PERIOPERATIVE PAIN MANAGEMENT GUIDANCE FOR PATIENTS ON CHRONIC BUPRENORPHINE THERAPY UNDERGOING ELECTIVE OR EMERGENT PROCEDURES FEBRUARY 2022

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at the *PBM INTERnet* or *PBM INTRAnet* site for further information.

Introduction and Background

The management of acute, post-operative pain presents many challenges and risks that are further amplified in patients receiving long-term opioid therapy for chronic pain. Perioperatively, these issues include: potentially higher postoperative analgesic dose requirements due to underlying physical tolerance to opioids, the absecnce of straightforward dose conversion methods, and the need to effect appropriate taper back to their original opioid regimen in the postoperative discharge course as acute pain begins to subside. These same difficulties remain in patients receiving medications for opioid use disorder (MOUD) namely the full mu-opioid receptor (μOR) agonist methadone and *partial* μOR agonist buprenorphine with the added pressure of trying to avoid triggering relapse or exacerbation of their substance use disorder (SUD).

Compounding these difficulties is the lack of firm evidence to guide the field, thus the following recommendations are mostly based on available evidence and expert opinion. It is strongly recommended that where available, X-waivered providers or an interdisciplinary team experienced with buprenorphine use be consulted to most effectively and safely help manage these patients. It is equally important in every single situation to communicate treatment plans with the buprenorphine prescriber, surgeon/proceduralist, anesthesiologist, pharmacist, and the PATIENT, as this will allow for the best transition of care plan back to the primary treating team. Active communication across the healthcare team will help reduce barriers to buprenorphine administration, dose adjustments, and the co-administration of buprenorphine with full opioid agonists where applicable. Patient education is crucial to assist with the shared decision-making process as some patients will refuse to take any opioid because they are worried about relapse and are proud of their work towards recovery. Setting early and realistic expectations for pain control bolsters trust and strengthens the patient-provider interaction. Clinical judgement is paramount regarding individual cases.

Receptor-binding studies utilizing positron emission tomography and radiolabeled (11C) carfentanil in buprenorphine-treated heroin-addicted persons confirmed the dose-dependent availability of μORs in

patients maintained on various doses of daily buprenorphine.[1] Fifty-nine percent of μORs are available at a 2 mg maintenance dose of BUP, meanwhile 20% and 16% of μORs are available at 16 mg and 32 mg maintenance dose of BUP, respectively. Occupancy is also time-dependent as observed in studies guided by ^{11}C-cPET data demonstrating the gradual increase in central nervous system μOR binding potential after BUP cessation.[1-3] For example, 40% of μOR receptors are clinically available for analgesia at 24 hours after omission of a 16mg BUP dose. Meanwhile withdrawal symptoms are suppressed at a μOR availability of 50-60%.[3] These observations have led to the development of protocols where buprenorphine is continued at reduced doses throughout the perioperative period to avoid withdrawal symptoms and to facilitate the analgesic efficacy of mu-opioid agonists administered in combination for acute postoperative pain.[4-8]

For this document, buprenorphine refers to both the buprenorphine mono-product and the buprenorphine/naloxone combination product for OUD, unless otherwise specified. An immediate-release (IR) opioid agonist refers to any IR or short acting opioid that provides six hours or less of analgesia.

Guidance

I. GENERAL TREATMENT PRINCIPLES

The first step in consideration of how to manage pain in this population of patients is to consider whether the planned procedure would result in minimal to no pain (e.g. endoscopy, cataracts, etc) or whether significant pain could be expected (e.g., laparoscopic, intra-abdominal, intra-thoracic, and orthopedic procedures). Buprenorphine may not need to be discontinued or have dose modification for minimally painful procedures. Non-opioid approaches should be used where appropriate in addition to baseline buprenorphine therapy.

