

PEDIATRIC FAST FACTS

THE FIRST AND ONLY FDA-APPROVED
LONG-ACTING LOCAL ANALGESIC FOR
AGES 6 AND ABOVE



EXPAREL 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.

Please see Important Safety Information [here](#) and refer to full Prescribing Information, which is available at www.EXPAREL.com.

EXPAREL IS A LONG-LASTING, NON-OPIOID ANALGESIC PROVEN TO MANAGE POSTSURGICAL PAIN

EXPAREL uses proprietary multivesicular liposome (pMVL) technology, an advanced drug-delivery platform, to extend analgesia.¹

DESIGNED

to deliver controlled levels of bupivacaine¹

COMPOSED

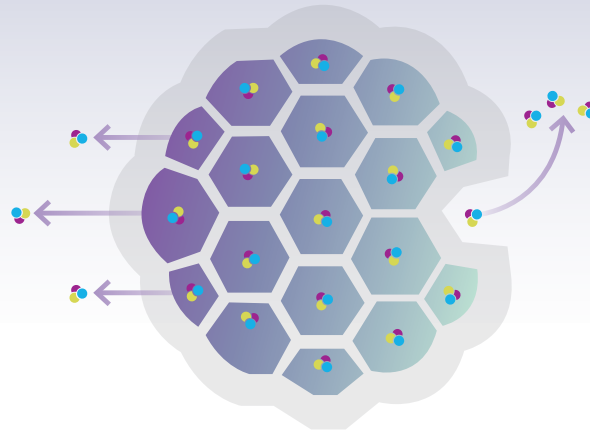
of naturally occurring, biocompatible lipids²⁻⁴

ENCAPSULATES

the bupivacaine in a suspension of multivesicular liposomes

RELEASES

bupivacaine over time¹



ACHIEVES

targeted analgesia at the surgical site

PROVIDES

safe, consistent levels of bupivacaine¹

ELIMINATES

the need for catheters and pumps that may hinder recovery⁵

EXTENDS

analgesic duration while reducing the need for opioids*

EXPAREL is administered differently than bupivacaine HCl, allowing for precise delivery of analgesia

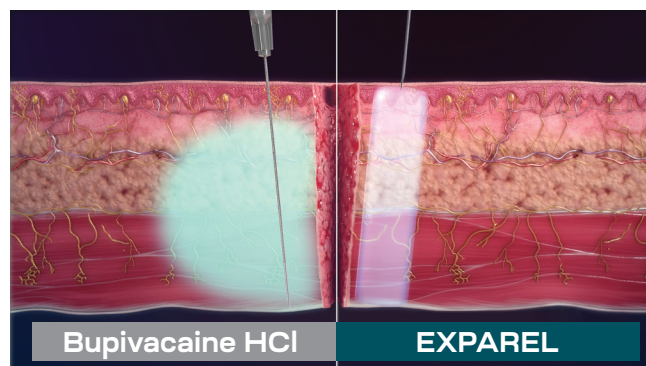
Since the bupivacaine in EXPAREL is encapsulated in multivesicular liposomes, it does not diffuse as widely throughout the tissues as bupivacaine HCl does.

Bupivacaine is an aqueous solution

- Readily diffuses into surrounding tissue throughout the surgical site
- Requires fewer injections for adequate pain-receptor coverage

EXPAREL is a suspension composed of multivesicular liposomes that carry bupivacaine

