

MANAGING POSTSURGICAL PAIN WITH OPIOID-REDUCING STRATEGIES

BREAST RECONSTRUCTION

Enhanced recovery goals following breast reconstruction procedures*

- Counsel patients and set pain expectations prior to the procedure^{1,2}
- Reduce the risk of developing chronic pain³
- Accelerate mobilization and rehabilitation^{4,5}
- Decrease the risk of postsurgical complications and delays^{3,6,7}

Breast reconstruction is considered an extremely painful procedure, regardless of technique. Poorly managed postsurgical pain can be debilitating and add further psychosocial distress, particularly in patients with a history of multiple treatments^{2,7}

Current opioid analgesic approach can have negative long-term effects



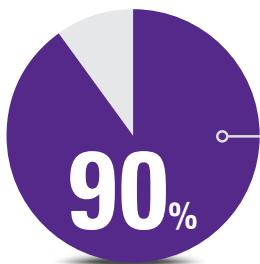
prescribed opioids for postsurgical pain will go on to long-term use⁸



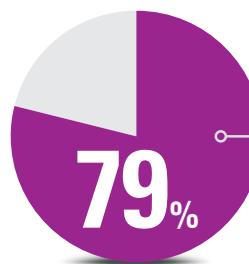
Incidence of chronic opioid use is higher in patients following simple mastectomy and breast reconstruction than most commonly performed procedures^{9,10}

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^{11,12}
- Many patients are aware of opioid-related risks and prefer non-opioid analgesic options¹³



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



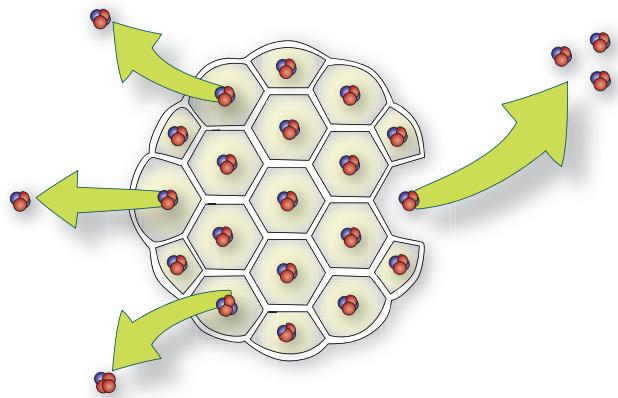
of patients prefer a non-opioid pain management option

*EXPAREL is not approved to treat chronic pain and has not been clinically proven to accelerate mobilization or rehabilitation, nor decrease the risk of postsurgical complications and delays.

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

EXPAREL provides long-lasting, non-opioid postsurgical pain control¹⁴

- 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 analgesia¹⁵
- Eliminates the need for catheters and pumps that may hinder recovery¹⁶



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 needs¹⁷
 - Adequate distribution of liposomes is essential for analgesic coverage¹⁸
 - 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 solution¹⁷
- 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.

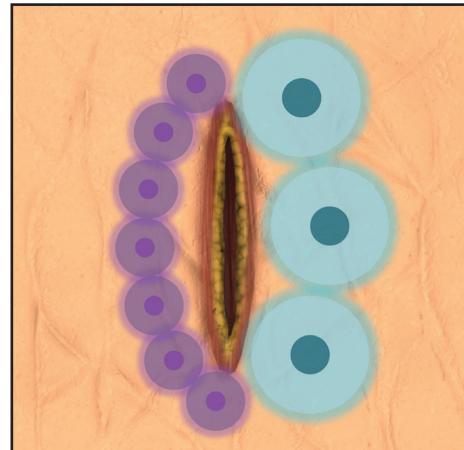
Please see additional Important Safety Information on back and accompanying full Prescribing Information for EXPAREL.

