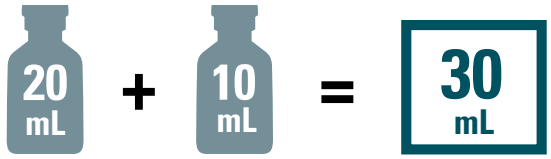
EXPAREL®
(bupivacaine liposome injectable suspension)

EXPAREL for hemorrhoidectomy:

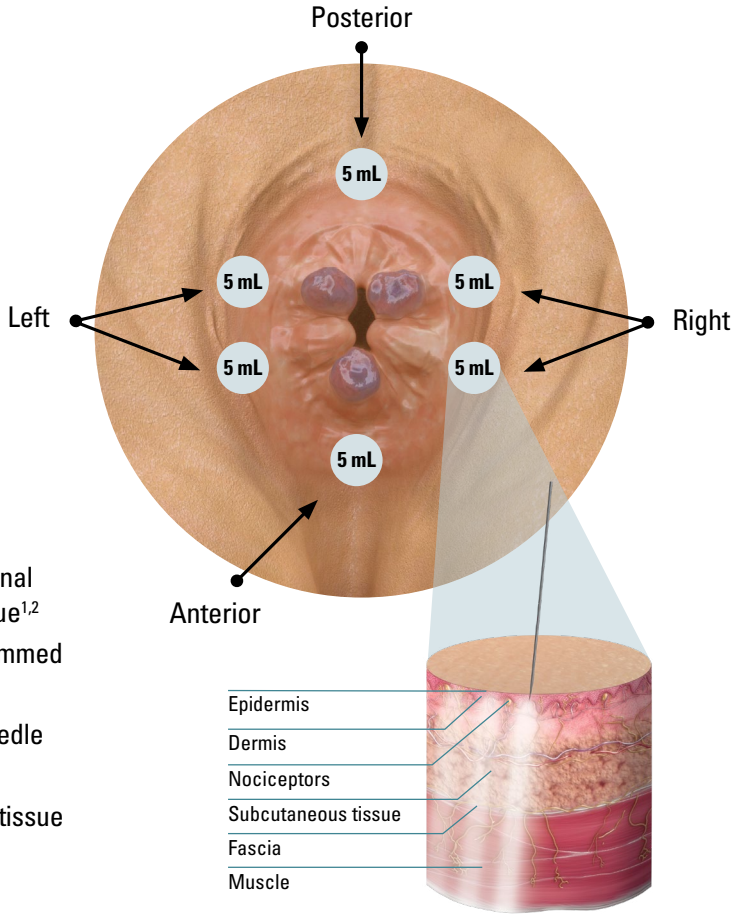
Infiltration technique and clinical efficacy results[1-3]

Dose of EXPAREL and total volume used



EXPAREL (266 mg) | **Normal saline 0.9%** | **Total**

- EXPAREL was administered at the conclusion of surgery as part of a standard field block with local anesthesia[1-3]
- Bupivacaine HCl can be admixed with EXPAREL in a 1:2 ratio to provide early onset analgesic coverage
- Avoid non-bupivacaine local anesthetics within 20 minutes of administration of EXPAREL



Infiltration technique protocol used

- Surgery was a 2- or 3-column excisional hemorrhoidectomy for internal or internal/external hemorrhoids using the Milligan-Morgan technique[1,2]
- A field block was created by visualizing the anal sphincter as diagrammed and 5 mL was infiltrated at each infiltration point as indicated below
  - —Injected slowly and deeply into the soft tissues using a moving needle technique (ie, injecting while withdrawing the needle)[1]
  - —Infiltrated above and below the fascia and into the subcutaneous tissue
  - —Aspirated frequently to minimize the risk of intravascular injection

Clinical efficacy results[1,3*]

Significantly lower OPIOID USE*
45% lower overall opioid consumption
P=0.0006†

Significantly better PAIN CONTROL
30% lower cumulative pain scores
P<0.0001†

Results from a phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group clinical trial that evaluated the safety and efficacy of 266 mg (20 mL) EXPAREL in 186 patients undergoing 2- or 3-column excisional hemorrhoidectomy. Primary end point: cumulative pain score reflected in area under the curve of numeric rating scale through 72 hours. Placebo was preservative-free saline for injection. Opioid rescue medication (up to 10 mg morphine administered intramuscularly) was available to all patients.[1,3]
*The clinical benefit of the decrease in opioid consumption was not demonstrated in the pivotal trials; †Through 72 hours. Opioid reduction was calculated based on geometric mean ratio.[3]

- 28% of EXPAREL patients were opioid free (*P*<0.0008)

Non-opioid EXPAREL provides significant long-lasting pain control *while* reducing opioid use[1,3*]

- Approved for use across surgical procedures in various surgical settings
- Critical component of a multimodal, opioid-minimizing pain management strategy[4]
- The infiltration indication includes regional field or interfascial plane blocks such as, but not limited to, transversus abdominis plane (TAP) block, pectoralis (PEC) and serratus plane blocks, erector spinae plane (ESP) block, and quadratus lumborum (QL) block

Please see Important Safety Information on reverse and refer to the full Prescribing Information, which is available at www.EXPARELpro.com.

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Indication

EXPAREL® (bupivacaine liposome injectable suspension) is indicated to produce postsurgical local analgesia via infiltration in patients aged 6 years and older and regional analgesia in adults via an interscalene brachial plexus nerve block, sciatic nerve block in the popliteal fossa, and an adductor canal block. 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, constipation, and vomiting; adverse reactions reported in adults with an incidence greater than or equal to 10% following EXPAREL administration via nerve block were nausea, pyrexia, headache, and constipation.

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, vomiting, constipation, hypotension, anemia, muscle twitching, vision blurred, pruritus, and tachycardia.

Do not admix lidocaine or other non-bupivacaine local anesthetics with EXPAREL. EXPAREL may be administered at least 20 minutes or more following local administration of lidocaine.

EXPAREL is not recommended to be used in the following patient populations: patients <6 years old for infiltration, patients younger than 18 years old for nerve blocks, 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.

EXPAREL is not recommended for the following types or routes of administration: epidural, intrathecal, regional nerve blocks **other than interscalene brachial plexus nerve block**, **sciatic nerve block in the popliteal fossa, and adductor canal 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.

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.

Methemoglobinemia: Cases of methemoglobinemia have been reported with local anesthetic use.

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

For more information, please visit www.EXPARELpro.com or call 1-855-793-9727.

References: 1. 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. **2.** Data on File. REF-0579. Clinical Study Report. Parsippany, NJ: Pacira Pharmaceuticals, Inc.; February 2010. **3.** Data on File. REF-2363. Parsippany, NJ: Pacira Pharmaceuticals, Inc.; June 2017. **4.** American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology.* 2012;116(2):248-273.

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