



MANAGING POSTSURGICAL PAIN WITH OPIOID-REDUCING STRATEGIES

ORTHOPEDIC

Enhanced recovery goals following orthopedic procedures*

- Optimize pain management¹
- Accelerate mobilization and rehabilitation¹
- Reduce hospital length of stay and readmission^{1,2}

Current opioid use can have short- and long-term effects

- Enhanced recovery pathways are complicated by opioid-related adverse events¹
- Orthopedic surgeons are the third highest prescribers of opioids³



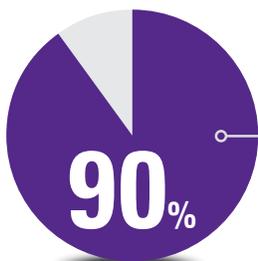
prescribed opioids for postsurgical pain will go on to long-term use⁴

- Incidence of chronic opioid use is higher in patients following total knee arthroplasty (TKA) and total hip arthroplasty (THA) than many other commonly performed procedures⁵

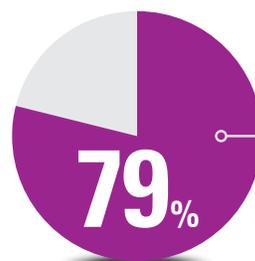


There is a growing demand to reduce postsurgical opioid use

- The Centers for Disease Control and Prevention and The Joint Commission call for a patient-centered multimodal treatment plan, noting that the best approach may be to start with a non-opioid^{6,7}
- Many patients are aware of opioid-related risks and prefer non-opioid analgesic options⁸



of patients are concerned about side effects, addiction, or dependence



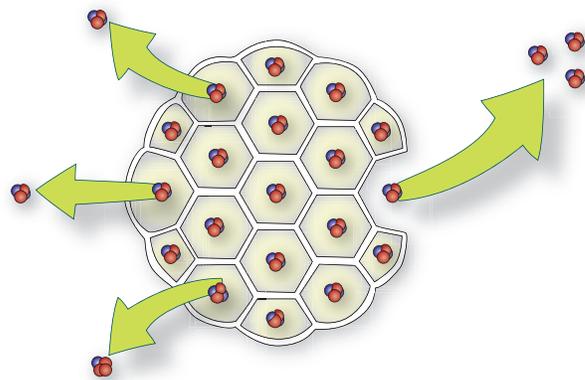
of patients prefer a non-opioid pain management option

*EXPAREL has not been clinically proven to reduce length of stay or rate of readmission, nor accelerate mobilization or rehabilitation.

CONSIDER **EXPAREL** AS PART OF YOUR ENHANCED RECOVERY AFTER SURGERY (ERAS) PROTOCOL

EXPAREL provides long-lasting, non-opioid postsurgical analgesia⁹

- Indicated for administration into the surgical site to produce postsurgical analgesia
 - Indication supports broad use across surgical procedures
- DepoFoam[®] technology uniquely delivers bupivacaine over time to extend postsurgical analgesia¹⁰
- Eliminates the need for catheters and pumps that may hinder recovery¹¹



Dose EXPAREL for optimal analgesic coverage of the surgical site

- The recommended dose of EXPAREL is based on the following factors:
 - Size of the surgical site
 - Volume required to cover the area
 - Individual patient factors that may impact the safety of an amide local anesthetic
 - Maximum dose should not exceed 266 mg (one 20 mL vial)
- Volume can be expanded to fit your analgesic coverage needs¹²
 - Adequate distribution of liposomes is essential for analgesic coverage¹³
 - A 20 mL vial of EXPAREL can be administered undiluted or expanded up to a total of 300 mL with normal (0.9%) saline or lactated Ringer's solution¹²
- Bupivacaine HCl may be administered immediately before EXPAREL or admixed in the same syringe, as long as the ratio of the milligram dose of bupivacaine HCl to EXPAREL does not exceed 1:2



Important Safety Information

EXPAREL is contraindicated in obstetrical paracervical block anesthesia.

In clinical trials, the most common adverse reactions (incidence $\geq 10\%$) following EXPAREL administration were nausea, constipation, and vomiting.

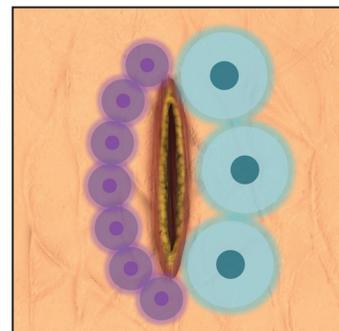
Please see additional Important Safety Information on back and accompanying full Prescribing Information for EXPAREL.