If the procedure is expected to result in meaningful postop pain, the next consideration is whether the planned surgery is elective or emergent. The major difference between them is that elective surgery allows for ample time prior to the procedure for preparation and proper planning for adequate perioperative pain management whereas emergent procedures allow minimal to no time for planning

The findings that a clinically significant proportion of opioid receptors remain available even at high stable doses of buprenorphine have led multiple expert consensus panels and clinical practice guidelines to make the following overall recommendations:[7-10]

A. **Buprenorphine treatment should not be routinely discontinued in the perioperative period**

Discontinuation of buprenorphine in a patient receiving stable MOUD therapy should generally be avoided, as discontinuing therapy may confer medical risk, including return to active opioid use (50-90%), risk of overdose, prolong hospital stay, and increase patient burden.[7-14] Patients who continue their usual buprenorphine dose during the perioperative period may also require less patient-controlled analgesia.[11]

B. A buprenorphine taper to ≤ 16 mg could be considered for patients prescribed higher doses of buprenorphine (eg, > 16 mg) with anticipated high postsurgical pain[7]

1. Higher potency (IV) full-agonist opioids in combination with multimodal pain treatment strategies (detailed below) are generally effective for analgesia in buprenorphine-maintained patients even at higher doses.

2. Alternatively, there may be cases in which it may be appropriate to temporarily lower the dose of buprenorphine in order to maximize the effect of these full-agonist medications (more details below).
3. For some patients it may be appropriate to temporarily divide and/or increase the dose of buprenorphine in consultation with the outpatient prescriber.

C. For all patients, utilize a multimodal pain approach to synergistically treat pain. Consider the following in addition to opioid medications as appropriate to the patient/situation:

1. **Systemic non-opioid analgesics** (e.g., acetaminophen, NSAIDS, gabapentinoids, ketamine, magnesium, systemic lidocaine, alpha-2 agonists, glucocorticoids.
2. **Regional/local analgesics** (e.g., epidural spinal blocks, local infiltration, local anesthetics)
3. **Psychosocial interventions** (e.g., Peer support, distraction activities, app-guided meditation or relaxation)

D. **In situations where a full μOR agonist medication is needed to adequately control perioperative pain, it is recommended that opioids with similar lipophilicity and binding affinity toward μORs be used.** Theoretically, similarly lipophilic molecules may be able to penetrate the blood-brain barrier (BBB) to the same or better degree than buprenorphine and more effectively compete with buprenorphine for the μOR. Fentanyl and hydromorphone are reasonable alternatives in this setting.[7]

II. PRE-OPERATIVE ASSESSMENT:

Pre-operatively, a patient evaluation including a pain history, physical examination, medication reconciliation and review, and assessment of patient's physical and psychiatric comorbidities should be performed in conjunction with urine drug monitoring (including specific testing for methadone, fentanyl and buprenorphine/metabolites). Providers should verify that the patient has been taking his/her buprenorphine as prescribed, and query the state prescription drug monitoring program (PDMP) database.[8] Special attention should be paid to any medications or substances that could cause withdrawal upon cessation or might interfere with the effect of opioid medication. A brief substance use disorder screening should be conducted universally, with more detailed questioning and appropriate referrals for positive responses.

Pre-operative counseling (including written instructions) should be part of the plan for all patients. The risks of exposure to opioid medications and/or undertreating pain as triggers for relapse to OUD should be discussed prior to treatment.

III. TREATMENT PLANNING:

A. **WHAT IS THE INDICATION FOR BUPRENORPHINE TREATMENT?** (i.e., OUD, pain with a history of OUD, or pain)

Patients receiving buprenorphine formulations for pain management (transdermal patch or buccal film) without a history of SUD (including opioid use disorder, OUD) may have more options from an overall perioperative pain management perspective. Those receiving buprenorphine for OUD and/or

those receiving it for pain with a history of SUD may have more limited or restricted opioid pain management options due to the patient's higher-risk status.[15]

B. **WHAT IS THE EXPECTED SEVERITY/DURATION OF PAIN?** Consider whether the planned procedure is likely to result in minimal to no pain (e.g. wisdom tooth removal, endoscopy, cataracts, etc) or whether more significant pain can be expected (e.g., laparoscopic, intra-abdominal, intra-thoracic, and orthopedic procedures). A procedure where minimal to no pain is expected may not require any adjustment of buprenorphine dose or dividing doses in the perioperative period to capitalize on buprenorphine's relatively short analgesic window. For procedures with anticipated moderate to severe pain it may be appropriate to temporarily lower the dose of buprenorphine as described above in order to maximize the effect of add-on full opioid agonist medications.