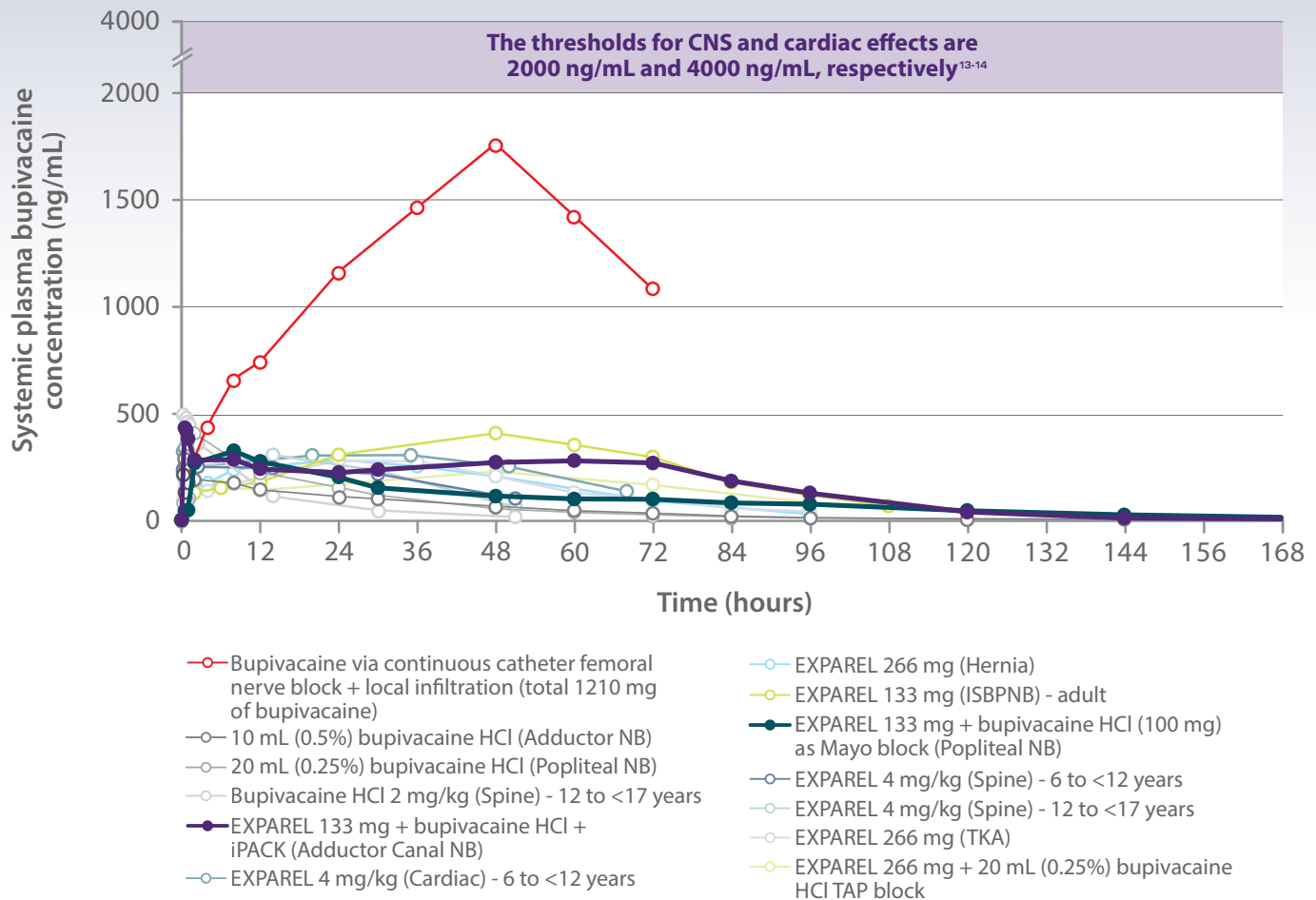
- Stays precisely where placed; does *not* diffuse into surrounding tissue
- Requires more injections to ensure adequate pain-receptor coverage



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

EXPAREL DELIVERS A CONSISTENT SLOW RELEASE OF BUPIVACAINE OVER TIME TO MAINTAIN PLASMA LEVELS BELOW CARDIAC AND NEUROTOXIC THRESHOLDS⁶⁻¹³

At all doses studied, including both doses of EXPAREL (266 mg and 133 mg), plasma bupivacaine levels are maintained well below toxic thresholds



