Buprenorphine/naloxone

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- **Suboxone®**
  - Sublingual tablet (under the tongue): 2 mg buprenorphine with 0.5 mg naloxone, 8mg buprenorphine with 2 mg naloxone
  - Sublingual film (under the tongue or inside the cheek): 2 mg buprenorphine with 0.5 mg naloxone, 4 mg buprenorphine with 1 mg naloxone, 8 mg buprenorphine with 2 mg naloxone, 12 mg buprenorphine with 3 mg naloxone
- **Bunavail®**
  - Buccal film (inside the cheek): 2.1 mg buprenorphine with 0.3 mg naloxone, 4.2 mg buprenorphine with 0.7 mg naloxone, 6.3 mg buprenorphine with 1 mg naloxone
- **Zubsolv®**
  - Sublingual tablet (under the tongue): 0.7 mg buprenorphine with 0.18 mg naloxone, 1.4 mg buprenorphine with 0.36 mg naloxone, 2.9 mg buprenorphine with 0.71 mg naloxone, 5.7 mg buprenorphine with 1.4 mg naloxone, 8.6 mg buprenorphine with 2.1 mg naloxone, 11.4 mg buprenorphine with 2.9 mg naloxone
- **Cassipa®**
  - Sublingual film (under the tongue): 16 mg buprenorphine with 4 mg naloxone

All FDA warnings are at the end of this fact sheet. Please consult them before taking this medication.

If you or someone you know is in crisis, please call 911 and/or the toll-free National Suicide Prevention Lifeline at 800-273-TALK (8255) to speak with a trained crisis counselor 24/7. A help line and other resources are also available through the National Alliance on Mental Illness at nami.org.

Medication Assisted Treatment (MAT)

Medication assisted treatment (MAT) is the use of medications in combination with counseling and behavioral therapies for the treatment of substance use disorders. A combination of medication and behavioral therapies is effective in the treatment of substance use disorders and can help some people to sustain recovery.

What is buprenorphine/naloxone and what does it treat?

Buprenorphine/naloxone is a medication that works in the brain to treat opioid use disorder. Opioids include heroin and prescription pain relievers such as hydrocodone, oxycodone, morphine, and fentanyl.

Buprenorphine is the active drug in buprenorphine/naloxone. Buprenorphine is known as a partial opioid agonist which means it partially works like an opioid and the effect is weaker than full agonists like heroin and methadone. It also has a "ceiling effect" so the opioid effects level off even with further dose increases which reduces the risk of misuse, dependency, and side effects. Buprenorphine lowers the effects of opioid withdrawal symptoms and cravings to use opioids without having full opioid potency or effects. This helps people who take the medication abstain from other opioids.

The naloxone part of buprenorphine/naloxone is known as an opioid antagonist or "blocker". It is only absorbed and activated in the body if the tablet or film is injected instead of being dissolved in the mouth as prescribed. If naloxone is injected into the bloodstream, it will cause someone who is dependent on opioids to have uncomfortable withdrawal symptoms. This helps discourage people who are dependent on intravenous (IV) opioids from injecting buprenorphine/naloxone.
It is important to combine buprenorphine/naloxone treatment with counseling and other support.

Symptoms of opioid use disorder include:

- Being unable to quit using opioids despite problems with health and relationships.
- Needing more opioids to achieve the same effect.
- Going through withdrawal symptoms (sweating, shaking, nausea, vomiting, diarrhea, body aches, anxiety, irritability, runny nose) when unable to use opioids.
- Spending the majority of time using or finding a way to use opioids.
- Having a desire but an inability to decrease the amount of opioids used.
- Giving up enjoyable activities in order to use opioids.

What is the most important information I should know about buprenorphine/naloxone?

Your health care provider will determine when buprenorphine/naloxone should be started. If it is started too early after using other opioids, you could experience withdrawal symptoms, such as sweating, shaking, nausea, vomiting, diarrhea, body aches, anxiety, irritability, or runny nose.