DELIVER LONG-LASTING PAIN CONTROL AT THE SURGICAL SITE

EXPAREL[®]
(bupivacaine liposome injectable suspension)
PATIENT-FOCUSED PAIN CONTROL

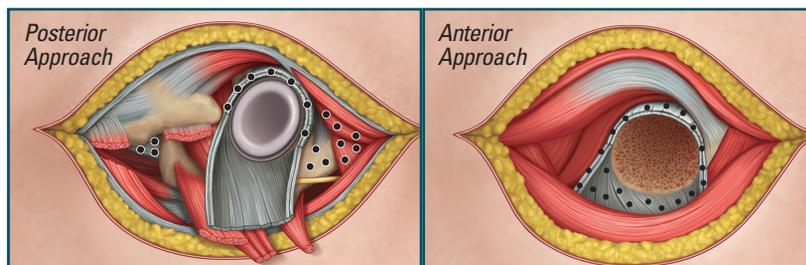
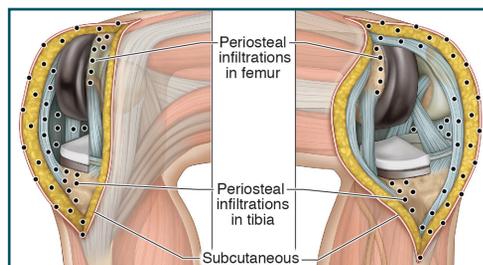
Utilize proper administration technique for targeted analgesia

- EXPAREL should be injected slowly into soft tissues of the surgical site using a deep tissue infiltration technique with frequent aspiration to check for blood and minimize the risk of intravascular injection
 - Administer with a 25-gauge or larger-bore needle
- Since EXPAREL does not diffuse throughout tissues in the same manner as traditional bupivacaine, use a series of injections to effectively cover the surgical area¹³



Infiltrating with EXPAREL: examples in TKA and THA procedures

- In large surgical sites (ie, hips, knees), consider expanding the volume to cover the surgical site
 - Volume ranges of 60 mL to 160 mL have been observed in clinical practice^{2,14,15}



Used with permission from International Guidelines Center (guidelinecentral.com)—Erin Daniel, illustrator.

In TKA procedures, EXPAREL may be infiltrated below and above the fascia, such as the posterior capsule, ligaments, subperiosteal, and musculature. Care should be taken to avoid the midline vascular bundle when injecting posteriorly and the peroneal nerve when injecting laterally.

With either the posterior or anterior approach to THA, EXPAREL may be infiltrated into the pericapsular soft tissues and then into the superficial muscular layers. Care should be taken to avoid the sciatic nerve.



Watch Dr Henderson and Dr Long infiltrate with **EXPAREL** at www.EXPAREL.com

Disclaimer: This individual experience is based on one methodology for using EXPAREL in a specific orthopedic procedure. Pacira Pharmaceuticals, Inc. recognizes that there are alternative methodologies for administering local anesthetics, as well as individual patient considerations, when selecting the dose for a specific procedure.

Important Safety Information

EXPAREL is not recommended for the following types or routes of administration: epidural, intrathecal, regional nerve blocks, or intravascular or intra-articular use.

Non-bupivacaine-based local anesthetics, including lidocaine, may cause an immediate release of bupivacaine from EXPAREL if administered together locally.

Please see additional Important Safety Information on back and accompanying full Prescribing Information for EXPAREL.

The clinical benefit of the decrease in opioid consumption was not demonstrated in the pivotal trials. EXPAREL is indicated for administration into the surgical site to produce postsurgical analgesia.

Important Safety Information

EXPAREL is contraindicated in obstetrical paracervical block anesthesia.

In clinical trials, the most common adverse reactions (incidence $\geq 10\%$) following EXPAREL administration were nausea, constipation, and vomiting.

EXPAREL is not recommended to be used in the following patient population: patients <18 years old and/or pregnant patients.

Because amide-type local anesthetics, such as bupivacaine, are metabolized by the liver, EXPAREL should be used cautiously in patients with hepatic disease. Patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally, are at a greater risk of developing toxic plasma concentrations.

Warnings and Precautions Specific to EXPAREL

EXPAREL is not recommended for the following types or routes of administration: epidural, intrathecal, regional nerve blocks, or intravascular or intra-articular use.

Non-bupivacaine-based local anesthetics, including lidocaine, may cause an immediate release of bupivacaine from EXPAREL if administered together locally. The administration of EXPAREL may follow the administration of lidocaine after a delay of 20 minutes or more. Formulations of bupivacaine other than EXPAREL should not be administered within 96 hours following administration of EXPAREL.

