

Non-opioid EXPAREL, powered by DepoFoam[®] technology, delivers precise pain control for the critical first few days after surgery to enable enhanced recovery.^{1,2}

The Era of Opioids as the Gold Standard for Pain Management Is Over

Opioids have been a mainstay in postsurgical pain control, but many who are prescribed opioids will go on to become persistent long-term users⁴



OF PATIENTS RECEIVE OPIOIDS TO MANAGE POSTSURGICAL PAIN*5



SURGICAL PATIENTS PRESCRIBED AN OPIOID MAY GO ON TO LONG-TERM USE OR ABUSE¹⁶

AMERICANS BECAME NEWLY PERSISTENT OPIOID USERS IN A SINGLE YEAR FOLLOWING INITIAL EXPOSURE AFTER SURGERY⁷

*In a retrospective study of hospital discharge data (N=37,301).

[†]In a prospective longitudinal study (N=109).

Most patients say they would prefer a non-opioid option to manage their pain after surgery^{‡8}

- 89% of patients said they were concerned about side effects of, addiction to, or dependence on opioids
- 79% of patients said they preferred a nonopioid pain management option

More than 8 million adult

patients have received non-opioid **EXPAREL** since **2012**³

EXPAREL Is a Non-opioid Component for Multimodal Pain Management and ERAS® Protocols



reduce opioid use and ORAEs can lead to enhanced clinical and economic benefits¹⁵⁻¹⁹

The 133 mg (10 mL) dose can be used for procedures that are limited to a small anatomical area as well as for ISBPNB Hand · Foot · Oral/Maxillofacial · BCB/TSA EXPARE The 266 mg (20 mL) dose is appropriate for procedures such as¹: Abdominal/Colorectal/General · Breast Gynecological · Orthopedic · Spine

*These are examples of procedures that typically require the above referenced dose of EXPAREL. Please use your professional clinical judgment when determining the appropriate dose of EXPAREL for a given surgical procedure and refer to the full Prescribing Information for complete dosing information before using.

EXPAREL Is a Long-lasting, Non-opioid Analgesic Proven to Manage Postsurgical Pain

INFILTRATION

[‡]From a survey of 500 adults in the United States who had an orthopedic or soft-tissue surgery.

Broad indication for infiltration across surgical procedures to provide local/regional analgesia

Versatility of Administration

FIELD BLOCKS

Indicated for a wide variety of blocks, including TAP, PEC, ESP, and QL

ISBP NERVE BLOCK

Indicated in adults for ISBP nerve block in procedures such as TSA and rotator cuff surgeries

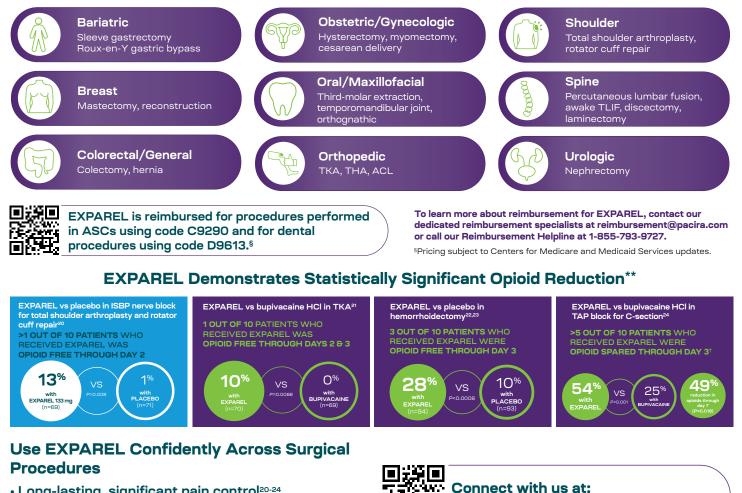
Proprietary DepoFoam® technology safely delivers bupivacaine over time for extended analgesia9

COMPOSED DELIVERS of naturally occurring biodegradable targeted local analgesia at the surgical site and biocompatible lipids¹⁰⁻¹ **ENCAPSULATES** DESIGNED to consistently deliver safe levels of bupivacaine in a multivesicular liposomal drug delivery technology bupivacaine to extend analgesic duration¹³ RELEASES **ELIMINATES** bupivacaine over time as lipid the need for catheters and pumps membranes reorganize⁹ that may hinder recovery¹⁴ UTILIZES PROVIDES

membrane components that are cleared by normal metabolic pathways¹⁰⁻¹²

long-lasting pain control while reducing the need for opioids

EXPAREL Can Be Used in a Wide Range of Procedures Across Specialties



- Long-lasting, significant pain control²⁰⁻²⁴
- Proven opioid reduction
 **20-24
- Proven safety and tolerability profile^{13,20,25,26}