   Also determine whether the main focus of pain control is expected to be perioperative or whether it is likely that pain control needs will extend long after the procedure.

C. **WHAT IS THE PLAN FOR CONTINUITY OF CARE?**

1. If short-acting opioids are used in an inpatient and controlled environment, it is recommended to taper the patient off the short-acting opioid prior to discharge so that they are discharged solely on buprenorphine.
2. The expectation should be that IR opioids will be used as short term rescue medications during the perioperative period only. This expectation should be discussed with the patient at the outset.
3. If the hospital length of stay is short or if outpatient procedures require a brief course of IR opioids, outpatient post-operative pain care should be offered in consultation with the patient's waivered provider or OUD team. Any outpatient opioid prescriptions should be time-limited.
4. Any changes to buprenorphine dose or schedule must be done in consultation with the patient's outpatient buprenorphine provider and a plan should be made to return the patient to his/her regular regimen (if appropriate).
5. Patients should be prescheduled with their OUD provider or chronic pain provider after discharge for close follow-up. Warm hand-off for continued buprenorphine adherence may be required upon discharge, especially for high risk patients. Patients should be discharged with sufficient quantity of buprenorphine to last them until their next follow-up appointment.

IV. THE FOLLOWING ARE SPECIFIC RECOMMENDED INTERVENTION OPTIONS FOR ELECTIVE AND EMERGENT PROCEDURES WITH VARYING LEVELS OF PAIN/OPIOID REQUIREMENT:

A. GUIDANCE FOR PERIOPERATIVE MANAGEMENT IN ELECTIVE PROCEDURES

1. Patients with OUD and/or chronic pain with history of OUD:

For most patients, buprenorphine should be continued throughout the operative period. The alternative for patients who will undergo procedures with expected high postoperative pain (e.g. open abdominal/thoracic surgeries and major orthopedic surgeries) is to reduce the dose of buprenorphine to ≤ 16 mg/day if on higher doses. Reduced doses throughout the perioperative period may help avoid withdrawal symptoms and facilitate the analgesic efficacy of μOR agonists administered in combination for acute postoperative pain (See algorithm) This would not be an option for patients maintained on the extended-release buprenorphine injection (BUP XR INJ) (see Buprenorphine Perioperative Guidance Supplemental Information). For these patients, we recommend referring to options for continuing buprenorphine throughout the perioperative process.).

a. Continue Buprenorphine Strategies:

For most patients it is not necessary to stop buprenorphine during the perioperative period in anticipation of the need for acute pain management. Buprenorphine could be continued throughout with maximization of non-opioids for analgesia as follows:

i. For Minimally Painful Surgery: Continue current home dose of buprenorphine unchanged. Alternatively, the home dose of buprenorphine may be divided and administered every 6 to 8 hours for more optimal pain coverage.[1, 12-15] The total daily dose of buprenorphine can be generally titrated up to 32 mg/day in divided doses if needed for pain management.[16] This option does not apply to the buprenorphine extended-release injection.

Examples of procedure with low risk of postoperative pain: tooth extraction, esophagoduodenoscopy, colonoscopy, bronchoscopy, etc.[16]

ii. For Painful Surgery: If a patient is on > 16 mg/day, the baseline dose of buprenorphine may be continued. Alternatively, the baseline dose may be reduced to ≤ 16mg/day to allow for the addition of an immediate release as needed full μOR agonist to the baseline SL buprenorphine dose. In situations where a full μOR agonist medication is needed to adequately control perioperative pain, it is recommended that opioids with similar lipophilicity and binding affinity toward μOR be used. Fentanyl and hydromorphone are reasonable alternatives in this setting. It should also be expected that the patient on baseline buprenorphine therapy in the perioperative setting may require a higher dose of full μOR agonist and therefore require close monitoring, e.g. in the ICU or step-down type unit. (see Buprenorphine Perioperative Guidance Supplemental Information).

