Opioid and Buprenorphine Use for Treating Opioid Use Disorder

A Retrospective Drug Utilization Review

Buprenorphine and full opioid agonists should not be used together to treat opioid use disorder.

The National Institute on Drug Abuse reports more than 130 individuals die from opioid overdose each day in the United States.[1] Overdose deaths from prescription opioids such as fentanyl, morphine, and oxycodone rose from 3,442 deaths in 1999 to 17,029 deaths in 2017 in the United States.[2] Some major contributing factors to this growing opioid epidemic are:

- Inadequately controlled pain
- Overprescribing, and
- The abuse or misuse of prescription opioid analgesics.

A better understanding of the drivers that fuel this epidemic and the pharmacological treatment options that are available can help combat the opioid crisis and optimize patient care.

> **Fentanyl** and morphine are a few of the most talked about "drivers" when referring to the opioid crisis. While these are catalysts, some of the other opioid analgesics can be overlooked such as tramadol and codeine. For most opioids, their analgesic effect is a result of activity at the mu-opioid receptor.
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> **Tramadol,** unlike other opioid analgesics, has a dual mechanism of action: it is a centrally acting full opioid agonist at the mu-opioid receptor and also a weak inhibitor of norepinephrine and serotonin reuptake. Tramadol gets metabolized by the liver to a much more active metabolite called "M1", which has a much higher affinity for the mu-opioid receptor.
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> **Codeine** is a more traditional full-opioid agonist, but has weak affinity for the mu-opioid receptor. Codeine is metabolized to morphine resulting in analgesic activity. Other full opioid-agonists that react at the mu-receptor include oxycodone, hydromorphone, and hydrocodone.
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> **Buprenorphine,** unlike full-agonists, is a mixed opioid agonist-antagonist. It is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor. Antagonizing the kappa receptor produces alterations in a patient's perception of pain as well as alters the emotional response to pain. Buprenorphine is more efficacious and safer when used as medication-assisted treatment (MAT) therapy than tapering opioids alone in patients with opioid use disorder. This is because buprenorphine helps lower a patient's psychological and physical dependence while providing a "ceiling effect" to decrease abuse and abuse potential.[3] Proper utilization of MAT options such as buprenorphine, methadone, and naltrexone by healthcare professionals in addition to safer prescribing practices can help manage the patient's pain more effectively and combat the opioid crisis.

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[1]National Institute on Drug Abuse. Opioid Overdose Crisis. Revised January 2019. https://www.drugabuse.gov/drugs-abuse/opioids/opioid-overdose-crisis#one. Accessed June 19, 2019.
[2]National Institute on Drug Abuse. Overdose Death Rates. Revised January 2019. https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates. Accessed June 19, 2019.
[3]The National Alliance of Advocates for Buprenorphine Treatment. Thorough Technical Explanation of Buprenorphine. http://www.naabt.org/education/technical_explanation_buprenorphine.cfm. Accessed June 19, 2019.

Drug Utilization Review Findings:

Concomitant use of Buprenorphine and Opioids

A retrospective analysis of the concurrent drug utilization review (DUR) point of sale rejects was conducted to evaluate the effectiveness of alerting dispensing pharmacists to potential medication related issues.

While reviewing the UnitedHealthcare Community Plan members on concomitant use of buprenorphine and opioids, 93 members were identified as having 5 or more overrides of the 5 or more overrides of the rejected claims. Many of these members received long term concurrent buprenorphine and opioids, most notably, tramadol.

Concurrent use is a major drug-drug interaction that leads to toxicities causing extreme central nervous system depression. Both buprenorphine and full opioid agonists have warnings regarding the use together due to both being CNS depressants.[4] Buprenorphine and other opioid analgesics compete for the binding site at the mu-opioid receptor. Buprenorphine has a higher affinity for these receptors and will displace morphine and other full opioid agonists at the mu-opioid receptor. This competition for receptors makes the safety and efficacy of other opioid analgesics unpredictable and additive which will result in an alteration of treating addiction and pain.[5]

Though there is essentially no time limit for buprenorphine treatment, the quicker the patient is able to taper off of the MAT, the faster the patient will reach complete remission. Therefore, because of the major drug interaction and the pharmacology of these two medicines, buprenorphine and full opioid agonists should not be used together to treat opioid use disorder and non-opioid analgesics are warranted to treat pain in patients with this disorder.

Goal of the Drug Utilization Review Team

The UnitedHealthcare Community Plan drug utilization review program is administered to promote the safe and efficacious use of medications. These interventions do not take into consideration patient-specific variables. The intent of this newsletter is to bring attention to potential medication related issues that have been found during an analysis of the DUR data regarding concomitant use of MAT and opioids. MAT has an important role in therapy especially with the current opioid crisis. UnitedHealthcare Community Plan is committed to continuing to provide the best possible care for our members.

Working to build healthier communities.

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[4]Subutex [package insert]. Richmond, VA: Reckitt Benckiser Pharmaceuticals; 2011.
[5]Niel JV, Schneider J, Tzschentke T. Efficacy of Full μ-Opioid Receptor Agonists is not Impaired by Concomitant Buprenorphine or Mixed Opioid Agonists/Antagonists – Preclinical and Clinical Evidence. Drug Research. 2016;66(11):562-570. doi:10.1055/s-0042-109393.

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