effective, clinicians should advise an initiation setting based on patients' experience, comfort, and preferences and clinicians' practice experience and support. (B2)
- **Precipitated withdrawal:** Clinicians should assess the potential for, educate patients about, and have a clear protocol for managing precipitated withdrawal. (A3)
- **Standard initiation:** To minimize the risk of precipitated withdrawal, clinicians should advise patients to wait for the onset of mild to moderate opioid withdrawal before starting BUP/NLX treatment. (A2)
  - As indicated, clinicians should provide adjunctive medications to relieve specific symptoms of acute opioid withdrawal. (B2)
- **Low-dose BUP with opioid continuation (LDB-OC)** (previously known as microdosing or micro-induction)**:** For patients who may be unable to tolerate opioid withdrawal before starting BUP/NLX, or for patients who have had prior experience with precipitated withdrawal with standard initiation, clinicians should offer LDB-OC as an alternative initiation approach. (A2)

BUP/NLX Dosing

- Clinicians should titrate BUP/NLX to the dose needed to control patients' cravings, reduce or prevent withdrawal symptoms, and support treatment goals. (A3)
  See Table: Buprenorphine/Naloxone for Treatment of Opioid Use Disorder in Nonpregnant Adults.
- If a patient has continued symptoms of opioid withdrawal, cravings, or opioid use despite the maximum dose of BUP/NLX approved by the FDA (24 mg/6 mg daily), the clinician should pursue 1 or more of the following strategies: :
  - Ensure the patient is taking the medication as prescribed. (A3) BUP/NLX should be dissolved under the tongue rather than swallowed.

ALL RECOMMENDATIONS *continued* P.3

BUP/NLX Dosing *continued*

  - Increase the total daily dose of BUP up to 32 mg, particularly for patients with chronic fentanyl exposure, and reassess the need for higher (>24 mg daily) long-term dosing when patients have stabilized. (A2)
  - Offer adjunctive medication and psychosocial treatment to relieve specific symptoms that persist after acute opioid withdrawal, known as protracted withdrawal or post-acute withdrawal syndrome. (B3)
  - Offer long-acting injectable BUP. (A2)
  - Offer referral to methadone treatment if available and preferred by the patient. (A3)
- If a patient chooses to discontinue BUP/NLX treatment, the clinician should:
  - Discuss alternative medication, including methadone and naltrexone. (A1)
  - Inform the patient about the risks of recurrence of use, reduced tolerance, and opioid overdose. (A3)
  - Offer the patient a slow, tapering decrease schedule to minimize withdrawal symptoms. (B3)
- Clinicians should consult with or refer the patient to a clinician experienced in treatment of SUD if encountering challenges with BUP/NLX dosing (e.g., increases beyond the FDA-approved maximum dose), switching to long-acting injectable BUP, or tapering or discontinuing treatment. (A3)

Methadone: Preferred Treatment

- Clinicians should recommend methadone as a preferred treatment for individuals with OUD. (A1)
- Methadone is available only through an OTP; therefore, the clinician should refer a patient for methadone treatment if methadone is preferred, if BUP/NLX is not available to the patient, or if the maximum dose of BUP/NLX does not control the patient's withdrawal symptoms or cravings. (A3)

Naltrexone: Alternative Treatment

- Clinicians should offer XR naltrexone to patients with OUD who prefer naltrexone treatment or who are not able to access or meet their treatment goals with methadone or BUP/NLX. (A3)
- When informing patients about XR naltrexone as a treatment option, clinicians should emphasize the strong motivation and adherence required for success. (B1)
- Before administering XR naltrexone, clinicians should administer an NLX (or low-dose naltrexone) challenge and confirm that patients do not react to ensure that opioids have been cleared from the system. (A2) See Table: Extended-Release Naltrexone for Treatment of Opioid Use Disorder in Nonpregnant Adults.

SELECTED KEY POINTS

- Harm reduction is a treatment goal.
- Provide overdose prevention counseling; prescribe, dispense, or offer resources for NLX; and dispense or offer resources for fentanyl and xylazine test strips as part of OUD treatment evaluation. See MATTERS > Harm Reduction online to request fentanyl and xylazine test strips (for individuals or organizations).
- BUP/NLX is generally initiated after the onset of mild to moderate opioid withdrawal symptoms and titrated in incremental doses. The goal is to reach a dose that will control a patient's opioid cravings, reduce or prevent withdrawal symptoms, and support the patient's treatment goals.
- Patients with chronic fentanyl exposure or other risk factors for precipitated withdrawal may benefit from a low-dose BUP with opioid continuation, in which full opioid agonists can be continued until a therapeutic level of BUP is achieved. Discussion and documentation of the risks of ongoing nonprescribed full opioid agonist use and strategies to maximize safe use is essential.
- Arranging for close follow-up by phone or in person throughout the initiation process is essential to patient success; follow-up may involve daily phone check-ins and in-person follow-up within 1 week of BUP/NLX initiation.
- Clinicians can contact expert consultants in OUD treatment through the CEI Line at 866-637-2342 and the Providers Clinical Support System (PCSS).
- The New York State Prescription Monitoring Program Registry must be consulted before providing each prescription for BUP/NLX (see New York State I-STOP/PMP—Internet System for Tracking Over-Prescribing—Prescription Monitoring Program). The database tracks individuals' history of pharmacy-dispensed controlled substances, but it does not include medications dispensed in OTPs.

