

NON-OPIOID
EXPAREL[®]
(bupivacaine liposome injectable suspension)

**BUILT TO WEATHER
POSTSURGICAL PAIN**



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.

Please see Important Safety Information throughout and refer to the full Prescribing Information, which is available at www.EXPAREL.com.

PACIRA
BIOSCIENCES, INC.

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 users¹

99%

OF PATIENTS RECEIVE OPIOIDS TO MANAGE POSTSURGICAL PAIN*²

1
out of
15

SURGICAL PATIENTS PRESCRIBED AN OPIOID MAY GO ON TO LONG-TERM USE OR ABUSE^{†3}

~3M

AMERICANS BECAME NEWLY PERSISTENT OPIOID USERS IN A SINGLE YEAR FOLLOWING INITIAL EXPOSURE AFTER SURGERY⁴



Most patients say they would prefer a non-opioid option to manage their pain after surgery^{‡5}

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

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

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

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

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.

Please refer to the full Prescribing Information for complete Dosage and Administration information before using EXPAREL.

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

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EXPAREL, also referred to as "liposomal bupivacaine," offers versatility of administration, enabling surgical site infiltration to produce local analgesia; fascial plane infiltration to produce regional analgesia as a regional field block; or interscalene brachial plexus nerve block

INFILTRATION

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

FIELD BLOCKS

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

ISBP NERVE BLOCK

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

Proprietary DepoFoam[®] technology safely delivers bupivacaine over time for extended analgesia⁶

COMPOSED

of naturally occurring biodegradable and biocompatible lipids⁷⁻⁹

ENCAPSULATES

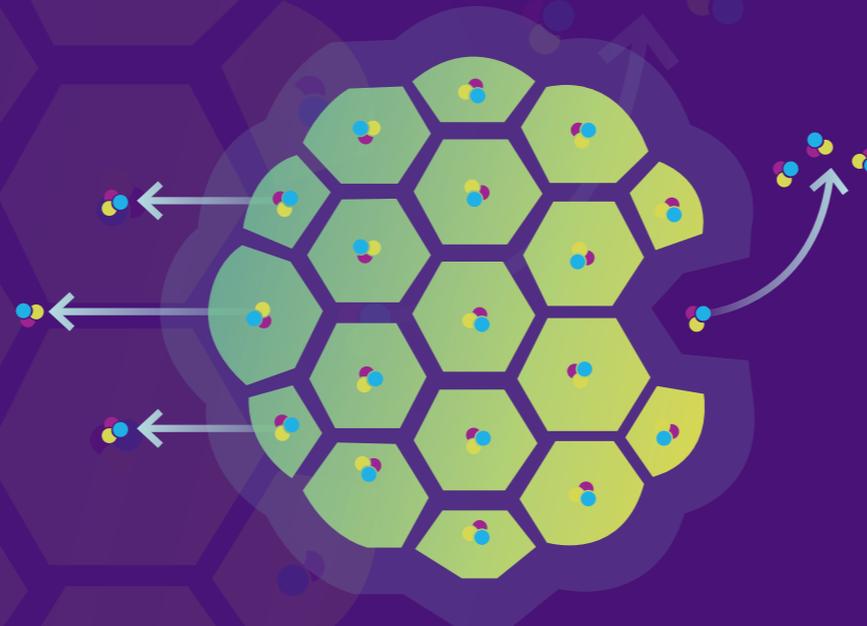
bupivacaine in a multivesicular liposomal drug delivery technology

RELEASES

bupivacaine over time as lipid membranes reorganize⁶

UTILIZES

membrane components that are cleared by normal metabolic pathways⁷⁻⁹



DELIVERS

targeted local analgesia at the surgical site

DESIGNED

to consistently deliver safe levels of bupivacaine to extend analgesic duration¹⁰

ELIMINATES

the need for catheters and pumps that may hinder recovery¹¹

PROVIDES

long-lasting pain control while reducing the need for opioids

TAP=transversus abdominis plane; PEC=pectoralis and serratus; ESP=erector spinae plane; TLIP=thoraco-lumbar interfascial plane; iPACK=interspace between the popliteal artery and capsule of the posterior knee; QL=quadratus lumborum; ISBP=interscalene brachial plexus; TSA=total shoulder arthroplasty.