Warnings and Precautions for Bupivacaine-Containing Products

Central Nervous System (CNS) Reactions: There have been reports of adverse neurologic reactions with the use of local anesthetics. These include persistent anesthesia and paresthesias. CNS reactions are characterized by excitation and/or depression.

Cardiovascular System Reactions: Toxic blood concentrations depress cardiac conductivity and excitability which may lead to dysrhythmias sometimes leading to death.

Allergic Reactions: Allergic-type reactions (eg, anaphylaxis and angioedema) are rare and may occur as a result of hypersensitivity to the local anesthetic or to other formulation ingredients.

Chondrolysis: There have been reports of chondrolysis (mostly in the shoulder joint) following intra-articular infusion of local anesthetics, which is an unapproved use.

Please see accompanying full Prescribing Information for EXPAREL.

For more information, please visit www.EXPAREL.com or call 1-855-RX-EXPAREL (793-9727).

References: 1. Barrington JW, Halaszynski TM, Sinatra RS; for Expert Working Group on Anesthesia & Orthopaedics: Critical Issues in Hip and Knee Replacement Arthroplasty. Perioperative pain management in hip and knee replacement surgery. *Am J Orthop.* 2014;43(suppl 4):S1-S16. 2. Joshi GP, Cushner FD, Barrington JW, et al. Techniques for periarticular infiltration with liposomal bupivacaine for the management of pain after hip and knee arthroplasty: a consensus recommendation. *J Surg Orthop Adv.* 2015;24(1):27-35. 3. Morris BJ, Mir HR. The opioid epidemic: impact on orthopaedic surgery. *J Am Acad Orthop Surg.* 2015;23(5):267-271. doi:10.5435/JAAOS-D-14-00163. 4. Alam A, Gomes T, Zheng H, Mamdani MM, Juurlink DN, Bell CM. Long-term analgesic use after low-risk surgery: a retrospective cohort study. *Arch Intern Med.* 2012;172(5):425-430. doi:10.1001/archinternmed.2011.1827. 5. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and risk factors for chronic opioid use among opioid-naïve patients in the postoperative period. *JAMA Intern Med.* 2016;176(9):1286-1293. doi:10.1001/jamainternmed.2016.3298. 6. The Joint Commission. Safe use of opioids in hospitals. *Sentinel Event Alert.* 2012;8(49):1-5. 7. Policy impact: prescription painkiller overdoses. Centers for Disease Control and Prevention website. <http://www.cdc.gov/drugoverdose/pdf/policyimpact-prescriptionpainkillerod-a.pdf>. Published November 2011. Accessed October 13, 2016. 8. New research: opioid addiction and dependence after surgery is significantly higher than previously known. Pacira Pharmaceuticals, Inc. website. http://investor.pacira.com/phoenix.zhtml?c=220759&p=irol-newsArticle_pf&ID=2191316. Accessed August 22, 2016. 9. Gorfine SR, Onel E, Patou G, Krivokapic ZV. Bupivacaine extended-release liposome injection for prolonged postsurgical analgesia in patients undergoing hemorrhoidectomy: a multicenter, randomized, double-blind, placebo-controlled trial. *Dis Colon Rectum.* 2011;54(12):1552-1559. doi:10.1097/DCR.0b013e18232d4c1. 10. About DepoFoam[®]. Pacira Pharmaceuticals, Inc. website. <http://www.exparel.com/hcp/about-EXPAREL/about-depofeam.shtml>. Accessed August 9, 2016. 11. Grissinger M. Improved safety needed in handling elastomeric reservoir balls used for pain relief. *P&T.* 2013;38(5):243-245. 12. Dosing EXPAREL[®]. Pacira Pharmaceuticals, Inc. website. <http://www.exparel.com/hcp/how-to-use/dosing.shtml>. Accessed August 18, 2016. 13. EXPAREL[®] administration. Pacira Pharmaceuticals, Inc. website. <http://www.exparel.com/hcp/how-to-use/EXPAREL-administration.shtml>. Accessed August 18, 2016. 14. Surdam JW, Licini DJ, Baynes NT, Arce BR. The use of EXPAREL (liposomal bupivacaine) to manage postoperative pain in unilateral total knee arthroplasty patients. *J Arthroplasty.* 2015;30(2):325-329. doi:10.1016/j.arth.2014.09.004. 15. Yu SW, Szulc AL, Walton SL, Davidovitch RI, Bosco JA, Iorio R. Liposomal bupivacaine as an adjunct to postoperative pain control in total hip arthroplasty. *J Arthroplasty.* 2016;31(7):1510-1515. doi:10.1016/j.arth.2016.01.004.