

**FDA warns about dental problems with buprenorphine medicines dissolved in the mouth to treat opioid use disorder and pain**

*Benefits for use outweigh these risks and oral care can help*

**1-12-2022 FDA Drug Safety Communication**

**What safety concern is FDA announcing?**

The U.S. Food and Drug Administration (FDA) is warning that dental problems have been reported with medicines containing buprenorphine that are dissolved in the mouth. The dental problems, including tooth decay, cavities, oral infections, and loss of teeth, can be serious and have been reported even in patients with no history of dental issues. Despite these risks, buprenorphine is an important treatment option for opioid use disorder (OUD) and pain, and the benefits of these medicines clearly outweigh the risks.

Regular adherence to buprenorphine to treat OUD reduces withdrawal symptoms and the desire to use opioids, without causing the cycle of highs and lows associated with opioid misuse. The comprehensive approach of buprenorphine combined with counseling and other behavioral therapies is often one of the most effective ways to treat OUD. This approach, called [medication-assisted treatment \(MAT\)](#), is tailored to meet each patient's needs and can help sustain recovery and prevent or reduce opioid overdose. According to the U.S. Substance Abuse and Mental Health Services Administration (SAMHSA), [MAT](#) has been shown to be effective in improving patient survival, decreasing opioid use, and allowing patients to live a self-directed life, including the ability to gain and maintain employment.

**What is FDA doing?**

We are requiring a new warning about the risk of dental problems be added to the prescribing information and the patient [Medication Guide](#) for all buprenorphine-containing medicines dissolved in the mouth. The prescribing and patient information will also include strategies to maintain or improve oral health while undergoing treatment with these medicines. These strategies will include recommending that prescribers refer patients to dental care services and encourage them to have regular checkups while taking these products. Patients should tell the dentist about all medicines they take, including buprenorphine.

**What is buprenorphine and how can it help me?**

Buprenorphine was approved in 2002 as a tablet to be administered under the tongue to treat OUD. In 2015, buprenorphine was approved as a film to be placed inside the cheek to treat pain. There are also buprenorphine products for pain and OUD delivered by other routes such as a skin patch and injection, but FDA has not identified a concern for dental health related to these other forms. Buprenorphine works by changing the way the brain and nervous system respond to pain. At proper doses, buprenorphine also decreases the pleasurable effects of other opioids, making misuse of them less appealing. The benefits of buprenorphine medicines clearly outweigh the risks, particularly in the treatment of OUD.

The buprenorphine medicines that are associated with dental problems are tablets and films dissolved under the tongue or placed against the inside of the cheek. They are available as single-ingredient products and also in combination with naloxone. Buprenorphine medicines are marketed under the brand names Belbuca, Bunavail, Cassipa, Suboxone, Subutex, and Zubsolv. They are also available as generics.

### **What should patients do?**

Continue taking your buprenorphine medicine as prescribed; do not suddenly stop taking it without first talking to your health care professional as it could lead to serious consequences. Suddenly stopping these medicines could cause you to become sick with withdrawal symptoms because your body has become used to the buprenorphine medicine, or to relapse to opioid misuse that could result in overdose and death. For those suffering from addiction to opioids, the benefits of using buprenorphine medicines clearly outweigh the risks and should be considered in conjunction with counseling and other behavioral therapies. This comprehensive [MAT](#) approach is often one of the most effective ways to treat OUD, and can help sustain recovery and prevent or reduce opioid overdose.

Patients using buprenorphine medicines dissolved in the mouth should take extra steps to help lessen the risk of serious dental problems. After the medicine is completely dissolved, take a large sip of water, swish it gently around your teeth and gums, and swallow. You should wait at least 1 hour before brushing your teeth to avoid damage to your teeth and give your mouth a chance to return to its natural state.

Inform your health care professional if you have a history of tooth problems, including cavities. Schedule a dentist visit soon after starting this medicine and inform your dentist that you are taking buprenorphine, and schedule regular dental checkups while taking this medicine. Your dentist can customize a tooth decay prevention plan for you. Notify both your health care professional and your dentist immediately if you experience any problems with your teeth or gums.