Do not stop taking buprenorphine/naloxone, even when you feel better. Only your health care provider can determine the length of treatment that is right for you. If buprenorphine/naloxone is stopped abruptly, you may have withdrawal symptoms.

Missing doses of buprenorphine/naloxone may increase your risk for relapse.

Respiratory depression (slowed breathing) and death can rarely happen when buprenorphine/naloxone is taken as prescribed. This risk is increased when buprenorphine/naloxone is injected into the body or when it is mixed with other depressants including benzodiazepine medications (such as lorazepam, diazepam, or alprazolam) and alcohol. Patients taking buprenorphine/naloxone or their caregivers should seek immediate medical attention if they start to experience unusual dizziness or lightheadedness, extreme sleepiness, slowed or difficulty breathing, or unresponsiveness.

Do not inject ("shoot-up") buprenorphine/naloxone. This can cause uncomfortable withdrawal symptoms, respiratory depression (slowed breathing), or death in someone dependent on opioids.

Buprenorphine/naloxone should not be used as a pain reliever. There have been deaths reported in people who have never used opioids before after using low doses of buprenorphine/naloxone.

Buprenorphine/naloxone is not recommended in people with severe liver disease. Liver injury is rare. This can be monitored through blood tests. Alert your doctor immediately if you experience any yellowing of your skin and/or eyes, severe stomach pain, or severe nausea or vomiting.

Tell all of your providers and pharmacists that you are on buprenorphine/naloxone. You should not take other medications with buprenorphine/naloxone without talking to your provider.

Do not drive or operate heavy machinery until you know how you will respond to buprenorphine/naloxone.

Store buprenorphine/naloxone out of the reach and sight of children. Buprenorphine/naloxone can cause serious respiratory depression (slowed breathing) and death in children.

Are there specific concerns about buprenorphine/naloxone and pregnancy?

If you are planning on becoming pregnant, notify your health care provider to best manage your medications. People living with substance use disorders that wish to become pregnant face important decisions and challenges. Active substance use disorders during pregnancy put the fetus at great risk. It is important to discuss the risks and benefits of continued treatment with your doctor and caregivers.

Opioid use disorder in pregnancy is associated with adverse outcomes such as low birth weight, preterm birth, and fetal death. Receiving treatment for opioid use disorder during pregnancy lowers these risks.

The effects of buprenorphine/naloxone on the fetus when used in pregnant women are unknown. Buprenorphine/naloxone did not appear to cause structural abnormalities during animal studies. There was evidence of obstructed labor, fetal death, neonatal death, and developmental delays in animal studies. These results cannot be applied to humans. Buprenorphine without naloxone did not show an increased risk of major structural abnormalities when studied in pregnant women. Opioid withdrawal symptoms may occur in newborn infants of women who were taking buprenorphine (without naloxone) during pregnancy. There have been reports of poor feeding, diarrhea, irritability, tremor, trouble breathing, low heart rate, rigidity, and seizure in infants exposed to buprenorphine.

Methadone is better studied for pregnant women needing medication for opioid use disorder. Buprenorphine without naloxone is a reasonable alternative to methadone for pregnant women. Buprenorphine/naloxone should only be used in pregnancy if the benefits outweigh the risk to the fetus.

Regarding breastfeeding, caution is advised since buprenorphine does pass into breast milk. Small studies of buprenorphine use in breastfeeding women did not show adverse events in breastfed infants. There is no data on buprenorphine/naloxone in breastfeeding. Nursing mothers who are taking buprenorphine/naloxone should monitor their infants for signs of increased drowsiness or trouble breathing.

What should I discuss with my health care provider before taking buprenorphine/naloxone?

