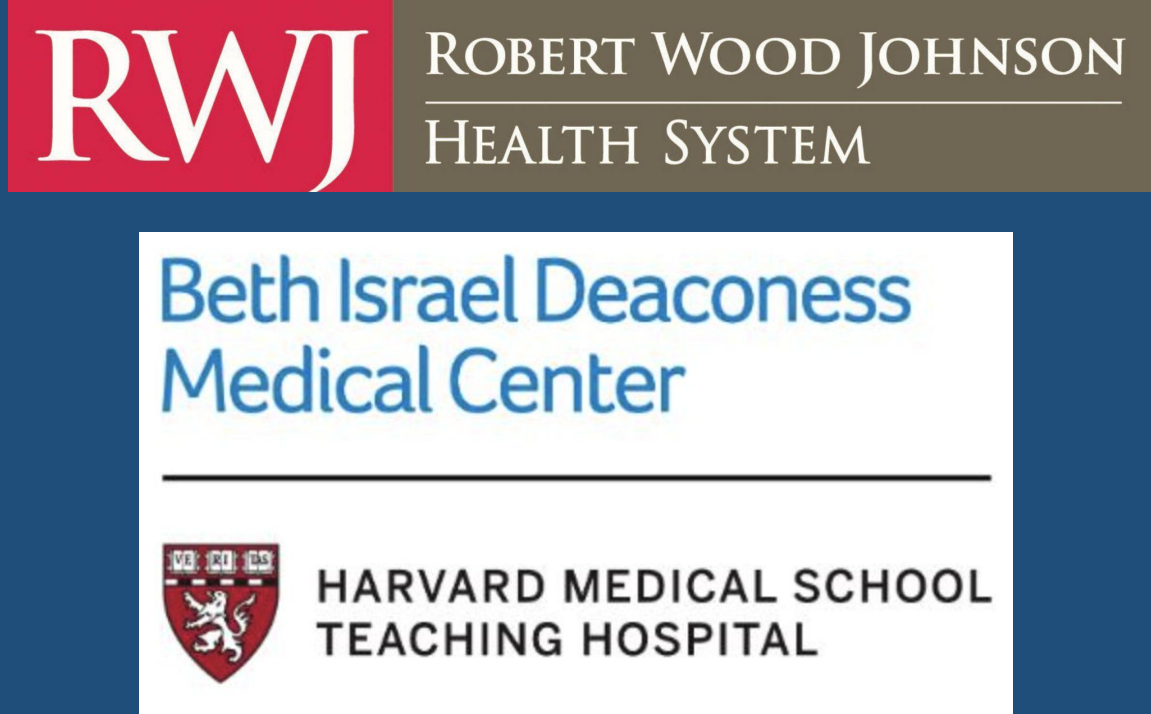




Sublocade® and Brixadi®: Perioperative pain management for patients on long-acting Buprenorphine injectables

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Introduction

- Buprenorphine is a high-affinity, long-acting, partial agonist at the mu-opioid receptor and antagonist at the kappa opioid receptor. Due to its high affinity with binding and low intrinsic activity at the mu-opioid receptor, it is beneficial regarding opioid use disorder and chronic pain while posing low risks for overdose.
- The FDA recently approved two long-acting, subcutaneous formulations of Buprenorphine: Sublocade® (2017) and Brixadi® (2023). These Buprenorphine formulations are novel in dosing and management for OUD
- Current recommendations for perioperative Buprenorphine management are available in existing literature. However, the discussion and consideration of long-acting injectables are minimally published.
- Our review evaluates the existing literature on current recommendations for perioperative Buprenorphine management and emphasizes the future consideration of long-acting Buprenorphine in perioperative pain management.

Methods

- A literature review of Pubmed was conducted using the keywords perioperative, Brixadi, and Sublocade, which yielded 30 results.
- The articles were sorted based on relevance, which yielded 7 articles. The search was limited to articles published within the past year.