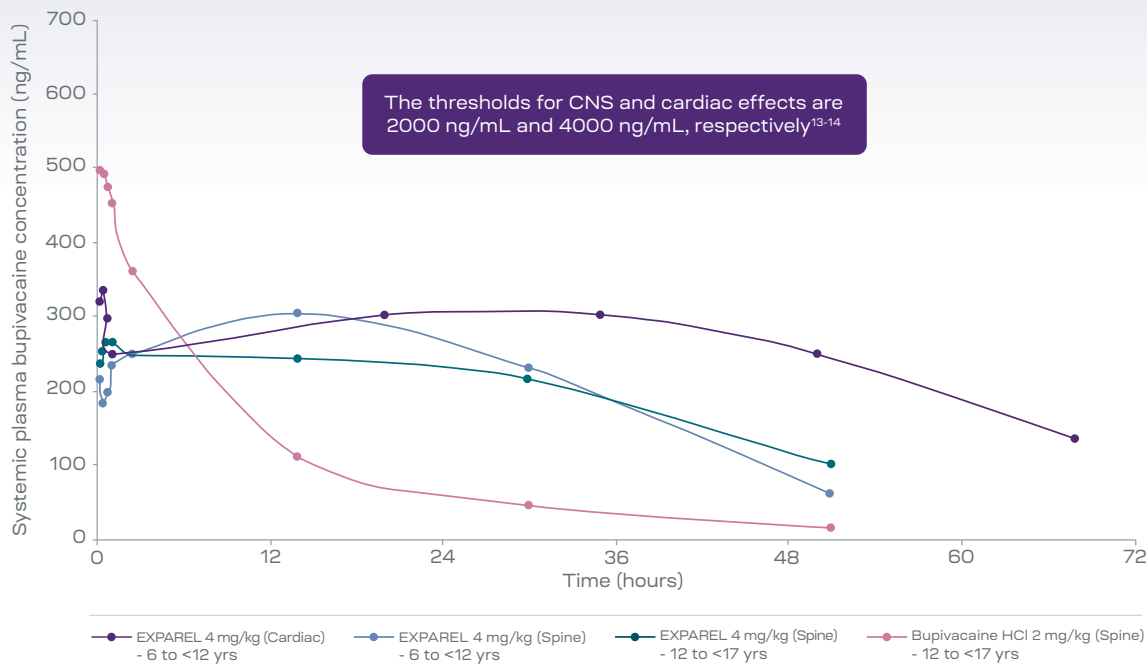
- Pharmacokinetics demonstrate plasma levels of bupivacaine that can persist for 96 hours^{1, 10}
- The rate of systemic absorption of bupivacaine is dependent upon the total dose of drug administered, the route of administration, and the vascularity of the administration site
- Systemic plasma levels of bupivacaine following administration of EXPAREL are not correlated with local efficacy

CNS=central nervous system; ISBPNB=interscalene brachial plexus nerve block; NB=nerve block; TAP=transversus abdominis plane; TKA=total knee arthroplasty.

THE PLAY STUDY WAS DESIGNED TO ESTABLISH THE SAFETY OF EXPAREL IN PEDIATRIC PATIENTS 6 TO <17 YEARS OLD⁹

The PLAY study findings were consistent with the PK and safety profiles of EXPAREL in adult patients. EXPAREL was studied in pediatric patients ages 6 to <17 years old for **single-dose infiltration at 4 mg/kg up to a maximum of 266 mg**. Treatment-emergent adverse events and treatment-related adverse events were mild or moderate in severity in both pediatric age groups.

PK Profile of EXPAREL in Pediatric Spine and Cardiac Surgery Was Comparable Across Age and Surgery Type



- Systemic plasma levels of bupivacaine following administration of EXPAREL are not correlated with local efficacy
- The rate of systemic absorption of bupivacaine is dependent upon the total dose of drug administered, the route of administration, and the vascularity of the administration site
- As seen in adults, EXPAREL PK levels remain well below toxic thresholds due to the pMVL technology, which allows for a consistent, steady, and safe release over time^{1,9}

Mean C_{max}

- EXPAREL Cardiac surgery: 447 ng/mL
- EXPAREL Spine surgery: 320 ng/mL
- EXPAREL Spine (12 to <17): 357 ng/mL
- Bupivacaine HCl Spine (12 to <17): 564 ng/mL

The PK curve represents the **mean plasma concentrations** of bupivacaine (ng/mL) for all patients **at each time point**.

C_{max} is calculated as the mean of the **maximum plasma concentrations** of bupivacaine (ng/mL) **for all patients**.