### **What should health care professionals do?**

Health care professionals should be aware the benefits of buprenorphine medicines clearly outweigh the risks and are an important tool to treat OUD. When combined with counseling and other behavioral therapies, this comprehensive [MAT](#) approach is often the most effective way for treating OUD, and can help sustain recovery and prevent or reduce opioid overdose.

Ask patients about their oral health history prior to prescribing treatment with a transmucosal buprenorphine medicine. These serious dental problems have been reported even in patients with no history of dental issues, so refer them to a dentist as soon as possible after starting transmucosal buprenorphine. Counsel patients about the potential for dental problems and the importance of taking extra steps after the medicine has completely dissolved, including to gently rinse their teeth and gums with water and then swallow. Patients should be advised to wait at least 1 hour before brushing their teeth. Dentists treating someone taking a transmucosal buprenorphine product should perform a baseline dental evaluation and caries risk assessment, establish a dental caries preventive plan, and encourage regular dental checkups.

### **What did FDA find?**

Since buprenorphine was approved, we identified 305 cases of dental problems (131 cases classified as serious) with buprenorphine medicines dissolved in the mouth. These only include cases reported to FDA\* or published in the medical literature,<sup>1,2</sup> so there may be additional cases about which we are unaware. The average age of the patients was 42 years, but those as young as 18 years were also affected. Most cases were in patients using the medicines for OUD; however, 28 cases of dental problems occurred in patients using it to treat pain. In 26 cases, patients had no prior history of dental problems. Some cases reported dental problems occurring as soon as 2 weeks after treatment began, with the median time to diagnosis being approximately 2 years after starting treatment. Many cases were reported by health care professionals and provided documentation of extensive dental adverse events. Of the 305 cases, 113 mentioned two or more teeth were affected. The most common treatment for these dental problems was tooth extraction/removal, which was reported in 71 cases. Other cases reported requiring root canals, dental surgery, and other procedures such as crowns and implants.

\*The cases were reported to the [FDA Adverse Event Reporting System \(FAERS\) database](#).

### **What is my risk?**

All medicines have side effects even when used correctly as prescribed, but in general the benefits of taking a medicine outweigh the risks. It is important to know that people respond differently to all medicines depending on their health, other medicines they are taking, the diseases they have, genetic factors, and many other reasons. As a result, we cannot determine how likely it is that someone will experience these side effects when taking buprenorphine medicines that dissolve in the mouth. However, the benefits of buprenorphine medicines for OUD and pain management clearly outweigh the risks. In particular, the comprehensive [MAT](#) approach of buprenorphine combined with counseling and other behavioral therapies is often one of the most effective ways to treat OUD, and can help sustain recovery and prevent or reduce opioid overdose.

### **How do I report side effects from buprenorphine medicines that are dissolved in the mouth?**

To help FDA track safety issues with medicines, we urge patients and health care professionals to report side effects involving buprenorphine or other medicines to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

### **How can I get new safety information on medicines I’m prescribing or taking?**

You can sign up for [email alerts](#) about Drug Safety Communications on medicines or medical specialties of interest to you.

### **Facts about buprenorphine medicines that are dissolved in the mouth**

- Buprenorphine-containing medicines that are dissolved in the mouth are approved to treat opioid use disorder (OUD), and one product is approved to treat pain. These medicines are

available as tablets and films to be placed under the tongue or on the inside of the cheek and kept there until completely dissolved.

- These medicines are available as single-ingredient products and in combination with [naloxone](#). Buprenorphine medicines are marketed under the brand names Belbuca, Bunavail, Cassipa, Suboxone, Subutex, and Zubsolv. They are also available as generics.
- Buprenorphine is an opioid and works by changing the way the brain and nervous system respond to pain.
- In patients taking buprenorphine for OUD, it reduces opioid withdrawal symptoms and the desire to use opioids, without causing the cycle of highs and lows associated with opioid misuse or abuse. At proper doses, buprenorphine also decreases the pleasurable effects of other opioids, making continued opioid use less appealing. When combined with counseling and other behavioral therapies, this comprehensive [medication-assisted treatment \(MAT\)](#) approach is often the most effective way for treating OUD. It can help sustain recovery and prevent or reduce opioid overdose.
- Common side effects of buprenorphine include headache, nausea, vomiting, constipation, pain, increased sweating, and insomnia.
- The use of buprenorphine-containing medicines that are dissolved in the mouth has been growing. The estimated number of prescriptions dispensed from U.S. outpatient retail and mail-order pharmacies increased from 11 million in 2014 to 16 million in 2020.<sup>3</sup>