Abbreviations: BUP, buprenorphine; DEA, Drug Enforcement Administration; ED, emergency department; FDA, U.S. Food and Drug Administration; LDB-OC, low-dose BUP with opioid continuation; NLX, naloxone; OTP, opioid treatment program; OUD, opioid use disorder; REMS, Risk Evaluation and Mitigation Strategy; SAMHSA, Substance Abuse and Mental Health Services Administration; SUD, substance use disorder; XR, extended-release.

← Use this code with your phone's QR code reader to go directly to a mobile-friendly version of the guideline.

This ¼-Folded Guide is a companion to the New York State Department of Health AIDS Institute guideline *Treatment of Opioid Use Disorder*. The full guideline is available at www.hivguidelines.org.

TABLE: BUPRENORPHINE/NALOXONE FOR TREATMENT OF OPIOID USE DISORDER IN NONPREGNANT ADULTS [a,b,c]

Formulations and Mechanism of Action	Dosing (individualized as indicated)	Considerations for Use
BUP/NLX sublingual film and tablet (multiple brands; see Medscape: Buprenorphine/Naloxone for more information) **Mechanism:** Partial opioid agonist	· **Standard initiation:** – **Initial BUP dose:** 2 mg to 8 mg once patient is experiencing mild to moderate opioid withdrawal – **Titration:** Increase BUP dose every 1 to 2 hours by increments of 2 mg to 4 mg over 2 to 7 days until opioid cravings and withdrawal symptoms are controlled. · **LDB-OC** (previously known as microdosing or micro-induction)**:** – **Initial BUP dose:** 0.25 mg to 0.5 mg while patient continues taking full opioid agonist [d] – **Titration:** Increase with low-dose increments of BUP over 7 days to reach therapeutic level; discontinue full opioid agonist. · **Long-term treatment:** The maximum dose of BUP is typically 24 mg taken once daily. – Increasing the dose up to 32 mg daily may be indicated for individuals with ongoing withdrawal, cravings, or opioid use. – The individualized dose that is most effective in supporting treatment goals should be continued as long-term treatment. – The total BUP dose can be divided by 2 or 3 for dosing throughout the day per patient preference.	· **Standard initiation:** Confirm opioid withdrawal symptoms and severity by observation or patient report before starting BUP/NLX. · Ensure that the patient understands the dosing schedule and how to take BUP/NLX: avoid swallowing and let the medication dissolve under the tongue. · **LDB-OC:** Does *not* require opioid withdrawal and can be an alternative for patients who may not be able to tolerate standard initiation. – Individualized patient protocols, pharmacy blister packing, and care coordination with close follow-up are essential to success of low-dose initiation. – Expert consultation may be helpful to guide individualization and coordination of low-dose initiation. – Discuss the risks of ongoing nonprescribed opioid use and strategies to maximize safe use. – Ensure that the patient understands the dosing schedule, how to cut the medication into smaller doses, and to avoid swallowing and let the medication dissolve under the tongue. · **Maximum dose:** If a patient has opioid withdrawal symptoms or cravings that are not controlled by the FDA-approved BUP maximum dose of 24 mg daily, dosing up to 32 mg daily may be beneficial but may require insurance prior authorization. In New York, as of January 18, 2024, the state Medicaid program covers up to 32 mg BUP daily for OUD treatment without prior authorization.
BUP monotherapy sublingual tablets (multiple brands)	See BUP/NLX dosing, above.	See BUP/NLX considerations for use, above.
XR-BUP subcutaneous depot injections (multiple brands) [e] **Mechanism:** Partial opioid agonist	**Sublocade** (monthly) · **Oral initiation:** Patients should tolerate taking sublingual BUP ≥8 mg per day for ≥7 days prior to injection initiation [e]. · **Injection initiation:** Administer the first 300 mg injection at week 1, and the second 300 mg injection 4 weeks after the first. · **Long-term treatment:** Administer maintenance dose of 100 mg or 300 mg every 4 weeks. The monthly dose that is most effective in managing opioid cravings and supporting treatment goals should be continued as maintenance treatment. **Brixadi** (weekly or monthly) · **Oral initiation:** Administer a 4 mg sublingual dose to test BUP tolerance without precipitated withdrawal. · **Injection initiation:** – *For patients not already taking sublingual BUP*, administer a first dose of Brixadi 16 mg followed by an additional dose of 8 mg within 3 days of the first dose for a total weekly dose of 24 mg. An additional 8 mg dose can be administered at least 24 hours after the previous injection for a total weekly dose of 32 mg. – *For patients already taking sublingual BUP*, administer the corresponding dose of Brixadi weekly or monthly for the initial dose. See prescribing information for dose equivalents. · **Long-term treatment:** Dose is individualized with a maximum dose of 32 mg weekly or 128 mg monthly.	· See manufacturers' restricted distribution programs: Brixadi REMS (Risk Evaluation and Mitigation Strategy or Sublocade Risk Evaluation and Mitigation Strategy (REMS). · Must be delivered from pharmacies or distributors that are certified by the manufacturer's REMS. **Sublocade** · Store in refrigeration; can only be stored at room temperature for up to 12 weeks. · Administer subcutaneously in abdominal region. · Maintenance doses can be administered up to 2 weeks late without clinically significant impact. **Brixadi** · Store at room temperature. · Administer subcutaneously in the abdomen, buttock, or thigh. · After 4 consecutive injections in one of the sites noted above, the injection can be administered subcutaneously in the upper arm.