Results

- Current RAPM guidelines indicate Buprenorphine can be used with full mu agonists for pain control. It is recommended to utilize multimodal therapy with non-opioid and non-pharmacologic agents, especially in opioid use disorder. Perioperatively, providers should continue the home dose of Buprenorphine.
- If patients are on a high dose of Buprenorphine, consider dose adjustments by discussing with the buprenorphine prescriber or the acute pain service. It is important to recognize the differences between the long-acting injectables Brixadii and Sublocade (Table 1).
- Long-acting injectables create a steady-state concentration, providing a longer-acting effect. The maximum dose of Sublocade is 300mg a month, and it is a monthly injection. Brixadii is a weekly or monthly injection, and the maximum dose is 32mg per week or 128mg per month. The half-life is 43-60 days for monthly Sublocade compared to 19-26 days monthly for Brixadii (3-5 days for weekly).

	Monthly Sublocade®	Weekly & Monthly Brixadi®
FDA Approval	November 2017	May 2023
Dosing	• 2 initial monthly doses of 300mg SQ followed by 100mg maintenance dose. Max dose: 300 mg a month • Doses should be separated by at least 26 days • Doses should be separated by at least 26 days	• Give test dose of 4 mg transcutaneous buprenorphine to ensure tolerated without precipitated withdrawal • If tolerated, administer first dose of 16 mg Brixadi weekly • Add 8 mg weekly dose within 3 days to reach recommended 24 mg weekly dose • An additional 8 mg (at least 24 hours apart) can be given for a total of 32 mg weekly (max dose), if needed • Weekly injection can be given up to 2 days before or after the weekly time point • Monthly injection can be given up to 1 week before or after the monthly time point *** Can convert weekly to monthly dosing with proper conversion of dose
Administration Site	Subcutaneous in the abdomen or gluteus • Rotate injection sites & expect formation of solid depot after injection for gradual release of buprenorphine	Subcutaneous in abdomen, arm, leg, buttock • No rotation required for monthly injection • Do not administer weekly injections at the same site for at least 8 weeks
Half-life	43-60 days	Weekly: 3 to 5 days, monthly: 19 to 26 days
Refrigerated and Formulation	Yes keep refrigerated. Depot formulation contains buprenorphine dissolved in biodegradable delivery system using Atigel® technology that releases at controlled rate over one-month period	No need to refrigerate. FluidCrystal® injection depot technology enables low-volume injection solution that transforms into nanostructured liquid-crystalline gel upon injection (gel allows for controlled gradual release over a week or one-month period)
Common Side Effects	Headache, nausea, injection site pain, vomiting, and fatigue	Headache, constipation, nausea, injection site pain, insomnia, and UTI
Removable	Depot can be surgically removed within 14 days, if needed	Not recommended. The depot may not be detectable or suitable for surgical removal.

Table 1: Long acting injectables brixadii and sublocade

Name	Induction	Maintenance
Sublingual buprenorphine	300 mcg IM/IV	300 mcg IM/IV q6-8 prn
Brixadii	16 mg SC qwk	8 mg SC qwk
Sublocade	300 mg SC	100 mg SC qmo

Table 2: Equivalent dosing: sublingual buprenorphine and long acting injectables (brixadii and sublocade)

Discussion

- A review of the literature shows a disparity regarding perioperative buprenorphine protocols between institutions, but there are general guidelines published by a multi-society panel.
- Additionally, multiple studies show that discontinuing buprenorphine before surgery led to worse outcomes, and that those on Buprenorphine required less narcotics postoperatively.
- Current guidelines suggest continuing or slightly decreasing the dose. Literature is lacking regarding the consideration of Sublocade and Brixadii, which is likely due to the novelty of these injectables since they have only recently been approved by the FDA.
- With new Buprenorphine formulations, providers will likely care for a growing subset of patients on long-acting Buprenorphine. Future considerations for perioperative pain management are necessary for long-acting Buprenorphine injectables versus daily oral Buprenorphine. Preoperative optimization of dosing should be considered for those on Sublocade or Brixadi, perioperative planning for pain management is vital, and considering pain medicine consultation early can be beneficial. Appropriate dose conversions between oral and injectable Buprenorphine should also be further evaluated and established in future literature.

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