### **Additional Information for Patients**

- FDA is warning that dental problems such as tooth decay, cavities, oral infections, and loss of teeth have been reported with buprenorphine medicines that are dissolved in the mouth to treat opioid use disorder (OUD) or pain. These problems, some of which have been serious, have been reported even in patients with no history of dental issues. Despite this, the benefits of buprenorphine medicines clearly outweigh the risks.
- Buprenorphine medicines are an important tool to treat OUD. When combined with counseling and other behavioral therapies, this comprehensive approach is often the most effective way for treating OUD. It can help sustain recovery and prevent or reduce opioid overdose. For help finding opioid treatment centers nearest to you, visit the U.S. Department of Health and Human Services [Treatment for Opioid Use Disorder and Addiction](#) webpage or [FindTreatment.gov](#).
- Additional information about MAT can be found on the following web pages: [FDA: Information about Medication-Assisted Treatment \(MAT\)](#) and [SAMHSA: Medication-Assisted Treatment \(MAT\)](#).
- Schedule an appointment with your dentist soon after starting this medicine and inform your dentist that you are taking it. Your dentist can customize a tooth decay prevention plan for you. Visit the dentist for regular checkups while taking this medicine.
- Notify your health care professionals immediately and seek dental treatment if you experience any problems with your teeth or gums while taking buprenorphine medicines that are dissolved in the mouth. If you are starting this medicine, tell your health care professional if you have any tooth problems, including a history of cavities.

- When taking your buprenorphine medicine and after it is completely dissolved, take a large sip of water, swish it gently around your teeth and gums, and swallow. Wait at least 1 hour before brushing your teeth.
- Do not suddenly stop taking your buprenorphine medicine without first talking to your health care professional as it could lead to serious consequences, including relapse to opioid misuse or abuse that could result in overdose and death. You could also become sick with withdrawal symptoms because your body has become used to the buprenorphine medicine.
- Read the patient [Medication Guide](#) every time you receive a prescription for buprenorphine. The Medication Guide will be updated with this new or other important information. It explains the important things that you need to know. These include the side effects, what the medicine is used for, how to take and store it properly, and other things to watch out for when you are taking the medicine.
- Talk to your health care professional if you have any questions or concerns.
- To help FDA track safety issues with medicines, report side effects from buprenorphine or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.
- You can sign up for [email alerts](#) about Drug Safety Communications on medicines or medical specialties of interest to you.

### **Additional Information for Health Care Professionals**

- FDA is warning that cases of dental adverse events, some severe, have been reported following the use of transmucosal buprenorphine-containing medicines. Reported events include cavities/tooth decay, including rampant caries; dental abscesses/infection; tooth erosion; fillings falling out; and, in some cases, total tooth loss. Multiple cases were reported in patients with no prior history of dental problems. The most common treatment for the dental adverse events was tooth extraction/removal.
- The benefits of buprenorphine medicines clearly outweigh the risks.
- Buprenorphine medicines are an important tool to treat opioid use disorder (OUD). When combined with counseling and other behavioral therapies, this comprehensive approach is often one of the most effective ways of treating OUD. It can help sustain recovery and prevent or reduce opioid overdose. Refer patients to find opioid treatment centers by visiting the U.S. Department of Health and Human Services [Treatment for Opioid Use Disorder and Addiction](#) webpage or [FindTreatment.gov](#).
- Additional information about MAT can be found on the following web pages: [FDA: Information about Medication-Assisted Treatment \(MAT\)](#) and [SAMHSA: Medication-Assisted Treatment \(MAT\)](#).
- Counsel OUD patients they should use their buprenorphine only as prescribed and should not stop it because they can experience serious consequences, including relapse, misuse or abuse of other opioids, overdose, and death.
- Screen patients for oral disease and ask about their oral health history prior to beginning therapy with a transmucosal buprenorphine medicine.

