VIEWPOINT

Buprenorphine for Cancer Pain—The Safest Opioid, and Patients With Cancer Cannot Get It

Amy A. Case, MD; Mellar P. Davis, MD; Marcin Chwistek, MD; Ali J. Zarrabi, MD

As palliative care clinicians who care for patients with cancer, managing cancer-related pain with opioids is our bread and butter. Opioids such as morphine, oxycodone, and fentanyl are our mainstays of therapy. Often, they provide a reprieve from suffering, making cancer-related pain and distress more manageable and allowing patients to function better. We prescribe these medications acknowledging that they also have short- and long-term harms that impact patients, which include depression,[1] addiction, and risk of overdose.[2] In this Viewpoint, we call for an older and safer opioid—buprenorphine—to be used as a first-line pain medication for patients with cancer for whom opioid therapies are considered.

For years, we have been dedicated to prioritizing the quality of life of patients with cancer while mitigating risk, and thus we have felt resigned to wield the double-edged sword of opioid therapy[2-4]; that is, until we became more familiar with buprenorphine, an opioid patented in 1965 as a so-called "improvement on codeine" with fewer adverse effects. Buprenorphine has become a prominent medication in our supportive oncology pain management toolkit.[5,6] Although an older medicine, buprenorphine was not commonly prescribed for pain until more recent years. Used today more commonly for addiction, it is also a powerful analgesic. While 30 times more powerful than morphine, buprenorphine used alone very rarely causes opioid-induced respiratory depression, even in high doses. It is not only an effective analgesic but also has fewer adverse effects, including sedation and overdose. Buprenorphine is a partial μ-opioid receptor agonist, which refers only to G protein activation, not partial analgesia. It is also a κ receptor antagonist, which results in antidepressant and blunted opioid craving effects.[7,8] Buprenorphine, simply put, is both an effective pain medicine and the safest opioid on the market as a schedule III opioid. It has been recognized as a safe first-line opioid by both the US Department of Veterans Affairs and the Department of Health and Human Services (HHS). At our national conferences, we ask each other, why are we not prescribing this as the first-line pain medication for patients with cancer?

The reason is US Food and Drug Administration (FDA)–approved formulations of buprenorphine for pain (Butrans and Belbuca, which are transdermal and buccal formulations, respectively) are prohibitively expensive, often even with insurance authorization. Furthermore, higher-dose formulations of buprenorphine—which are often necessary to manage malignant pain—are not FDA approved for pain. These higher-dose formulations, such as Suboxone, are inexpensive; however, insurance almost never pays for them off label to treat pain.

We have called insurance companies, written letters, and sent many appeals to get our patients with cancer access to buprenorphine, only to still have insurance denials. Which medications are we asked to prescribe first? Morphine and oxycodone, with their associated risks of craving, sedation, and other adverse effects. The out-of-pocket cost of Butrans—which we often use for patients who do not require high doses of an opioid—can be more than $400 per month. Generic sublingual forms are less expensive, ranging from $30 to $50 per month. However, many insurance companies do not list generic or brand-name buprenorphine on their formulary or are selective about which type—generic or brand name—they will cover, leading to mixed messages to clinicians. For patients who require higher doses of buprenorphine, GoodRx offers coupons for Suboxone or generic sublingual buprenorphine, which can lower the price to $30 monthly; however, this is still expensive for some patients. Often, even with insurance approval, patients must pay more than $100 in co-pays for a month's supply.

We offer these real-life encounters that inform our call for reform: a young female individual with young children with metastatic cancer in her bones, lungs, and liver with pain so severe that morphine, oxycodone, hydrocodone, and methadone were ineffective due to adverse effects? Denied by insurance. While hospitalized, she was started on buprenorphine, which treated her pain with fewer adverse effects; however, upon discharge from the hospital, her insurer denied the medication, which resulted in several communications, appeals, and gaps in her pain management until it was finally approved weeks later, resulting in a period of uncontrolled pain and a gap in her care.

A middle-aged man with cancer with diffuse pain in his joints from cancer treatment who was sedated on morphine? Denied. The insurance company recommended that we prescribe oxycodone instead. He did not want to try it. Assenting to the insurance company to make our medical decisions, we prescribed a few tablets, which he never took and then prescribed buprenorphine again. After another rejected prior authorization followed by an appeal, his insurance ultimately covered it, but with a $175 monthly co-pay. He eventually used the medication with success and stated that the improvement in his quality of life was dramatic.