Notes:
a. Federal regulations effective in 2023 eliminated the waiver requirement for prescribing BUP. Any clinician with an active DEA license to prescribe controlled substances can prescribe BUP. To contact clinicians or programs who provide BUP for OUD treatment, call the HOPEline (1-877-8-HOPENY) (New York State), see NYC Health: Treatment for Opioid Use Disorder With Buprenorphine and Methadone > How to Find Treatment (New York City), or see SAMHSA: Buprenorphine Practitioner Locator.
b. Consult full prescribing information for each medication before prescribing.
c. For OUD treatment in pregnant individuals, see NYSDOH AI guideline Substance Use Disorder Treatment in Pregnant Adults.
d. Low-dose initiation requires splitting the BUP/NLX 2 mg/0.5 mg films or tablets. A quarter of a film or tablet is a 0.5 mg BUP dose; half of a film or tablet is a 1 mg BUP dose.
e. Under specialist guidance, XR-BUP initiation approaches may vary; in some patients, the first injection may be administered <7 days after starting sublingual BUP.

TABLE: EXTENDED-RELEASE NALTREXONE FOR TREATMENT OF OPIOID USE DISORDER IN NONPREGNANT ADULTS [a,b]

Formulations and Mechanism of Action	Dosing	Considerations for Use
XR naltrexone (Vivitrol) **Mechanism:** Opioid antagonist	**Initial and long-term treatment** (intragluteal injections)**:** 380 mg every 28 days · Before starting XR naltrexone, confirm appropriate washout period from last opioid use with an NLX challenge: – Administer intranasal NLX as available (e.g., 4 mg/0.1 mL) and observe the patient's reaction. In individuals with recent opioid use, this may precipitate opioid withdrawal. – If intranasal NLX is not available, consider use of oral naltrexone, starting with a low dose (e.g., a quarter of a 50 mg tablet). – If a patient is already taking oral naltrexone, an NLX challenge is not necessary. · Before administering the initial injection, inform patients of the potential adverse effects of naltrexone and initiate oral naltrexone. Advise the patient to: – Take 25 mg of oral naltrexone (half of a 50 mg naltrexone tablet). – After 1 hour, if no adverse effects are experienced, take another 25 mg of oral naltrexone (second half of the 50 mg tablet). – If adverse effects are not experienced, take 50 mg of oral naltrexone once daily for 2 to 3 days. – If adverse effects are experienced, stop taking oral naltrexone.	· Inform patients of risk of precipitated and protracted opioid withdrawal if opioids are used before taking naltrexone [c]. · Emphasize the strong motivation and adherence needed for treatment success. · Do not initiate naltrexone in patients with concomitant use of opioid analgesics or opioid agonists (e.g., methadone or BUP) with no plans for tapering or discontinuation. · **Contraindications:** Concomitant use of opioid analgesics or opioid agonists (e.g., methadone or BUP), current physiologic opioid dependence, acute opioid withdrawal, and failure on the NLX challenge test or a positive urine screen for opioids. · Warn patients of the increased risk of opioid overdose due to increased sensitivity after discontinuing naltrexone.

Notes:
a. See full prescribing information for XR naltrexone (Vivitrol).
b. For OUD treatment in pregnant individuals, see NYSDOH AI guideline Substance Use Disorder Treatment in Pregnant Adults.
c. When withdrawal is precipitated abruptly by the administration of an opioid antagonist to an opioid-dependent patient, the resulting withdrawal syndrome can be severe. Symptoms of withdrawal usually appear within 5 minutes of ingestion of naltrexone and can last for up to 48 hours. Changes in mental status include confusion, somnolence, and visual hallucinations, and patients can experience significant fluid losses from vomiting and diarrhea requiring intravenous fluid administration.