Examples of procedure with intermediate or moderate risk of postoperative pain: laparoscopic procedures, video-assisted thoracoscopic procedures, arthroscopic procedures, open neurosurgical procedures, etc.[16]

Examples of procedure with severe postoperative pain or high opioid requirement in the postoperative period: open intra-abdominal surgery, open intra-thoracic surgery, and orthopedic procedures.[16]

B. GUIDANCE FOR PERIOPERATIVE MANAGEMENT IN EMERGENT PROCEDURES: [10, 15-21]

This scenario represents a potentially more difficult challenge, as emergency procedure leaves no time to sufficiently and completely taper the patient off buprenorphine. Even if stopped abruptly, up to five days would still be needed to entirely clear the drug from the body for most formulations. Thus, although the specific use of chronic buprenorphine is still important to consider for emergency procedures, anticipated pain level should also be considered.

1. **Emergency Procedure with Anticipated Minimal to no Pain:**

   In this situation, buprenorphine would be anticipated to offer enough analgesia to cover the patient during the procedure and postoperatively. Buprenorphine can be continued throughout the procedure along with non-opioid medications for anesthesia and postoperative analgesia. The buprenorphine dose could be increased until adequate pain relief is achieved. If short-acting opioids are used in an inpatient and controlled environment, it is recommended to taper the patient off the short-acting opioid prior to discharge so that they are discharged solely on buprenorphine. If the hospital length of stay is short or if outpatient procedures require a brief course of IR opioids, outpatient post-operative pain care should be offered in consultation with the patient's waivered provider or OUD team.

2. **Emergency Procedure with Anticipated Moderate to Severe Pain:**

   In the case of an emergency procedure with anticipated moderate to severe pain there are two options:

   a. Continue buprenorphine method:

   Buprenorphine could offer enough analgesia to cover the patient during the operation and postoperatively. It could be continued throughout the operation utilizing non-opioids for anesthesia and postoperative analgesia. In the postoperative setting, the dose of buprenorphine could be increased (EXCEPT the buprenorphine Implant or BUP XR INJ) until adequate pain levels are achieved or short-acting opioids could be used. As above, in situations where a full μOR agonist medication is needed to adequately control perioperative pain, it is recommended that opioids with similar lipophilicity and binding affinity toward μOR be used. If short-acting opioids are used postoperatively in addition to buprenorphine, it would still be recommended to taper the patient off the short-acting opioid prior to discharge or shortly after discharge.

   b. Discontinue buprenorphine method: See Section V. DISCONTINUING BUPRENORPHINE

V. DISCONTINUING BUPRENORPHINE

Although the continuation of buprenorphine methods described above are preferred, providers may choose to discontinue buprenorphine prior to the procedure if they anticipate moderate to severe postoperative pain or if they anticipate that postoperative pain may be hard to control.[15-21] The rationale for stopping buprenorphine is to ensure opioid receptor availability for pain management purposes; this would allow the team to freely utilize scheduled opioid agonist analgesics or their institution's acute pain management policy. While there have been historical concerns about buprenorphine's effectiveness as an analgesic (and particularly its capacity to interfere with the

action of other mu- agonists), recent clinical evidence suggests that it allows for greater binding potential of other opioids than previously thought. In addition, while it is a partial agonist, buprenorphine is nonetheless a potent analgesic. Finally, the fact that buprenorphine confers lower risks in terms of overdose and hyperalgesia than full-agonist opioids should be taken into consideration. Taken together, this suggests that there should be extremely few situations that warrant completely removing a patient from buprenorphine perioperatively. Among them are:

1. The patient is asking to stop buprenorphine and the pros and cons of this decision have been discussed with the patient and his/her outpatient OUD provider as well as a plan for follow-up OUD care identified

2. There is a medical contraindication to continuing buprenorphine treatment;

3. It has become clear that all of the other options available (maximizing buprenorphine dose; splitting buprenorphine dose; adjunctive multimodal pain treatment; etc.) have been considered and are insufficient to manage pain. In addition, it must be clear that both the provider and the patient have carefully weighed the pros and cons of potential added pain control against the risks of exacerbating withdrawal and return to active illicit opioid use and there must be a plan in place for returning the patient to buprenorphine post-operatively.

