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Safety Alert: Dental Issues with Transmucosal Buprenorphine

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Background: Buprenorphine is a partial mu-opioid agonist approved by the Food and Drug Administration (FDA) for the treatment of acute and chronic pain and opioid use disorder (OUD).[1-2] This medication is available in many different dosage forms including buccal film, subcutaneous implant, transdermal patch, injectable solution, and sublingual tablet.[3] A combination therapy of buprenorphine-naloxone (Suboxone®; Indivior Pharmaceutical) is also available as a sublingual film or tablet.[2] Only providers associated with an OUD program and those possessing a DATA 2000 waiver may prescribe buprenorphine for substance abuse.[4] Despite these prescribing limitations, the estimated number of buprenorphine-containing prescriptions in the United States has increased from 11 million in 2014 to 16 million in 2020.[3] A common side effect, which has become more apparent with increased use of buprenorphine, is xerostomia or dry mouth, a contributing factor to various dental problems. Buccal buprenorphine has between a 1 to 5% incidence of dry mouth.[1] Consequently, several post-marketing reports have linked the use of the transmucosal dosage forms of buprenorphine (sublingual and buccal) with dental issues.[3] These dental problems occurred regardless of the patient's baseline dental health, including dental decay, tooth loss, and tooth fractures. One case series noted that the majority of patients experiencing dental issues due to buprenorphine had a low or moderate salivary buffering capacity.[5] Therefore, it has been theorized that the medication's acidity combined with the lack of salivary buffer contributed to dental problems in these patients.

FAERS Reports: Between December 2018 and January 2022, 305 cases of dental adverse events were identified in the medical literature and reported to the FDA Adverse Event Reporting System (FAERS) regarding sublingual and buccal forms of buprenorphine-containing products.[3] The effects included a combination of dental decay, tooth loss, and tooth fractures. Two or more teeth were involved in 113 cases, with 11 reporting the involvement of all teeth. Cases were classified as serious in 131 reports. In addition, 26 reports described severe dental adverse effects in patients with no history of dental problems. These dental issues were reported in patients using buprenorphine-containing products for OUD, as well as, a subset of patients (n=28) using these medications for pain management. Patients included in the FAERS reports ranged from 18-71 years old (average age=41.8 years) and had a median time to diagnosis of approximately 2 years after starting the medication (range: 0.5-182 months). As a result of those medication-related dental issues, patients sought treatment in 151 re-

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ported cases, most commonly with tooth extraction in 71 cases. Additional treatment measures included root canals, dental surgery, crowns, and implants.

Post-Marketing Data: A study conducted in Boston, Massachusetts between May and November 2012 included 11 patients treated for OUD that reported worsening dental health after starting buprenorphine.[5] The average duration of buprenorphine treatment was 45.7 months and the average baseline Summated Xerostomia Inventory score was 8.5, which is comparable to a healthy community sample. Patients in this study reported experiencing dental caries and cracked teeth that required fillings, crown placements, root canals, and/or tooth extractions. Additionally, more than half of the patients reported experiencing tooth pain. Over 90% of patients developed a low or moderate salivary buffering capacity which likely contributed to their dental issues.

FDA Changes: The FDA required new warnings about the risk of dental problems to be added to the prescribing information and patient medication guides of all buprenorphine-containing transmucosal products.[3] As of June 2022, the prescribing information and medication guides for all buprenorphine-containing transmucosal products have been updated to include a warning about "Dental Adverse Events" under section 5 (Warnings and Precautions) in the package insert and throughout the patient medication guides.[1-2] This warning summarizes the dental effects reported to FAERS and suggests potential mitigation strategies for patients and providers.

Pharmacists Considerations: Buprenorphine is one of the most effective treatments for OUD.[3] Because of this, providers should continue to utilize this medication when necessary and take the appropriate steps to mitigate the incidence of dental effects. Patients prescribed transmucosal forms of buprenorphine should be referred to a dentist upon initiation of therapy and counseled on the risk of severe dental problems. Patients can be educated on strategies to minimize risk including waiting at least 1 hour after taking this medication to brush their teeth and rinsing their teeth and gums with water once the medication has completely dissolved. Keeping the mouth moisturized with sprays or hydrating mouth rinses, avoiding dehydrating drinks, such as coffee or alcohol, and chewing sugarless gum may help prevent dental issues. Patients should be encouraged to practice good dental hygiene by brushing their teeth twice a day and having regular dental cleanings and check-ups. Patients experiencing adverse effects should be counseled against abruptly discontinuing buprenorphine without first speaking to a healthcare provider, as this could trigger relapse of their OUD.

Formulary Status: Transmucosal buprenorphine-containing products including Belbuca® and Suboxone® are on the Adult CCHS Formulary. Details can be found in Lexicomp regarding restriction criteria and prescriber qualifications.

References:

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