METHADONE TO BUPRENORPHINE TRANSFERS

TRANSITIONING FROM METHADONE MAINTENANCE TO BUPRENORPHINE/NALOXONE

Work with methadone clinic staff to coordinate the methadone taper, with the transition to buprenorphine/naloxone:

- Establish with both patient and methadone clinic that, if the transition to buprenorphine/naloxone is unsuccessful (e.g., patient begins to experience withdrawal that interferes with functioning or leads to return to use, or patient does not tolerate the medication), the patient may return to methadone treatment without a gap in treatment.

- Educate patients regarding appropriate methadone dose levels for transferring to buprenorphine/naloxone. To decrease the level of physical opioid dependence and minimize the chance for precipitated withdrawal, most patients will need to have their dose tapered to 30mg before beginning buprenorphine/naloxone treatment.

Inform patient that the tapering and transitioning period may include discomfort and increased risk for relapse.

Choose approach:

- Provide target methadone dose: 20–30 mg daily for one to two weeks prior to transition is optimal, but not always necessary.

- Alternate approach: taper methadone dose to the point of patient discomfort, with objective withdrawal symptom documentation via COWS, then initiate buprenorphine/naloxone.

- Inpatient detoxification is another option to assist a patient in the transition from methadone to buprenorphine/naloxone.

Advise patient to arrange for time off from work and family support with childcare and other responsibilities during the transition, as discomfort may last 1–2 weeks.

Timing for last methadone dose/first buprenorphine/naloxone dose is difficult to predict:

- Generally, at least 36–96 hours after last methadone dose, but utilizing clinical assessment and judgment is essential.

- Long half-life of methadone (storage in body tissues, especially liver) causes unpredictable clearance.

- Initiation of buprenorphine/naloxone should be guided by withdrawal symptoms objectively documented with a COWS score of 13–15, rather than by time since last methadone dose.

Clonidine, anxiolytics (including benzodiazepines), and NSAIDs may be used to manage distressing withdrawal symptoms and be continued during induction if prescribed by provider.

More intensive stabilization support may be needed (e.g., telephone contact up to 3 times daily, until maintenance dosing is attained). Frequent visits, adequate supports, and a supportive environment to assist in the transition are important.

Providers should be experienced in induction prior to transitioning a patient from methadone maintenance to buprenorphine/naloxone.

Having the patient go to an inpatient detoxification clinic to make this transition can be a safer, more effective way to get the patient from methadone maintenance to buprenorphine/naloxone.

Induction recommendations:

- Once a COWS score of 13–15 is documented, start buprenorphine/naloxone at 2mg/0.5mg sublingually, as prescribed.

- Continue to dose patient as prescribed until physical withdrawal symptoms have been reduced to manageable levels or are absent. Patients transitioning from methadone may require higher dosing initially and then a taper down over time.

- Continue induction according to patient's prescription order, assessing symptoms of withdrawal and cravings.

- Manage symptoms with adjunctive medications, as appropriate, with provider input.

- Support and access to providers are critical components to assist patients make this transition and not jeopardize their recovery.

BUPRENORPHINE TO NALTREXONE TRANSFERS

TRANSITIONING FROM BUPRENORPHINE/NALOXONE MAINTENANCE TO NALTREXONE

There have been several observation pilot studies conducted to explore the transition from buprenorphine to naltrexone.[i, ii, iii] The vast majority were not randomized controlled trials.

Review the potential benefits of transitioning from buprenorphine/naloxone to naltrexone:

- Naltrexone is a long-acting medication.
- Naltrexone tablets have a half-life of 14 hours and can/should be dosed on a once-daily regimen.
- The extended-release injectable formulation lasts 28 days. Patients receive one injection in the clinic every 4 weeks, thus reducing the need for self-discipline and the burden of daily medication dosing.
    - Naltrexone mutes the reinforcing effects of alcohol.
- No opioid dependency.
    - Patients may choose to stop naltrexone treatment at any time without having to undergo opioid withdrawal.
- No psychoactive effects.
- Treatment is also provided within an established medical system, with integration of addiction treatment alongside medical care and the ability to obtain FDA-approved medications for opioid use disorder and alcohol use disorder.
    - Insurance may require use of a specialty pharmacy and prior authorization.
- Antagonist medications such as naltrexone accelerate the opioid-agonist detoxification process and are often prescribed post-detoxification to help prevent relapse.