Important Safety Information (continued)

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.

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

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Enhanced Recovery After Surgery (ERAS®) protocols are patient-centered, evidence-based multimodal pathways for perioperative care that accelerate recovery and reduce general morbidity,¹² as well as:

Reduce pain¹³

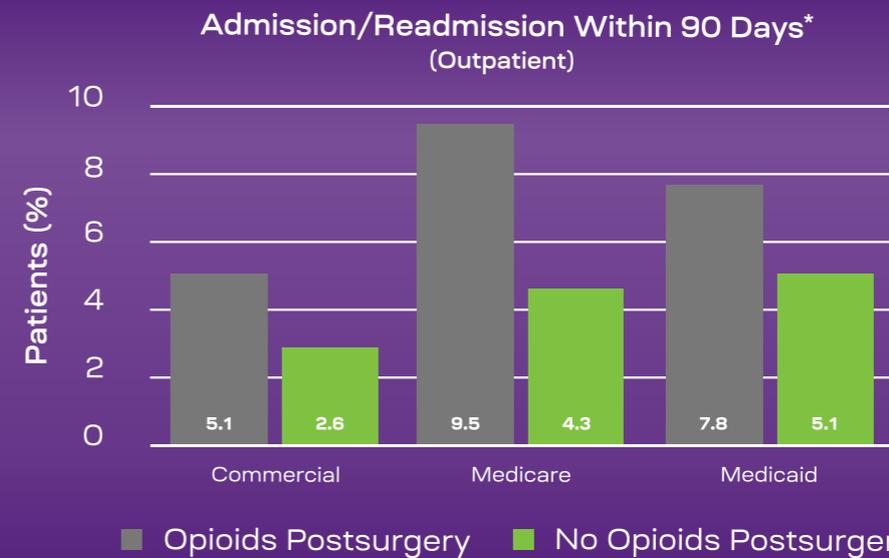
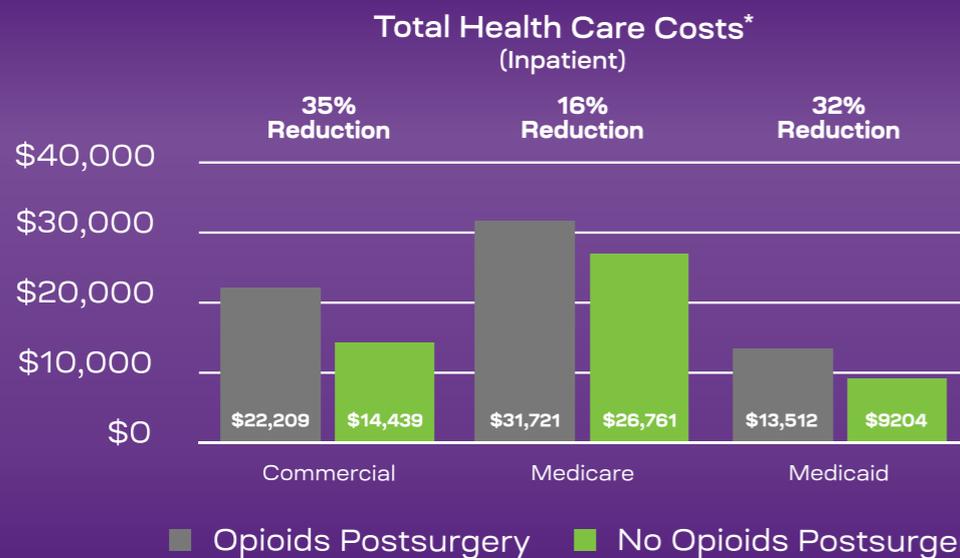
Minimize ORAEs¹⁴

Reduce time to discharge¹⁵

Decrease costs¹⁶

Multimodal postsurgical pain management protocols that reduce opioid use and ORAEs can lead to enhanced clinical and economic benefits¹³⁻¹⁷

In a study of the burdens of opioid use in multiple payer channels in the United States¹⁷:



Retrospective, observational cohort study of medical claims, health care utilization, and costs in opioid-naïve patients who received and those who did not receive opioids after surgery in large, nationally representative claims databases (N=4,105,121). Surgery types included general, orthopedic, plastic, obstetric/gynecologic, and other surgery.

