FREQUENTLY ASKED QUESTIONS

Fentanyl

A Guide for Hospital Providers

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Frequently Asked Questions

Is buprenorphine a good treatment for people who use fentanyl?

Yes. Buprenorphine is a great treatment for people who use fentanyl, as is methadone in communities where it is available. Current studies show no difference between rates of treatment initiation, retention, and opioid abstinence with buprenorphine treatment for people who use fentanyl compared to those who use other opioids.[1,2] An ongoing, multi-site trial of buprenorphine initiation at twenty-eight emergency departments (EDs) across the United States shows a 1% risk of precipitated withdrawal in a population with urine drug screens that are positive for fentanyl in 76% of cases.[3]

How should I start a patient who uses fentanyl or fentanyl analogs on buprenorphine?

An empathetic, reassuring provider makes a big difference. Ask patients about prior experience with buprenorphine (prescribed or from the street), including buprenorphine use while using fentanyl. Explain that most buprenorphine starts are smooth and any complications can be managed.

In most cases, our recommended protocol is to:

- stop all opioids,
- wait for *objective evidence* of withdrawal (will often take >24 hours in people who use fentanyl daily),
- give a first dose of 8-16 mg of buprenorphine, and
- rapidly increase as needed up to 32 mg or more.[4,5]

See our Buprenorphine Hospital Quick Start for more details.

This strategy allows rapid titration to therapeutic doses, increasing the probability of overdose protection and retention in treatment. If a patient is not in withdrawal prior to ED discharge, they may be discharged with a

buprenorphine prescription to begin once they are experiencing significant withdrawal. Adjunctive medications, motivational interviewing, and very low-dose buprenorphine (e.g., 20 mcg/hr buprenorphine patch applied prior to discharge) may help patients better tolerate the wash-out period.

In the inpatient setting or for outpatients with chronic pain on prescribed opioids, patients may receive short-acting oral full opioid agonists (e.g., morphine for 72 hours) to support fentanyl wash-out. After 72 hours, stop the short-acting opioids, and, once the patient is in withdrawal, start the first buprenorphine dose at 8 mg, then repeat as needed every hour up to 32mg total on day 1.

In certain cases, cross tapering (also referred to as microdosing) can be considered. Cases where this may be beneficial include treating people with a history of severe precipitated withdrawal, planned prolonged hospitalization with significant pain, a medically unstable situation, or methadone in their systems.[6–8] We do not generally advise cross tapering buprenorphine starts in the ED due to logistical barriers to patient adherence, safety concerns, and minimal data in this population. For more information on cross tapering, see Starting Buprenorphine with Microdosing and Cross Tapering.

Cautionary Note

Doses in the low-moderate range (2-4 mg) are high enough to cause precipitated withdrawal but not high enough to adequately treat withdrawal in patients who regularly use fentanyl.

What should I do if buprenorphine causes withdrawal in my patient?

Persistent or worsening symptoms after the first buprenorphine dose may be due to insufficiently treated withdrawal, co-occurring withdrawal (especially benzodiazepine or alcohol withdrawal), intoxication, side effects of buprenorphine, or medical mimics (e.g., sepsis, diabetic ketoacidosis). However, a significant and sudden worsening of withdrawal symptoms within one hour of the first buprenorphine dose is consistent with precipitated withdrawal. If this occurs:

- Give an additional dose of 16 mg sublingual (SL) buprenorphine as soon as possible—this dosing can also be given in the outpatient setting and should not be delayed.

In the acute care setting:

- Add 1-2 mg lorazepam by mouth (PO) to reduce anxiety.
- If withdrawal does not improve with the first dose of 16 mg buprenorphine and 1-2 mg lorazepam, quickly administer an additional 16mg SL buprenorphine. In most cases, precipitated withdrawal can be managed with repeat buprenorphine doses up to a total of 32-48 mg in 24 hours.
- Consider the addition of ketamine to treat hyperalgesia, pain, and to potentiate buprenorphine mu receptor signaling. Ketamine can be provided in a bolus (e.g., 0.3 mg/kg slow IV push q 30 min) or an infusion (0.3-1 mg/hr).[9]
- Additional treatments of potential but unclear value include clonidine, antipsychotics, NSAIDS, acetaminophen, antiemetics, as well as full opioid agonists.

After the management of precipitated withdrawal, most patients who received at least 16 mg buprenorphine on their start day can continue buprenorphine normally the next day without further withdrawal.

What dose of buprenorphine works best for people who use fentanyl?

Most patients who use fentanyl do extremely well on buprenorphine. Immediately after a buprenorphine start, higher doses of buprenorphine (24-32 mg SL daily or divided dosing) may be required to adequately control symptoms for people who use fentanyl regularly. For some patients, the first-week dosing may be higher than subsequent weeks. In the ED, we suggest discharging patients who use fentanyl with at least 7 days supply for 24-32 mg buprenorphine per day. In some cases, and in the outpatient setting, doses can subsequently be tapered to 16-24 mg. Subcutaneous, long-acting buprenorphine (Sublocade) may better control cravings and withdrawal, as is it achieves high serum levels of buprenorphine.[10,11] For more information on subcutaneous, long-acting buprenorphine, see our Extended-Release Buprenorphine guide.

How is fentanyl use different from any other opioid?