Considerations:

When transitioning from buprenorphine to naltrexone, work with current buprenorphine clinic staff to coordinate the buprenorphine taper with the transition to naltrexone:

- Establish with both the patient and buprenorphine clinic that, if the transition to naltrexone fails (e.g., patient begins to experience withdrawal that interferes with functioning or leads to return to use or patient does not tolerate the medication), the patient may return to buprenorphine treatment without a gap in treatment.

- Long half-life of buprenorphine and slow dissociation for *mu* opioid receptor causes unpredictable clearance.

  → Timing for last buprenorphine dose/first naltrexone dose is difficult to predict.

  → The limited amount of available data suggests that patients may do best when tapered to 2–4mg of buprenorphine/naloxone daily for one week, waiting 5–7 days between last dose of buprenorphine/naloxone and the first dose of naltrexone, and then starting with low-dose naltrexone by mouth.

  → The tapering and transitioning period will include discomfort and an increased risk for relapse.

  → Advise patient to arrange for time off work and family support with childcare and other responsibilities during the transition, as discomfort may last several days.

- Initiation of naltrexone should be guided by patient motivation, clinical judgment, and negative UTS result for ALL opioids, rather than by last buprenorphine dose, family pressure, or law enforcement desire for patient to be on antagonist treatment.

- Withdrawal signs and symptoms will occur, causing patient discomfort.

  → Intensive stabilization and support may be needed (e.g., telephone contact up to 3 times daily until free of withdrawal signs/symptoms and patient is stable), as well as frequent visits, adequate supports, and a supportive environment to assist in the transition.

  → Clonidine, anxiolytics (including benzodiazepines), and NSAIDs may be used to manage distressing withdrawal symptoms and be continued during induction, if prescribed by provider and closely monitored.

- Begin with naltrexone tablets before administering extended-release injectable naltrexone.

- Having the patient go to an inpatient detox clinic to make this transition can be a safer, more effective way to get the patient from buprenorphine maintenance to naltrexone.

- Assess mental stability.

  → Evaluate for suicidal and/or homicidal concerns and take appropriate action.

  → Antagonist medications may be contraindicated in the setting of unstable mental health.

Suggested Buprenorphine to Naltrexone Protocol:

- Patient to reduce daily buprenorphine dose to 2mg for one week.

- Establish last dose date with patient. Five to seven days after final buprenorphine dose, patient to come to clinic with naltrexone tablet prescription bottle for naltrexone induction appointment with OBAT nurse.

- Ensure that UTS is negative for all opioids and illicit substances.

- Ensure a negative naloxone/naltrexone challenge.

- Always initiate naltrexone treatment with oral naltrexone formulation versus extended-release injectable formulation to mitigate allergic reactions, side-effects, and adverse reactions.

- Ensure that patient has support and access to providers, as these are critical components for assisting patients with making this transition and not jeopardizing their recovery.

[i] Mannelli P, Peindl KS, Lee T, Bhatia KS, Wu LT. Buprenorphine-mediated transition from opioid agonist to antagonist treatment: state of the art and new perspectives. *Curr Drug Abuse Rev.* 2012 Mar;5(1):52-63.

[ii] Kosten TR, Morgan C, Kleber HD. Phase II clinical trials of buprenorphine: detoxification and induction onto naltrexone. *NIDA Res Monogr.* 1993;121:101–101.

[iii] Sigmon SC, Dunn KE, Badger GJ, Heil SH, Higgins ST. Brief buprenorphine detoxification for the treatment of prescription opioid dependence: a pilot study. *Addict Behav.* 2009;34(3):304–311.