C_{max} = maximum concentration; PK=pharmacokinetics.

Bupivacaine HCl data is for reference purposes only and does not reflect an active comparator in the study.

DETERMINING THE EXPAREL DOSE

The dose of EXPAREL (mg) is determined by weight at 4 mg/kg not to exceed 266 mg*

$$\text{Patient weight (kg)} \times 4 \text{ mg/kg} = \text{EXPAREL dose (mg)}$$

Example based on a 25-kg patient

EXPAREL dose (mg)

$$25 \text{ kg} \times 4 \text{ mg/kg} = 100 \text{ mg of EXPAREL}$$

Calculate the volume of EXPAREL (mL) by dividing the EXPAREL dose (mg) by 13.3 mg/mL

$$\text{EXPAREL dose (mg)} \div 13.3 \text{ mg/mL} = \text{volume of EXPAREL (mL)}$$

Example based on a 25-kg patient

EXPAREL volume (mL)

$$100 \text{ mg} \div 13.3 \text{ mg/mL} = 7.5 \text{ mL of EXPAREL}$$

Expanding and/or admixing with EXPAREL

Consider the size, vascularity, and neuroanatomy of the surgical site.

Admixing may impact the pharmacokinetic/pharmacodynamic properties of EXPAREL; this effect is concentration dependent.

For optimal analgesic coverage

Expand volume of EXPAREL

Normal (0.9%) saline or lactated Ringer's solution
Up to a total volume of 300 mL
(for the 266 mg vial)

To ensure the effectiveness of EXPAREL, **maintain a minimum concentration of 0.89 mg/mL**

For early analgesic onset

Admix with EXPAREL

Bupivacaine HCl[†] *only*

Ensure ratio of milligram dose of bupivacaine HCl to EXPAREL does not exceed 1:2

If expanding and admixing, consider the amount of normal saline or lactated Ringer's solution, bupivacaine HCl, and EXPAREL as part of the total maximum volume

*For patients 66.5 kg and above, do not exceed 266 mg (20 mL).

†Bupivacaine HCl is indicated for use in patients aged 12 years and older.

ADMINISTERING EXPAREL

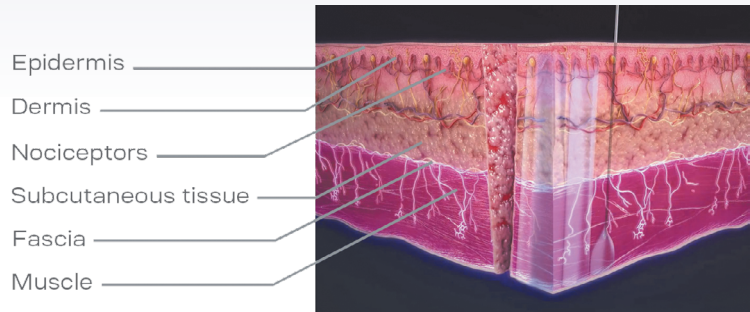
In patients 6 and above, EXPAREL can be administered via single-dose infiltration into the surgical site to produce local analgesia or be infiltrated into the fascial plane to produce regional analgesia as a regional field block.

Surgical site infiltration

To produce local analgesia across surgical procedures

When infiltrating into the surgical site with EXPAREL

- 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)

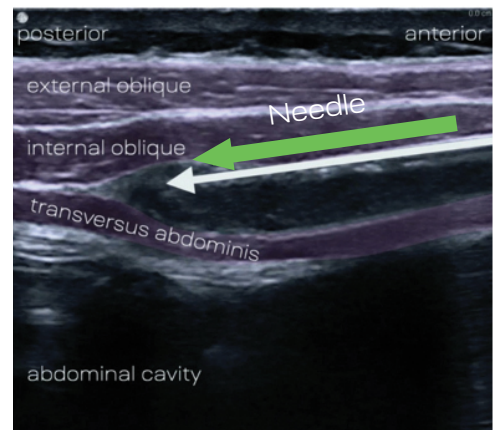


Fascial plane infiltration for regional field blocks

To produce regional analgesia using regional techniques such as ESP, QL, and TAP

When infiltrating into the fascial plane with EXPAREL

- Use a regional field block technique, such as ESP, PECS I and II, QL or TAP, for postsurgical regional analgesia
- Deposit EXPAREL within the musculofascial plane so that it can spread and provide sensory blockade to nerve(s) contained within the anatomical plane
- Multiple blocks can be used in combination to achieve full coverage of the surgical site(s)
- Perform using ultrasound guidance or laparoscopic visualization to enable precise placement of EXPAREL within the plane



ESP=erector spinae plane; PECS=pectoralis; QL=quadratus lumborum; TAP=transversus abdominis plane.