"The clinical benefit of the decrease in opioid consumption was not demonstrated in the pivotal trials.

t"Opioid-spared" was defined as patients who took no more than 10 mg of oxycodone (15 mg of morphine or equivalent) with no bother or stress from vomiting, itching, sweating, freezing, or dizziness through 72 hours.

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https://www.exparel.com/hcp/connectwithus

Indication

EXPAREL[®] (bupivacaine liposome injectable suspension) is indicated for single-dose infiltration in patients aged 6 years and older to produce postsurgical local analgesia and in adults as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia. Safety and efficacy have not been established in other nerve blocks. Important Safety Information

EXPAREL is contraindicated in obstetrical paracervical block anesthesia. Adverse reactions reported in adults with an incidence greater than or equal to 10% following EXPAREL administration via infiltration were nausea Adverse reactions with an incidence greater than or equal to 10% following EXPAREL administration via infiltration in pediatric patients six to less than 17 years of age were nausea, yomiting, constipation, hypotension, anemia, muscle twitching, vision blurred, pruritus, and tachycardia. If EXPAREL administration via infiltration in pediatric patients six to less than 17 years of age were nausea, vomiting, constipation, hypotension, anemia, muscle twitching, vision blurred, pruritus, and tachycardia. If EXPAREL administration via infiltration in pediatric patients are administered at the same site, there may be an immediate release of bupivacaine from EXPAREL Therefore, EXPAREL may be administered to the same site 20 minutes after injecting lidocaine. EXPAREL is not recommended to be used in the following applications; patients <6 years old for infiltration, patients younger than 18 years old for interscalene brachial plexus nerve block, 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.

Warnings and Precautions Specific to EXPAREL

Avoid additional use of local anesthetics within 96 hours following administration of EXPAREL is not recommended for the following types or routes of administration: epidural, intrathecal, regional nerve blocks other than interscalene brachial plexus nerve block, or intravascular or intra-articular use. The potential sensory and/or motor loss with EXPAREL is temporary and varies in degree and duration depending on the site of injection and dosage administered and may last for up to 5 days, as seen in clinical trials.

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 paresthesia. CNS reactions are characterized by excitation and/or depression. 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 (e.g. 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. Methemoglobinemia: Cases of methemoglobinemia have been reported with local anesthetic use.

Full Prescribing Information is available at www.EXPAREL.com.

