Methadone, naltrexone, and buprenorphine are all approved by the U.S. Food and Drug Administration for the treatment of OUD. These medications reduce opioid cravings and create opioid blockade, thus preventing reward from any opioids taken concurrently. Which medication to recommend depends on many factors, including:

- Patient preference
- Schedule III opioid
  - Can prolong the corrected half-life, methadone
- Clinician’s assessment of the risks and benefits of each medication for the individual patient
- Opioid
  - Schedule II opioid
  - Naltrexone
- Prior treatment experience (successes and challenges)

Diazepam’s assessment of the risks and benefits of each medication for the individual patient (e.g., medical comorbidities, overdose risk)

Here is an overview of the three medications:

**Methadone**
- Buprenorphine
- Naltrexone

**Mechanism of action**
- Methadone: Full opioid agonist
- Buprenorphine: Partial opioid agonist
- Naltrexone: Opioid antagonist

**Classification**
- Methadone: Schedule II opioid
- Buprenorphine: Schedule II opioid
- Naltrexone: Schedule III opioid

**Factors affecting use and frequency**
- Amount, route, or order in which daily doses are taken
- Methadone:
  - Undergoing treatment program (OTP) with observed dosing, at least weekly
  - Maintenance dose
- Buprenorphine:
  - Transmucosal formulations (e.g., buccal film, sublingual tablet)
  - Extended-release tablets
  - Effective at one or two doses per day
- Naltrexone:
  - For every daily dose

**Can this medication be prescribed legitimately for OUD (treatment)?**
- Methadone
  - Yes
  - Must be ordered and dispensed by a licensed physician
  - Schedule II opioid
  - May be prescribed in a combination with other medications
- Buprenorphine:
  - Yes
  - Can be used in conjunction with other medications
- Naltrexone:
  - Yes
  - Only for patients in recovery

**Can use for the extended-release formulation (e.g., methadone) be used?**
- Methadone
  - Yes
  - It can be used in the hospital setting
  - Methadone is often used as a part of a comprehensive opioid treatment program (OTP)
- Buprenorphine:
  - Yes
  - Highly structured treatment with potential for patient self-completion
  - Potential relapse following treatment
- Naltrexone:
  - Yes
  - Effective for patients in recovery

**Evidence of benefit for OUD treatment**
- Methadone
  - More effective when used with opioid antagonists
  - Methadone induction performed
- Buprenorphine
  - More difficult to induce

**Rate of retention**
- Methadone
  - More than 50 years of use
  - Obstetric
  - Risk of relapse
- Buprenorphine
  - Less than 5 years of use
  - Opioid agonist
  - Risk of relapse
- Naltrexone:
  - No evidence
  - Opioid antagonist
  - Risk of relapse

**Risk of outcome**
- Methadone
  - Reduced risk of mortality
  - Reduced risk of overdose
- Buprenorphine
  - Reduced risk of mortality
  - Reduced risk of overdose
- Naltrexone:
  - No risk
  - High risk of overdose

**Other safety concerns**
- Methadone:
  - None
  - Reduced risk of mortality
- Buprenorphine:
  - None
  - Reduced risk of mortality
- Naltrexone:
  - None
  - Reduced risk of mortality

**For more information**
- Last reviewed Oct 2023. Last modified Oct 2023. The information included here is provided for educational purposes only. It is not intended as a sole source on the subject matter or as substitute for the professional judgment of qualified healthcare professionals. Users are advised, whenever possible, to confirm the information through additional sources.