- Fentanyl is a synthetic opioid, therefore it is not detected on many immunoassay urine drug tests. Clinical diagnosis of fentanyl use or withdrawal is often needed.
- Fentanyl is about 40 times more potent than heroin[12,13] and has a high affinity for and high efficacy at the mu opioid receptor. Fentanyls include a widening number of available analogues of varying potency. The variations in fentanyl type, potency, and purity increase the risk of overdose.
- Fentanyl is highly lipophilic. While a single bolus dose of fentanyl has a short half life[14], repeated use of fentanyl leads to accumulation in adipose tissue. In addition, reduced renal clearance occurs with chronic use. Clinically, daily fentanyl use leads to delayed withdrawal (often >24 hours) and longer urine toxicology positivity.[15]

The resulting increased time to withdrawal and increased tolerance can sometimes make starting buprenorphine more challenging in people who use fentanyl regularly.[16] Waiting for objective evidence of withdrawal and using high doses of buprenorphine can improve patient experiences with treatment.

Why is there fentanyl in the drug supply?

Most street fentanyl is not pharmaceutical fentanyl that has been diverted, rather it is synthesized in clandestine labs internationally. Supply side advantages of fentanyl production and distribution include the relatively low cost of synthesizing fentanyl and ease of transporting it in small packages.[17] Some people who use opioids intentionally purchase fentanyl because of the cost effectiveness, high potency, rapid effect, and the convenience and safety of smoking over injecting.[18,19]

Drugs that are not sold as fentanyl may be contaminated unintentionally during packaging or preparation of drugs, or intentionally by sellers. Furthermore, there is widespread availability of counterfeit pills across drug classes (e.g., counterfeit Xanax), which may contain varying amounts of fentanyls. Additionally, intentional use of fentanyl and stimulants to balance each other out is common and may cloud the picture of stimulant adulteration with fentanyl.

Can you overdose by touching or being in the same room as fentanyl?

No. Touching fentanyl, touching someone who uses fentanyl, or breathing air near fentanyl does not cause an overdose.[20] Standard precautions, such as nitrile gloves, are more than adequate when handling fentanyl.

Does naloxone work to reverse a fentanyl overdose?

Yes. In some cases, repeat naloxone doses or higher doses may be needed to reverse fentanyl overdoses.[21,22] Management of fentanyl overdose may be challenging because of the rapid onset of overdose,[21,23] risk of wooden chest syndrome, which may not respond to naloxone,[24] and frequency of complex overdose with multiple sedating substances such as benzodiazepines.[25] Rapid use of naloxone following overdose symptoms remains the most important factor.

Can a person who uses fentanyl that is in precipitated withdrawal from a naloxone overdose reversal be treated with buprenorphine?

Yes.[26–28] 16 mg SL buprenorphine is the most common initial treatment. For more information, see Starting Buprenorphine Immediately After Reversal of Opioid Overdose with Naloxone.

Caring for People Who Use Fentanyl

ED Buprenorphine Treatment For People Who Use Fentanyl

If objective signs of withdrawal are clear and the patient feels ready: Dose 8-16mg SL buprenorphine and repeat as needed every 60 min. It is only in rare cases that 32 mg SL is not sufficient.

If there are no or unclear signs of withdrawal: Support the patient in stopping fentanyl use and waiting for withdrawal. The wash-out period may take several days. Once the patient feels very sick from withdrawal, they can take 8 mg SL buprenorphine and repeat q 1 hour as needed with up to 32 mg total on day 1. They may also come to the ED for a directly supported buprenorphine start when in withdrawal. Example prescription: buprenorphine-naloxone 8-2 mg films, 2-4 films SL q day, #28, 0 refills.

- To support abstinence during fentanyl wash-out period: While still in the ED, consider administering morphine PO x 1 to mitigate withdrawal. This can support motivational interviewing and help patients wait for full fentanyl withdrawal in the outpatient setting.

If precipitated withdrawal occurs at any time:

1. Give the patient 16 mg SL buprenorphine (if the patient is unable to tolerate SL, use 0.9 mg IV buprenorphine) AND a single dose of benzodiazepine (e.g., 1-2 mg lorazepam PO, monitor for sedation/respiratory depression). Repeat buprenorphine until the patient's pupils are small. Only in rare cases is 32 mg SL not sufficient.
2. If withdrawal persists: give the patient 0.3 mg/kg IV ketamine at a slow push every 30 minutes as needed until the patient is calm and lightly sedated. Hold for excessive sedation (moderate to deep) or if dissociative symptoms develop.

Reducing Harms of Fentanyl

Universal precautions for all people who use drugs (including those who use fentanyl)

- Provide buprenorphine to any patient who uses opioids, regardless of whether they plan to stop use of nonprescribed opioids. Wait for objective evidence of withdrawal before starting buprenorphine. Methadone is also a good option when available.
- Provide harm reduction kits, including safer injection supplies and safer smoking supplies. Fentanyl can be snorted or smoked from a foil or bubble pipe–these supplies decrease the risk of injection complications.
- Provide naloxone, including distribution without prescription, to anyone who uses drugs or may be near someone who uses drugs.
- Counsel on universal overdose precautions:
  - Always start with a small test dose, much less than usual or more dilute than usual, to gauge the potency of a drug.[29]
  - Use with a companion, who should have naloxone available. Take turns using/stagger use.
  - If no companion is available, call the Never Use Alone line at (800) 484-3731.[30]

Additional precautions for people trying to avoid fentanyl use (including drugs sold as heroin, opioid pills, benzodiazepine pills, and stimulants)

Offer fentanyl test strips so that patients can check their drugs before use. Share our step-by-step guidance, Prevent Overdose with Fentanyl Test Strips. *Note that fentanyl test strips do not indicate how much fentanyl is in a batch, just its presence.*

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