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 area¹⁸



Infiltrating with EXPAREL: example in breast reconstructive procedures



In a case study done on a patient undergoing a delayed right latissimus dorsi breast reconstruction following mastectomy, Dr Mark Brzezinski infiltrated EXPAREL into the back, taking care when infiltrating the inferior portion of the dissection where the muscle is detached, as discomfort is commonly noted in that area.



He also infiltrated EXPAREL into the front of the dissection, taking care when infiltrating the axilla, which is also a commonly reported site of discomfort after surgery.



Watch Dr Brzezinski infiltrate with EXPAREL
at www.EXPAREL.com

Disclaimer: This individual experience is based on one methodology for using EXPAREL in a specific reconstructive 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 ≥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. Pusic AL, Klassen AF, Snell L, et al. Measuring and managing patient expectations for breast reconstruction: impact on quality of life and patient satisfaction. *Exper Rev Pharmacoecon Outcomes Res.* 2012;12(2):149-158. doi:10.1586/erp.11.105. 2. Parker PA. Breast reconstruction and psychosocial adjustment: what have we learned and where do we go from here? *Semin Plast Surg.* 2004;18(2):131-138. doi:10.1055/s-2004-829047. 3. Hutchins JL. Improving patient outcomes through state-of-the-art pain control in breast cancer surgery. *Am J Hematol Oncol.* 2015;11(5):29-32. 4. Gnaneshwaran N, Perera M, Perera N, Peters M. Enhanced recovery after surgery (ERAS) pathways in autologous breast reconstruction: a systematic review. *Eur J Plast Surg.* 2016;39(3):165-172. doi:10.1007/s00238-016-1189-3. 5. The Pennine Acute Hospitals NHS Trust. Enhanced recovery after breast surgery, an information guide. 2012;1-31. 6. Alderman A, Gutowski K, Ahuja A, Gray D; for Postmastectomy Expander Implant Breast Reconstruction Guideline Work Group. ASPS clinical practice guideline summary on breast reconstruction with expanders and implants. *Plast Reconstr Surg.* 2014;134(4):648e-655e. doi:10.1097/PRS.0000000000000541. 7. Butz DR, Shenaq DS, Rundell VL, et al. Postoperative pain and length of stay lowered by use of Exparel in immediate, implant-based breast reconstruction. *Plast Reconstr Surg Glob Open.* 2015;3(5):1-5. doi:10.1097/GOX.0000000000000355. 8. Alam A, Gomes T, Zheng H, Mandani 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. 9. 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. 10. Bar-Meir ED, Yueh JH, Hess PE, et al. Postoperative pain management in DIEP flap breast reconstruction: identification of patients with poor pain control. *Eplasty.* 2010;10:483-491. 11. The Joint Commission. Safe use of opioids in hospitals. *Sentinel Event Alert.* 2012;8(49):1-5. 12. 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. 13. 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. 14. Gorfine SR, Onel E, Patou G, Krivakovic ZV. Bupivacaine extended-release liposome injection for prolonged postsurgical analgesia in patients undergoing hemicolectomy: a multicenter, randomized, double-blind, placebo-controlled trial. *Dis Colon Rectum.* 2011;54(12):1552-1559. doi:10.1097/DCR.0b013e18232d4c1. 15. About DepoFoam®. Pacira Pharmaceuticals, Inc. website. <http://www.exparel.com/hcp/about-EXPAREL/about-depofoam.shtml>. Accessed August 9, 2016. 16. Grissinger M. Improved safety needed in handling elastomeric reservoir balls used for pain relief. *P&T.* 2013;38(5):243-245. 17. Dosing EXPAREL®. Pacira Pharmaceuticals, Inc. website. <http://www.exparel.com/hcp/how-to-use/dosing.shtml>. Accessed August 18, 2016. 18. EXPAREL® administration. Pacira Pharmaceuticals, Inc. website. <http://www.exparel.com/hcp/how-to-use/EXPAREL-administration.shtml>. Accessed August 18, 2016.