

ADMINISTRATION AND DOSING GUIDE

EXPAREL[®]

(bupivacaine liposome injectable suspension)

OPIOID FREE

CHOOSE EXPAREL TO MANAGE PAIN WITH FEWER OPIOIDS

EXPAREL is indicated for single-dose infiltration in adults to produce postsurgical local analgesia and as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia. Safety and efficacy have not been established in other nerve blocks.

Consider patients who would benefit from an alternative to opioids

- Patients whose use of opioids may impact recovery goals¹
- Patients at high risk for opioid-related adverse events²⁻⁴
- Patients at risk for misuse or abuse of opioids^{5,6}



Please see Indication and Important Safety Information on the back cover and refer to accompanying full Prescribing Information.

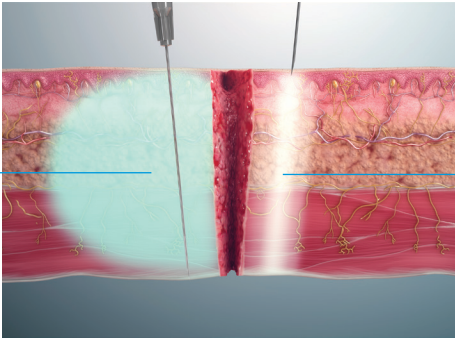
For more information, please visit www.EXPAREL.com
or call 1-855-RX-EXPAREL (793-9727).

HOW TO ADMINISTER EXPAREL FOR OPTIMAL ANALGESIA

HOW

Administer EXPAREL differently than bupivacaine HCl

- When infiltrating, utilize a frequent and consistent injection technique throughout the surgical site



BUPIVACAINE HCl IS AN AQUEOUS SOLUTION

- Readily diffuses into surrounding tissues and spreads throughout site
- Requires fewer injections for adequate pain-receptor coverage

EXPAREL IS A SUSPENSION COMPOSED OF MULTIVESICULAR LIPOSOMES THAT CARRY BUPIVACAINE

- Stays precisely where placed; does *not* readily diffuse into surrounding tissue
- Requires more injections to ensure adequate pain-receptor coverage

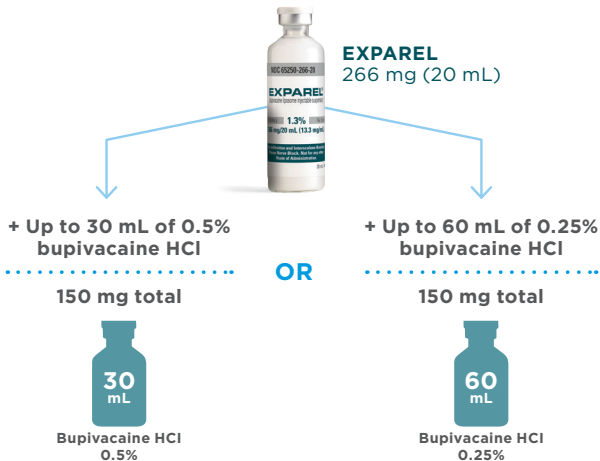
Please refer to accompanying full Prescribing Information.

ENSURE EARLY ANALGESIC ONSET BY ADMIXING EXPAREL WITH BUPIVACAINE HCl

Bupivacaine HCl may be administered immediately before EXPAREL or admixed as part of the total expanded volume

- Keep a 1:2 ratio of the milligram dose of bupivacaine HCl to EXPAREL. In determining the ratio, consider
 - One 20 mL vial of EXPAREL contains 266 mg free-base bupivacaine, which is molar equivalent to 300 mg bupivacaine HCl
 - One 30 mL vial of 0.5% bupivacaine contains 150 mg bupivacaine HCl

Example of admixing



- Admixing may impact the pharmacokinetic and/or pharmacodynamic properties of EXPAREL; the effect is concentration dependent

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WHERE TO ADMINISTER EXPAREL

WHERE

Inject deep into surgical site or into the fascial plane

SURGICAL-SITE INFILTRATION

- Inject EXPAREL slowly and deeply (generally 1-2 mL per injection) into soft tissues using a moving needle technique (ie, inject while withdrawing the needle)
- Infiltrate above and below the fascia and into the subcutaneous tissue
- Aspirate frequently to minimize risk of intravascular injection
- Use a 25-gauge or larger-bore needle to maintain the structural integrity of liposomes
- Inject frequently in small areas (1-1.5 cm apart)