A. IF BUPRENORPHINE IS TO BE STOPPED PRIOR TO THE PROCEDURE:

1. **Emergency (unplanned) procedures**: Discontinue buprenorphine immediately upon admission in lieu of high dose, short-acting μOR agonist.
2. **Elective (planned) procedures**:
    a. Discontinue buprenorphine 24-72 hours prior the surgery[4, 10, 17]
    b. Restart after resolution of acute postoperative pain.
    c. In this situation, it is recommended to carefully titrate the short-acting opioid in the short-term to overcome buprenorphine's tight binding affinity and overwhelming occupation of μORs.
3. **Generally**:
    a. These patients may require an extended hospital stay after initial discontinuation of buprenorphine, as the dose of the short-acting opioid may need to be continually adjusted (most likely decreased) to prevent short-acting μOR agonist-related adverse effects.
    b. For patients on high doses of full μOR agonists, monitoring for respiratory function is recommended. As buprenorphine clears from systemic circulation, more μORs will become available for the short-acting opioid to bind to. If the short-acting opioid dose is not continually monitored and adjusted appropriately, there is an increased risk of opioid induced respiratory depression (OIRD) and other adverse effects.
    c. Preoperative planning should include coordination for the use of alternative pain regimen and/or other supportive care planning between all members of the team. As needed, short-acting full opioid agonists may be used for pain management and to mitigate withdrawal symptoms. Non-opioid treatment

options for withdrawal symptom management (e.g., alpha-2 receptor agonists; loperamide or odansetron; diphenhydramine) may also be useful adjunctive options as appropriate.

4. Post-Operative Planning:

a. If a short-acting opioid is utilized postoperatively, it is recommended to ensure that the plan includes taper off the short-acting opioid and conversion back to their previous dose of buprenorphine in consultation with their waivered provider or OUD team. Notably, the patient should be converted back to buprenorphine if they have a history of OUD and/or pain with substance abuse ***prior to discharge***.

VI. RESTARTING BUPRENORPHINE

If a short-acting opioid is utilized postoperatively, it is recommended to ensure that the plan includes taper off the short-acting opioid and conversion back to their previous dose of buprenorphine in consultation with their waivered provider or OUD team. A simple way to restart buprenorphine post surgically would be to discontinue the peri/postoperative full opioid receptor agonist and restart buprenorphine when the initial withdrawal signs are observed by the provider for clinic induction or by the patient (for home induction). Buprenorphine may be started at 2 mg or 4 mg. If and when withdrawal is alleviated, the remaining prior buprenorphine maintenance dose may be started on day 1. Alternatively, the patients may be re-induced as follows:[10]

Patients may begin buprenorphine when they are exhibiting clear signs of opioid withdrawal. Buprenorphine is typically started with a 2 mg to 4 mg dose or a 2 mg/0.5 mg to 4 mg/1 mg dose of buprenorphine/naloxone. Depending on the formulation used and whether a given patient has a dry mouth, the dose can take between 3 and 10 minutes to dissolve fully. After approximately 2 hours, an additional 2 mg to 4 mg dose of buprenorphine or buprenorphine/naloxone can be given if there is continued withdrawal and lack of sedation.

Always individualize dosing. The FDA label recommends a maximum buprenorphine/naloxone dose of 8 mg on Day 1 and 16 mg on Day 2. When dosing outside of FDA recommendations, document the clinical rationale, including risks and benefits. Remember that some patients stabilize on lower doses.

