

Q. What is buprenorphine/naloxone?

A. The combination of buprenorphine/naloxone medication plus counseling is approved by the U.S. Food and Drug Administration (FDA) as an induction and maintenance treatment for opioid use disorder (OUD). Buprenorphine/naloxone is available in three different formulations: buccal film, sublingual film, or sublingual tablet.

Q. What are the potential mechanisms of action underlying buprenorphine/naloxone for the treatment of OUD?

A. Buprenorphine is the active drug in buprenorphine/naloxone. Buprenorphine is a partial opioid agonist; it has a function similar to an opioid but has a weaker effect than full agonists such as heroin and methadone (Lutfy & Cowan, 2004). It also has a “ceiling” at which the opioid effect levels off as dose increases. The ceiling effect reduces the risk of misuse, dependency, and side effects. Buprenorphine also reduces withdrawal symptoms and cravings and helps with abstinence from other opioids. The naloxone component of buprenorphine/naloxone serves as an opioid antagonist or “blocker.” When absorbed and activated in the body, naloxone causes an individual who is dependent on opioids to have uncomfortable withdrawal symptoms. However, naloxone is absorbed and activated only if a tablet or film is snorted or injected into the bloodstream rather than dissolved in the mouth as prescribed (Naloxone Hydrochloride, 2020). Consequently, individuals who are dependent on nasal or intravenous (IV) opioids are discouraged from snorting or injecting buprenorphine/naloxone. Rates of misuse of buprenorphine/naloxone in the United States appear to be lower than with other opioids (Yokell, Zaller, Green, & Rich, 2011).

Q. Is buprenorphine/naloxone recommended as a treatment for OUD in the Military Health System (MHS)?

A. **Yes.** The 2015 VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders (SUDs) recommends buprenorphine/naloxone for patients with OUD, with a “strong for” strength of recommendation.

The MHS relies on the VA/DoD CPGs to inform best clinical practices. The CPGs are developed under the purview of clinical experts and are derived through a transparent and systematic approach that includes, but is not limited to, systematic reviews of the literature on a given topic and development of recommendations using a graded system that takes into account the overall quality of the evidence and the magnitude of the net benefit of the recommendation. A further description of this process and CPGs on specific topics can be found on the VA clinical practice guidelines website.

Q. Do other authoritative reviews recommend buprenorphine/naloxone as a treatment for OUD?

A. **Yes.** Other authoritative reviews have substantiated the use of buprenorphine/naloxone as a treatment for OUD.

Several other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. These include the Agency for Healthcare Research and Quality (AHRQ) and Cochrane.

- AHRQ: No comparative effectiveness reviews on buprenorphine/naloxone for OUD were identified.
- Cochrane:
 - A 2014 systematic review of buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence found that buprenorphine retained people in treatment better than placebo, and, at high doses, reduced illicit opioid use compared to placebo (Mattick, Breen, Kimber, & Davoli, 2014). Buprenorphine prescribed at fixed doses was found to be equivalent to methadone prescribed at fixed doses in treatment adherence and suppression of illicit opioid use.
 - A 2016 systematic review of six trials of buprenorphine, methadone, and other opioid agonist treatments for pharmaceutical opioid dependence found low to moderate quality of evidence

supporting their use for maintenance treatment (Nielsen et al., 2106). Buprenorphine and methadone appeared to be equally effective for maintenance, and buprenorphine also was reported to be more effective than detoxification or psychological treatments for maintenance.

Q. What conclusions can be drawn about the use of buprenorphine/naloxone as a treatment for OUD in the MHS?

A. Buprenorphine/naloxone has met the burden of evidence for inclusion in VA/DoD guidelines and is considered a first-line pharmacological treatment for OUD. The CPG states that this medication should be used in conjunction with a psychosocial intervention. The U.S. National Institute on Drug Abuse has identified the medication as a first-line treatment for opioid dependence (Bridge, Fudala, Hebert, & Leiderman, 2003). Providers should take into account factors such as potential adverse effects, comorbidities, and availability to inform treatment choice for patients with OUD.

References

- Bridge, T. P., Fudala, P. J., Hebert, S., & Leiderman, D. B. (2003). Safety and health policy considerations related to the use of buprenorphine/naloxone as an office-based treatment for opiate dependence. *Drug and Alcohol Dependence*, 70(Suppl 2), s79–85.
- Department of Veterans Affairs/Department of Defense. (2015). *VA/DoD clinical practice guideline for the management of substance use disorders. Version 3.0*. Washington, DC: Department of Veterans Affairs/Department of Defense.
- Lutfy, K., & Cowan, A. (2004). Buprenorphine: A unique drug with complex pharmacology. *Current Neuropharmacology*, 2(4), 395–402.
- Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2014). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database of Systematic Reviews*, 2, CD002207.
- Naloxone Hydrochloride. (2020, May 12). Drugs.com. Retrieved June 12, 2020, from <https://www.drugs.com/monograph/naloxone-hydrochloride.html>
- Nielsen, S., Larance, B., Degenhardt, L., Gowing, L., Kehler, C., Lintzeris, N. (2016). Opioid agonist treatment for pharmaceutical opioid dependent people. *Cochrane Database of Systematic Reviews*, 5, CD011117.
- Yokell, M. A., Zaller, N. D., Green, T. C., & Rich, J. D. (2011). Buprenorphine and buprenorphine/naloxone diversion, misuse, and illicit use: An international review. *Current Drug Abuse Reviews*, 4(1), 28–41.