Sonoanatomy showing abdominal wall muscles and the needle direction for the lateral TAP block. The pool of EXPAREL mixture is seen in the correct plane.

Compatibility considerations with EXPAREL



Wait 20 minutes after administering lidocaine, ropivacaine, or other non-bupivacaine-based local anesthetics before administering EXPAREL into the same surgical site



Allow topical antiseptics such as Betadine® to dry before administering EXPAREL into the same surgical site



EXPAREL should not be admixed with local anesthetics other than bupivacaine prior to administration
Remember to be mindful of the total bupivacaine exposure



Do not dilute EXPAREL with water or other hypotonic agents, as it will result in disruption of the liposomal particles



Avoid additional use of local anesthetics within 96 hours following administration of EXPAREL

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Storage and handling recommendations for EXPAREL

The 133 mg (10 mL) and 266 mg (20 mL) doses of EXPAREL are available in cartons of 4 and 10 single-dose vials.

Storage

- EXPAREL vials should be stored and refrigerated between 2°C to 8°C (36°F-46°F)
- Sealed, intact (unopened) EXPAREL vials may be held at a controlled room temperature of 20°C to 25°C (68°F-77°F) for up to 30 days



Do not do the following to EXPAREL vials:

- Freeze
- Expose to high temperatures (>40°C or 104°F) for an extended period
- Rerefrigerate

Handling

- Vials should be visually inspected before use
- Invert vials multiple times to resuspend the particles immediately prior to withdrawal from the vial
- Use within 4 hours of opening



Do not administer EXPAREL if:

- Vial stopper is bulging
- The vial is suspected of having been frozen or exposed to high temperatures

Use this wristband as an identifier for care teams as well as a way to educate patients and parents about the use of EXPAREL and the potential to minimize opioid use.

Click [here](#) to contact your local sales representative to order wristbands for your institution.



INDICATION AND IMPORTANT SAFETY INFORMATION

Indication

EXPAREL 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.

References: 1. 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 HCl for postsurgical analgesia in total knee arthroplasty. *Knee*. 2012;19(5):530-536. 2. 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. 3. 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. 4. 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. 5. Grissinger M. Improved safety needed in handling elastomeric reservoir balls used for pain relief. *P T*. 2013;38(5):243-245. 6. Patel MA, et al. *Pain Medicine*. 2020;21(2):387-400. 7. Gadsden et al. Presented at: American Society for Regional Anesthesia (ASRA) 48th Annual Regional Anesthesiology and Acute Pain Medicine Meeting; April 20, 2023. Hollywood, FL. 8. Schwartz et al. Presented at: American Society for Regional Anesthesia (ASRA) 48th Annual Regional Anesthesiology and Acute Pain Medicine Meeting; April 20, 2023. 9. Tirotta CF, et al. *J Clin Anesth*. 2021;75:11050. 10. Hu D et al. *Clin Drug Invest*. 2013;33:109-115. 11. Mustafa HJ, et al. *Obstet Gynecol*. 2020;36(1):70-76. 12. Marino J et al. *J Arthroplasty*. 2019;34(3):495-500. 13. Knudsen K et al. *Br J Anaesth*. 1997;78(5):507-514. 14. New York School of Regional Anesthesia. *Clinical Pharmacology of Local Anesthetics*. 2019. <https://www.nysora.com/foundations-of-regional-anesthesia/pharmacology/clinical-pharmacology-local-anesthetics/>. Accessed December 21, 2023.

Connect with us to learn how EXPAREL can help support pain management in your practice

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



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EXPAREL[®]
(bupivacaine liposome injectable suspension)