References

1. Greenwald MK, Johanson CE, Moody DE, Woods JH, Kilbourn MR, Koeppe RA, Schuster CR, Zubieta JK. Effects of buprenorphine maintenance dose on mu-opioid receptor availability, plasma concentrations, and antagonist blockade in heroin-dependent volunteers. Neuropsychopharmacology. 2003 Nov;28(11):2000-9.
2. Greenwald M, Johanson CE, Bueller J, Chang Y, Moody DE, Kilbourn M, Koeppe R, Zubieta JK. Buprenorphine duration of action: mu-opioid receptor availability and pharmacokinetic and behavioral indices. Biol Psychiatry. 2007 Jan 1;61(1):101-10.
3. Greenwald MK, Comer SD, Fiellin DA. Buprenorphine maintenance and mu-opioid receptor availability in the treatment of opioid use disorder: implications for clinical use and policy. Drug Alcohol Depend. 2014 Nov 1;144:1-11.
4. Quaye AN, Zhang Y. Perioperative Management of Buprenorphine: Solving the Conundrum. Pain Med. 2019 Jul 1;20(7):1395-1408. doi: 10.1093/pm/pny217
5. Lembke A, Ottestad E, Schmiesing C. Patients Maintained on Buprenorphine for Opioid Use Disorder Should Continue Buprenorphine Through the Perioperative Period. .Pain Med. 2019 Mar 1;20(3):425-428. doi: 10.1093/pm/pny019.
6. Hickey T, Abelleira A, Acampora G, Becker WC, et al. Perioperative buprenorphine management: a multidisciplinary approach. Med Clin N Am 2022; 106:169-85. https://doi.org/10.1016/j.mcna.2021.09.001
7. Kohan L, Potru S, Barreveld A, Sprintz M, et al. Buprenorphine management in the perioperative period: educational review and recommendations from a multisociety expert panel. Reg Anesth Pain Med 2021; **0**: 1–20. doi:10.1136/rapm-2021-103007.
8. The ASAM National Practice Guidelines: For the Treatment of Opioid Use 2020 Focused Update. www.asam.org/docs/default-source/quality-science/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2 Accessed on October 20, 2021
9. Webster L, Gudin J, Baffa R, et al. Understanding buprenorphine for use in chronic pain: Expert opinion. Pain Medicine. 2020; 21(4): 714-723.
10. Substance Abuse and Mental Health Services Administration. *Medications for Opioid Use Disorder*. Treatment Improvement Protocol (TIP) Series 63 Publication No. PEP21-02-01-002. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2021.
11. Macintyre PE, Russell RA, Usher KA, Gaughwin M, Huxtable CA. Pain relief and opioid requirements in the first 24 hours after surgery in patients taking buprenorphine and methadone opioid substitution therapy. Anaesth Intensive Care 2013;41 (2):222–30.
12. Harrison TK, Kornfeld H, Aggarwal AK, Lembke A. Perioperative considerations for the patient with opioid use disorder on buprenorphine, methadone, or naltrexone maintenance therapy. Anesthesiol Clin 2018;36(3):345–59.
13. Ward EN, Quaye AN-A, Wilens TE. Opioid use disorders: perioperative management of a special population. Anesthesia and Analgesia. 2018;127(2):539-547.
14. Bentzley BS, Barth KS, Back SE, et al. Discontinuation of buprenorphine maintenance therapy: perspectives and outcomes. J Subst Abuse Treat 2015;52:48–57.
15. Alford DP, Compton P, Samet JH. Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. Ann Intern Med. 2006;144(2):127-134.

16. Jonan AB, Kaye AD, Urman RD. Buprenorphine formulations: clinical best practice strategies recommendations for perioperative management of patients undergoing surgical or interventional pain procedures. Pain Phy. 2018;21:E1-E12.
17. Anderson TA, Quaye ANA, Ward EN, et al. To stop or not, that is the question: acute pain management for the patient on chronic buprenorphine. Anesthesiology. 2017;126(6):1180-1186.
18. Fiellin DA, Schottenfeld RS, Cutter CJ et al. Primary care-based buprenorphine taper vs maintenance therapy for prescription opioid dependence. JAMA Intern Med. 2014;174(12):1947-1954.
19. Sigmon SC, Dunn KE, Saulsgiver K, et al. A randomized, double-blind evaluation of buprenorphine taper duration in primary prescription opioid abusers. JAMA Psychiatry. 2013;70(12):1347-1354.
20. Bryson EO. The perioperative management of patients maintained on medication used to manage opioid addiction. Anesth and Medical Disease. 2014;27:359-364.
21. Coluzzi F, Bifulco F, Cuomo A, et al. The change of perioperative pain management in opioid-tolerant patients. Therapeutics and Clinical Risk Management. 2017;13:1163-1173.

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