Methadone & Buprenorphine: Understanding the Difference

American Association for the Treatment of Opioid Dependence, Inc.

METHADONE	&	BUPRENORPHINE
Both methadone and buprenorphine are long-acting synthetic opioid medications that can be used in the treatment of opioid use disorder. Both have a robust evidence base to support their efficacy in treating opioid use disorder.		
DEA Schedule		**DEA Schedule**
Schedule II		Schedule III
Drug Properties		**Drug Properties**
Methadone is a full opioid agonist drug. This means that when methadone binds to an opioid receptor, it fully activates the receptor.		Buprenorphine is a partial opioid agonist drug. This means that when buprenorphine binds to an opioid receptor, it only partially activates the receptor.
Induction Risks		**Induction Risks**
Significant caution must be used when starting someone on methadone (called induction). Because methadone is long-acting, methadone can accumulate and cause delayed toxicity. High starting doses, doses that are increased too quickly, or inadequate assessment of a patient's opioid tolerance can result in overdose and even death. These risks are particularly high in the first two weeks of treatment. Close monitoring during methadone induction is required to prevent adverse outcomes.		Overdose risks associated with starting buprenorphine are low. Buprenorphine has significantly less risk of sedation and respiratory depression (the primary cause of overdose) during induction. As a result, buprenorphine starting doses are often administered at home by the patient with instructions from the prescriber. If buprenorphine is started too soon after the last dose of another opioid it can cause the abrupt onset of withdrawal symptoms.
Overdose Risks		**Overdose Risks**
As a full opioid agonist, increasing doses of methadone result in increased opioid effects, including sedation, respiratory depression, and overdose. Overdose risks extend beyond the first two weeks of treatment if patients take more than their daily dose of methadone. Overdose risks are also increased in elderly patients, patients with COPD or other respiratory illnesses, or in patients taking other contraindicated or sedative medications (legally or illegally) Risk of overdose when taken by someone not tolerant to methadone or other opioids is high. The DEA requires that patients store methadone received from an OTP in a locked container to prevent against access by unintended recipients, including children.		As a partial agonist, buprenorphine is unable to produce maximal activation of the opioid receptors, regardless of the amount of drug applied. As a result, there is a ceiling effect where increased doses of buprenorphine do not result in increased opioid effects, including respiratory depression. This reduces the likelihood and occurrence of overdose involving buprenorphine. Overdose with buprenorphine is possible when taken by someone not tolerant to opioids or in combination with other commonly prescribed medications; however, these risks are significantly less than that associated with methadone. Buprenorphine is absorbed under the tongue or cheek and is less effective when swallowed (due to poor oral bioavailability) resulting in reduced risks of overdose with accidental ingestion.

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FDA Black Box warnings		**FDA Black Box warnings**
Because of the increased risks of respiratory depression, methadone carries a FDA black box warning on the increased risks of respiratory depression.		No black box warning
Additional Risks		**Additional Risks**
In some people methadone may interfere with normal electrical circuits in the heart and can cause an EKG change called QTc Prolongation. Because of genetic differences and other medications being taken, some people are at higher risk of this than others. QTc Prolongation may be seen at higher doses of methadone. If this is not addressed it could lead to a cardiac arrhythmia called Torsades de Pointes, which can be fatal. This risk can be addressed by careful monitoring.		Cardiac arrhythmia (QTc Prolongation/Torsades de Pointes) is *not* a risk with buprenorphine.
Formulations/Route of Administration		**Formulations/Route of Administration**
Liquid Tablet Dispersible Tablets (restricted to opioid treatment programs and hospitals) All forms are taken orally. No abuse deterrent formulations.		Tablet Film Strip Subdermal implant Extended-release injection Both the tablet and film are dissolved under the tongue or inside the cheek. Buprenorphine tablets and film strips are also available in an abuse deterrent formulation which combines buprenorphine with naloxone (common brand name: Suboxone). When a buprenorphine/ naloxone combo drug is injected (in an attempt to divert or get greater effect) the naloxone is activated and results in opioid withdrawal.
Risks associated with diversion		**Risks associated with diversion**
Methadone carries a high diversion and misuse potential. Due to the overdose risks associated with methadone, methadone diversion carries significant risk for adverse consequences including death. When methadone prescriptions for pain increased in the late 1990's and early 2000's, there was a significant increase in methadone deaths. At least three federal reports showed the increase in methadone mortality was directly related to patients receiving methadone by a prescription.		Buprenorphine is known to have high rates of diversion; however, the lower risks of overdose with buprenorphine misuse means less risk of fatal consequences are associated with buprenorphine diversion.