Patients with cancer are experiencing pain, and clinicians are frustrated by the added administrative barrier and constant fight to get their patients with cancer the opioid analgesics they need. Moreover, although HHS recommended buprenorphine as a first-line opioid in 2019, Medicare, Medicaid, and private insurers have not followed through with the recommendation. It is simply common sense to use buprenorphine as a first-line opioid for cancer pain rather than full-agonist opioids.

We believe the FDA should expand approval for all formulations of buprenorphine to treat cancer pain. We need collective pressure on insurance payors to cover the cost of buprenorphine for patients with cancer. Manufacturers could provide it at a discount or even for free to patients needing an opioid but not able to afford it.

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For example, Butrans is made by Purdue Pharma, the company responsible for infamous excessive marketing of highly addicting oxycodone[9] and contributing to the related opioid epidemic. Purdue states that it now distributes nalmefene, its proprietary version of naloxone, "for no profit" as part of its new commitment, so perhaps Butrans could be offered in a similar program.[10] Perhaps Purdue or other buprenorphine manufacturers, such as BioDelivery Sciences International, which manufactures Belbuca, could make these forms of buprenorphine more affordable so patients with cancer do not need to be faced with deciding whether to manage their pain or put food on the table.

What if we can grant easier access to a medicine that can more safely treat cancer pain and reduce the societal risk of addiction? Sounds like a medical miracle.

ARTICLE INFORMATION

Author Affiliations: Department of Supportive and Palliative Care, Roswell Park Comprehensive Cancer Center, Buffalo, New York (Case); Department of Supportive Oncology, Levine Cancer Institute, Charlotte, North Carolina (Davis); College of Public Health, Temple University, Philadelphia, Pennsylvania (Chwistek); Supportive Oncology and Palliative Care Program, Fox Chase Cancer Center, Philadelphia, Pennsylvania (Chwistek); Division of Palliative Medicine, Department of Family and Preventive Medicine, Emory University School of Medicine, Atlanta, Georgia (Zarrabi).

Corresponding Author: Amy A. Case, MD, Department of Supportive and Palliative Care, Roswell Park Comprehensive Cancer Center, 665 Elm St, Buffalo, NY 14203 (amy.case@roswellpark.org).

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Caring for Fasting Patients With Cancer During Ramadan

Javier Mora, MD; Mina Bakhtiar, MD; Nadia A. Saeed, MD; Tracy A. Balboni, MD, MPH

Ramadan is the ninth month of the Islamic lunar calendar and represents a holy time for Muslims worldwide to dedicate themselves to prayer, fasting, and community. During Ramadan, some observant Muslim patients with cancer may elect to fast. While some studies explore the impact of intentional caloric restriction on cancer therapy,[1] the effect of repetitive daytime fasting for religious purposes has not been well characterized. Nevertheless, oncology clinicians should familiarize themselves with this cultural practice due to the potential clinical implications for patients.

In 2025, the month of Ramadan began on March 1 in the US and concluded on March 30, following the first sighting of the crescent moon. In this month, daily fasting occurs during the hours between dawn and sunset; observers often eat a predawn meal and break their fast after sunset with an evening meal, followed by prayer and communal time with family and friends. Due to the lunar calendar being 11 days shorter than the solar calendar, the start of Ramadan shifts each year, resulting in variable fasting lengths annually, which also depends on observers' location of worship on the globe. Ramadan fasting practices may vary culturally but often involve abstaining from food, drink, sexual activity, and oral medications during the day. Ramadan ends with the holiday Eid al-Fitr, during which Muslims gather for prayer, food, and exchanging gifts.[2,3]

There are notable exemptions to fasting in Islam. Children are not expected to fast. Practicing adult Muslims may abstain from fasting if they are menstruating, pregnant, breastfeeding, elderly, traveling, sick, in need of standing medications, or have a medical condition that makes fasting harmful to their health. However, despite these permitted exceptions, some Muslims with a cancer diagnosis may still choose to fast.[2-5] In one study, a majority of the sampled practicing Muslim patients with breast, colorectal, bladder, lung, or head and neck cancers fasted for the entirety or part of Ramadan.[3] As such, the following considerations and patient scenarios can help guide oncology clinicians to optimize their care and understanding of patients fasting during Ramadan:

Identification of Fasting Practices

- Clinicians should gain an understanding of observant Muslim patients' plans around fasting. In some studies, even while living in Muslim-majority countries, only 20% to 50% of Muslim oncology patients sought advice from their clinicians regarding fasting.[4,5] The standard inclusion of spiritual histories as part of a simple, time-limited patient intake—such as the FICA (Faith, Importance and Influence, Community, and Address) Spiritual History Tool—aids clinicians in recognizing a patient's faith as part

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