- Counsel patients that severe and extensive tooth decay, tooth loss, and tooth fracture have been reported with the use of this medicine and it is important to visit their dentist to closely monitor their teeth.
- Refer patients to a dentist as soon as possible after starting transmucosal buprenorphine for a baseline dental evaluation, dental caries risk assessment and preventive plan, and encourage them to have regular dental checkups while taking the medicine.
- Educate patients on strategies to maintain or improve oral health while being treated with transmucosal buprenorphine medicines. Counsel them that after the medicine has completely dissolved in the oral mucosa, to gently rinse their teeth and gums with water and then swallow. Patients should wait at least 1 hour before brushing their teeth after using the medicine, which will allow the mouth to gradually return to oral homeostasis and avoid any mechanical damage that may occur due to brushing.
- Encourage patients to read the [Medication Guide](#) they receive with each prescription, which explains the safety risks and provides other important information.
- To help FDA track safety issues with medicines, report adverse events involving transmucosal buprenorphine or other medicines to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of this page.
- You can sign up for [email alerts](#) about Drug Safety Communications on medicines or medical specialties of interest to you.

## Data Summary

A search of the [FDA Adverse Event Reporting System \(FAERS\) database](#) and the medical literature<sup>1,2</sup> through December 31, 2018, identified 305 cases of dental adverse events reported with transmucosal buprenorphine use. Patients with opioid use disorder (OUD) may have a higher incidence of poor dental health;<sup>4</sup> however, many cases described severe dental issues in patients with no reported prior history of dental problems (n=26). In addition, although most of the cases were in patients using transmucosal buprenorphine products for OUD, there was a subset of patients (n=28) who experienced severe dental adverse events while receiving pain-only indicated products (e.g., Belbuca) or stated the indication was for pain.

The average age of the patients in this case series was 41.8 years (range 18-71), and the median time to diagnosis was 24.25 months (range 0.5-182). Many cases reported a combination of dental decay, tooth loss, and tooth fractures in numerous teeth. Many cases were reported by health care professionals and provided documentation of extensive dental adverse events including "all upper," "all lower," "all," "majority," "most," "multiple teeth," and "rampant decay." The cases often noted the number of teeth involved, with 113 cases mentioning two or more teeth. Some cases specifically mentioned involvement of 11 to 12 or more teeth, as well as all teeth in 11 cases. Of the 305 cases, 151 reported the treatment for the adverse event, with tooth extraction/removal as the most common, which was reported in 71 cases. Other treatments included root canal, dental surgery, and other restorative procedures such as crowns and implants.

## References

1. Suzuki J, Park EM. Buprenorphine/naloxone and dental caries: a case report. *Am J Addict* 2012;21:494-5.
2. Suzuki J, Mittal L, Woo SB. Sublingual buprenorphine and dental problems: a case series. *Prim Care Companion CNS Disord* 2013;15:PCC.13101533.
3. Symphony Health Metys™. Data 2010-2020. Data extracted May 2021.
4. Yazdanian M, Armoon B, Noroozi A, Mohammadi R, Bayat AH, Ahounbar E, et al. Dental caries and periodontal disease among people who use drugs: a systematic review and meta-analysis. *BMC Oral Health* 2020;20:44.

## Related Information

[Buprenorphine Transmucosal Products for Opioid Dependence \(BTOD\) Shared System Risk Evaluation and Mitigation Strategy \(REMS\)](#)

[Suboxone/Subutex REMS](#)

[Opioid Analgesic REMS](#)

[Information about Medication-Assisted Treatment \(MAT\)](#)

[HHS: Treatment for Opioid Use Disorder and Treatment](#)

[SAMHSA: Medication-Assisted Treatment \(MAT\)](#)

[Information about Naloxone](#)

[The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective](#)

[Think It Through: Managing the Benefits and Risks of Medicines](#)