- Symptoms of your condition that bother you the most
- If you have allergies to any medications
- If you have thoughts of suicide or harming yourself
- Medications you have taken in the past for your condition, whether they were effective or caused any adverse effects
- If you experience side effects from your medications. Some side effects may pass with time, but others may require changes in the medication.
- Any other psychiatric or medical problems you have, including a history of liver disease
- All other medications you are currently taking (including over the counter products, herbal and nutritional supplements) and any medication allergies you have
- Other non-medication treatments you are receiving, such as talk therapy or counseling. Your provider can explain how these different treatments work with the medication.
- If you are pregnant, plan to become pregnant, or are breastfeeding
- If you use illegal drugs or narcotics

How should I take buprenorphine/naloxone?

Buprenorphine/naloxone is available as a tablet or film that dissolves in the mouth. On the first day of buprenorphine/naloxone treatment, a starting dose up to 8mg/2mg per day is usually recommended. This starting dose should be carefully adjusted under the supervision of a certified health care provider to find the safest and most effective dose for you. The recommended daily maintenance dose of buprenorphine/naloxone tablets or films is usually 16mg/4mg taken once per day. Only your health care provider can determine the correct dosage form or dose.

Buprenorphine/naloxone tablets should be dissolved under the tongue. Do not swallow. Keep the tablets in place under the tongue until completely dissolved. Do not eat or drink anything until the tablets are completely dissolved. If more than one tablet is needed to reach the prescribed dose, place all tablets in different places under the tongue at the same time. If this is not possible, see the detailed instructions on the medication guide that came with your prescription or ask your health care provider.

When you first begin using buprenorphine/naloxone film, it should be dissolved under the tongue. Place one film under the tongue until it is completely dissolved. Do not move the film after placement. You can place the film under the tongue on either the left or right side close to the base of the tongue. If a second film is needed, the second should be placed on the opposite side. If a third film is required, place it on either side after the first two films have dissolved. After a few days, you can decide to dissolve buprenorphine/naloxone films under the tongue or on the inside of the cheek.

Patients taking Bunavail® will apply the film using a dry finger directly to the inside of their cheek. Place the film with the text (BN2, BN4, BN6) against the inside cheek and press for 5 seconds. Keep film in place until it dissolves. If using more than 1 film, then place the second film on the opposite cheek. No more than 2 films should be placed on the inside of one cheek at the same time.

Patients should be stabilized on another buprenorphine-containing product at a dose of 16 mg before starting Cassipa®. Do not cut, chew, or swallow Cassipa®.

Drink water to moisten your mouth before taking the film to help it dissolve better. Buprenorphine/naloxone films will not work as well if swallowed. Buprenorphine/naloxone film should be taken whole. Do not cut, chew, or swallow the film.

Your provider or pharmacist can show you how to take buprenorphine/naloxone. You can find detailed instructions on how to use buprenorphine/naloxone tablets or films in the medication guide that comes with your prescription from the pharmacy.

Do not switch from one dosage form of buprenorphine/naloxone to another medication that contains buprenorphine without talking with your doctor. The amount of buprenorphine may be different than other buprenorphine containing medications and your doctor will prescribe a starting dose that is right for you.

Consider using a calendar, pillbox, alarm clock, or cell phone alert to help you remember to take your medication. You may also ask a family member or friend to remind you or check in with you to be sure you are taking your medication.

What happens if I miss a dose of buprenorphine/naloxone?

If you miss a dose of oral buprenorphine/naloxone, take it as soon as you remember unless it is closer to the time of your next dose. Do not double your next dose or take more than what is prescribed.

What should I avoid while taking buprenorphine/naloxone?

Avoid drinking alcohol, using sedatives, or other opioid pain medications (such as codeine, hydrocodone, oxycodone, or morphine), or using illegal drugs while you are taking buprenorphine/naloxone. They may increase adverse effects (e.g., sedation, overdose, death) of the medication.

Keep in mind that some cough syrups may contain opioid pain medication. Discuss all medications with your doctor and pharmacist prior to taking buprenorphine/naloxone.

What happens if I overdose with buprenorphine/naloxone?

If an overdose occurs, call your doctor or 911. You may need urgent medical care. You may also contact the poison control center at 1-800-222-1222.