1. Lambert WJ, Los K. DepoFoam' multivesicular liposomes for the sustained release of macromolecules. In: Rathbone MJ, Hadgraft J, Roberts MS, Lane ME, eds. Modified-Release Drug Delivery Technology. Vol 2. 2nd ed. New York, NY: Informa Healthcare USA, Inc; 2008:207-214. 2. 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. 3. Data on File. 6450. Parsipany, NJ: Pacira BioSciences, Inc.; January 2021. 4. Brunmett CM, Waljee JF, Goesling J, et al. New persistent opioid use after minor and major surgical procedures in US adults. JAMA Surg. 2017;152(6):e170504. 5. Kessler ER, Shah M, Gruschuss KR, Raji A. Cost and quality implications of opioid-based postsurgical pain control using administrative claims data from a large health system: opioid-related adverse events and their impact on clinical and economic outcomes. Pharmacetherapy. 2013;33(3):33-391. 6. Carroll I, Barelika P, Wang CKM, et al. A pliot cohort study of the determinants of longitudinal opioid use after surgery. Anesth Analg. 2012;1153(3):647-702. 7. Pacira Pharmacetticals, Inc. United States for Non-Dependence: An Analysis of the Impact of Opioid Overprescribing in America. September 2017. (Analysis in the report was based on research conducted by the Quintiles/NB Institute.) 8. Data on File. 2014. Discinged release of macromolecules In: 2 Hadynaft I. Roberts MS (Lang ME). 2914. Parsipany, NJ: Pacifica BioSciences, Inc.; June 2016. **9**. Lambert W. J. Los K. DepoFoam' multivesicular lingsome for the sustained release of macromolecules. In: Rathbone MJ, Hadgraft J, Roberts MS, Lane ME, eds. *Modified-Release Drug Delivery Technology*. Vol 2. 2nd ed. New York, NY: Informa Healthcare USA, Inc; 2008;207-214. **10**. Angst MS, Drover DR. Pharmacology of drugs formulated with DepoFoam: a sustained release drug delivery system for parenteral administration using multivesicular liposome technology. *Clin Pharmacokinet*. 2006;45(12):1153-1176. **11**. Kohn FR, Malkmus SA, Brownson EA, Bossi SS, Yaksh TL. Fate of the release drug delivery system for parenteral administration using multivescular liposome technology. *Clin Pharmacokinet*. 2006;45(12):1153-1176. **11**. Kohn FR, Malkmus SA, Brownson EA, Rossi SS, Yaksh TL, Fate of the predominant phospholipid component of DepoFoam drug delivery matrix after intrathecal administration of sustained-release encapsulated cytarabine in rats. *Drug Deliv*. 1998;5(2):143-151. **12**. Richard BM, Newton P, Ott LR, et al. The safety of EXPAREL' (bupivacaine liposome injectable suspension) administered by peripheral nerve block in rabbits and dogs. *J Drug Deliv*. 2012;2012:962101. **13**. Bramlett K, Onel E, Viscusi ER, Jones K. A randomized, double-blind, dose-ranging study comparing wound infiltration of DepoFoam bupivacaine, an extended-release liposomal bupivacaine, to bupivacaine HCI for postsurgical analgesia in total knee arthroplasty. *Knee*. 2012;9(5):530-536. **14**. Grissinger H. Improved safety needed in handling elastomeir creservoir balls used for pain relief. *P T*. 2013;38(5):247-245. **15**. Gottschalk A, Smith DS. New concepts in acute pain therapy: preemptive analgesia. *Am Fam Physician*. 2001;63(10):1979-1984. **16**. Gandhi K, Viscusi E. Multimodal pain management techniques in hip and knee arthroplasty. *J NYSORA*. 2009;13:1-10. **17**. White PF. The changing role of non-opioid analgesic techniques in thermangement of postoperative pain after transforminal lumbar interbody fusion: a clinical study. *World Neurosurg*. 2016;91:460-467. **19**. Brummett CM, England C, Evans-Shields J, et al. Health care burden associated with outpatient or outpatient or outpatient science approximately. *J Mang Care Spec Pharm*. 2019;2(5):97:973-983. **20**. Patel MA, Gadsden JC, Nedeljikovic SS, et al. Brachial plexus block with liposomal bupivacaine for chardbard and partice and reduce covicid equation for contropicia and and/outpace and reduce covicid equation of contropicia and reduce covicid equation for the analyzed analgesia and reduce analgesia and reduce covicid equation of postoperative pai With outpatient opioid use following inpatient or outpatient surgery. J Manag Care Spec Pharm. 2019;25(9):9/3-983. **20**, Patel MA, Gadsden JC, Nedeljkovic SS, et al. Brachial plexus block with liposomal bupivacane for shoulder surgery improves analgesia and reduces opioid consumption: results from a multicenter, randomized, double-blind, controlled trial. Pain Med 2020;21(2):387-400. **21**. Mont MA, Beaver WB, Dysart SH, Barrington JW, Del Gaizo DJ. Local infiltration analgesia with liposomal bupivacaine improves pain scores and reduces opioid use after total knee arthroplasty: results of a randomized, double-blind, placebo-controlled trial. J Arthroplasty: analgesia with liposomal bupivacaine extended-release liposome injection for prolonged postsurgical analgesia in patients undergoing hemorrhoidectomy: a multicenter, randomized, double-blind, placebo-controlled trial. J S Colon Rectum. 2011;54(12):1552-1559. **23**. Data on File. 2363. Parsippany, NJ: Pacira BioSciences, Inc.; June 2017. **24**. Nedeljkovic SS, Kett A, Vallejo MC, et al. Transversus abdominis plane block with liposomal bupivacaine injection following a single administration at the surgical site. *Clin Drug Investine*; 2013;26(1):019-115. **26**. Gadsden J, Long WJ. Time to analges onset and pharmacokinetic profile of liposome bupivacaine and bupivacaine and bupivacaine HCI: considerations for clinicians. *Open Orthop J.* 2016;10:94-104.