Epidermis

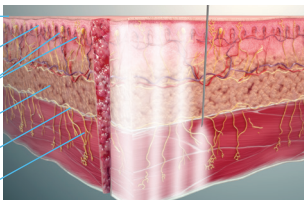
Dermis

Nociceptors

Subcutaneous tissue

Fascia

Muscle



TRANSVERSUS ABDOMINIS PLANE BLOCK

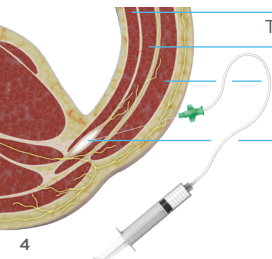
- Use regional field block technique for postsurgical analgesia in the abdomen
- Place EXPAREL in the fascial plane between the internal oblique and transversus abdominis muscles
- Perform using ultrasound guidance or laparoscopic visualization

Transversus abdominis

Internal oblique

External oblique

Local anesthetic



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HOW MUCH EXPAREL TO ADMINISTER TO ENSURE PAIN-RECEPTOR COVERAGE

HOW
MUCH

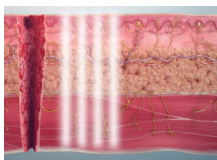
Determine the right dose and how much to expand the volume

DOSING CONSIDERATIONS

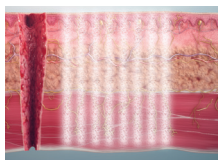
- Size of the surgical site
- Volume required to cover the area
- Individual patient factors that may impact the safety of an amide local anesthetic
- Maximum dose should not exceed 266 mg (20 mL)
- Intended for single-dose administration only

DETERMINE THE RIGHT VOLUME TO COVER THE SURGICAL SITE

- Consider the size of the surgical site and the neuroanatomy
- Expand the volume to disperse liposomes throughout the surgical site
- Enough multivesicular liposomes must be available at the pain receptors to continuously release bupivacaine, ensuring long-lasting analgesia



EXPAREL unexpanded



EXPAREL expanded

EXPAREL 266 mg (20 mL) CAN BE EXPANDED UP TO 300 mL FOR LARGE SURGICAL SITES

- Expand with normal (0.9%) saline or lactated Ringer's solution
- Add up to 280 mL for a total of 300 mL, a 1:14 ratio

Please refer to accompanying full Prescribing Information.

Indication

EXPAREL is indicated for single-dose infiltration in adults to produce postsurgical local analgesia and 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 with an incidence greater than or equal to 10% following EXPAREL administration via infiltration were nausea, constipation, and vomiting; adverse reactions reported with an incidence greater than or equal to 10% following EXPAREL administration via interscalene brachial plexus nerve block were nausea, pyrexia, and constipation. If EXPAREL and other non-bupivacaine local anesthetics, including lidocaine, 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 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.

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**, 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.

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Please refer to accompanying full Prescribing Information.

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1. Gan TJ, Robinson SB, Oderda GM, Scranton R, Pepin J, Ramamoorthy S. Impact of postsurgical opioid use and ileus on economic outcomes in gastrointestinal surgeries. *Curr Med Res Opin.* 2015;31(4):677-686. 2. Kessler ER, Shah M, Gruschus SK, Raju 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. *Pharmacotherapy.* 2013;33(4):383-391. 3. The Joint Commission. Safe use of opioids in hospitals. https://www.jointcommission.org/assets/1/18/SEA_49_opioids_b_2_12_final.pdf. Accessed July 20, 2018. 4. Minkowitz HS, Gruschus SK, Shah M, Raju A. Adverse drug events among patients receiving postsurgical opioids in a large health system: risk factors and outcomes. *Am J Health Syst Pharm.* 2014;71(18):1556-1565. 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. 6. Seal KH, Shi Y, Cohen G, et al. Association of mental health disorders with prescription opioids and high-risk opioid use in US veterans of Iraq and Afghanistan. *JAMA.* 2012;307(9):940-947.