Evzio® (naloxone) injection or Narcan® (naloxone) nasal spray is a medication that can be used to reverse overdose from opioids including buprenorphine/naloxone. You should always call 911 after giving someone naloxone to treat an overdose. Ask your provider if naloxone is right for you.

What are the possible side effects of buprenorphine/naloxone?

Common side effects

- Headache, nausea, vomiting, increased sweating, constipation, trouble sleeping (insomnia), pain, and swelling in the arms and legs (peripheral edema)
- Signs and symptoms of withdrawal from opioids (such as shaking, stomach cramps, diarrhea, restlessness, irritability, anxiety, body aches, or runny nose)
- Numbness of the mouth, redness of the mouth, and burning or painful tongue may occur with the buprenorphine/naloxone film

Rare/serious side effects

- Orthostatic hypotension (low blood pressure when standing)
- Changes in liver function or liver failure
- Changes in adrenal gland function
- Sleep-related breathing disorders
- Allergic reactions
    - Avoid with known hypersensitivity (rashes, hives, itching) to buprenorphine, naloxone or any of the ingredients with them
- Overdose and death
    - Signs of overdose include pinpoint pupils, sedation, low blood pressure, and respiratory depression (slowed breathing)
    - This risk is higher when buprenorphine/naloxone is used IV or at the same time as sedatives (like benzodiazepines) or other depressants (like alcohol)

Are there any risks for taking buprenorphine/naloxone for long periods of time?

Buprenorphine is a partial opioid agonist. Like other opioids, buprenorphine causes physical dependency when taken daily for a long period of time. This means that you may have withdrawal symptoms if buprenorphine/naloxone is stopped abruptly. Withdrawal symptoms when stopping buprenorphine/naloxone are usually not as severe as with other full opioids. Talk to your provider before stopping buprenorphine/naloxone.

What other medications may interact with buprenorphine/naloxone?

There have been reports of respiratory depression (slowed breathing) and death in patients taking buprenorphine/naloxone with benzodiazepine medications such as alprazolam (Xanax®), clonazepam (Klonopin®), diazepam (Valium®), lorazepam (Ativan®), and temazepam (Restoril®). These medications should be taken exactly as prescribed. It is very dangerous to take buprenorphine/naloxone with benzodiazepines if you do not have a prescription.

The following medications may increase the effects of buprenorphine/naloxone

- Certain antibiotics such as clarithromycin (Biaxin®) and erythromycin (Ery-Tab®)
- Certain antidepressants such as fluoxetine (Prozac®), phenelzine (Nardil)
- Antifungals, such as fluconazole (Diflucan®), ketoconazole (Nizoral®), and itraconazole (Sporanox®)
- Certain HIV medications known as protease inhibitors: indinavir (Crixivan®), ritonavir (Norvir®), saquinavir (Fortovase®, Invirase®), and lopinavir/ritonavir (Kaletra®)

The following medications may decrease the effects of buprenorphine/naloxone:

- Certain seizure medications such as phenobarbital, carbamazepine (Tegretol®), and phenytoin (Dilantin®)
- The antibiotic rifampin (Rifadin®)
- The opioid "blocker" naltrexone (Revia®, Vivitrol®)

How long does it take for buprenorphine/naloxone to work?

Buprenorphine/naloxone will begin working shortly after taking one dose.

Summary of Black Box Warnings

This medication has an opiate drug in it. The FDA has found that the use of opiate drugs with benzodiazepine drugs or other sedating medications can result in serious adverse reactions including slowed or difficult breathing and death. Benzodiazepine drugs include drugs like alprazolam, clonazepam, and lorazepam. Benzodiazepine drugs are used to treat health problems like anxiety, trouble sleeping, or seizures. Patients taking opioids with benzodiazepines, other sedating medications, or alcohol, and caregivers of these patients, should seek immediate medical attention if they start to experience unusual dizziness or lightheadedness, extreme sleepiness, slowed or difficulty breathing, or unresponsiveness.