ORAEs=opioid-related adverse events.

*All comparisons of postsurgical opioid use were statistically significant (P<0.001).

Important Safety Information (continued)

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.

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National Medical Societies Across Surgical Specialties Support Multimodal Pain Management Strategies That Include EXPAREL

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AAOMS – Oral/Maxillofacial

AAOMS also supports multimodal pain management strategies, such as the use of long-acting anesthetics during surgery...¹⁸



ERAS Society – Breast Reconstruction

A single injection of liposomal bupivacaine lasts for several days, potentially avoiding the need for catheter-based infusions.¹⁹



APS, ASRA, ASA – Anesthesiology

...clinicians should be knowledgeable regarding specific local anesthetic infiltration techniques (including the use of extended-release formulations of local anesthetics, such as liposomal bupivacaine)...²⁰



ERAS Society – Gynecologic Oncology

Incisional injection of liposomal bupivacaine has no systemic side effects when used appropriately and should be incorporated into all ERAS protocols as a component of multimodal analgesia.²¹



ASCRS, SAGES – Colorectal Surgery

...liposomal bupivacaine wound infiltration and transversus abdominus plane (TAP) blocks "have shown promising results in patients undergoing open and laparoscopic colorectal surgery."²²



ERAS Society, ESTS Thoracic Surgery

Liposomal bupivacaine also shows promise when delivered as multilevel intercostal injections, potentially providing blockade of intercostal nerves for up to 96 hours.²³

AAOMS=American Association of Oral and Maxillofacial Surgeons; APS=American Pain Society; ASRA=American Society of Regional Anesthesia and Pain Medicine; ASA=American Society of Anesthesiologists; ASCRS=American Society of Colon and Rectal Surgeons; SAGES=Society of American Gastrointestinal and Endoscopic Surgeons; ESTS=European Society of Thoracic Surgeons.

Important Safety Information (continued)

Warnings and Precautions Specific to EXPAREL

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.

Please refer to the full Prescribing Information for complete Dosage and Administration information before using EXPAREL.

EXPAREL Provides Long-lasting, Significant Pain Control While Reducing Opioid Use*

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EXPAREL vs placebo in ISBP nerve block for total shoulder arthroplasty and rotator cuff repair²⁴

78% FEWER OPIOIDS

Postsurgical opioid consumption over 48 hours

P<0.0001

SIGNIFICANTLY BETTER PAIN CONTROL

Cumulative pain scores over 48 hours

P<0.0001

Results from a phase 3, double-blind, randomized, placebo-controlled trial that compared the postsurgical analgesia efficacy, safety, and pharmacokinetics of EXPAREL 133 mg (10 mL) (n=69) and placebo (n=71) in patients undergoing total shoulder arthroplasty or rotator cuff repair. Primary and secondary end points: pain intensity through 48 hours postsurgery, as measured by area under the curve (AUC) of visual analog scale (VAS) pain intensity scores, and total postsurgical opioid consumption. Rescue opioids for pain were available upon patient request. Incidence of AEs were comparable between groups, with the most common being nausea, headache, pyrexia, and constipation.

EXPAREL vs bupivacaine HCl in TKA²⁵

78% FEWER OPIOIDS

Overall opioid consumption over 48 hours

P=0.0048

SIGNIFICANTLY BETTER PAIN CONTROL

Cumulative pain scores from 12 to 48 hours

P=0.0381

Results from a phase 4, double-blind, randomized, placebo-controlled trial that compared the efficacy and safety of EXPAREL 266 mg (20 mL) (n=70) and bupivacaine HCl (n=69) in a TKA study. Primary end points: AUC of VAS pain intensity scores 12 to 48 hours postsurgery; total opioid consumption 0 to 48 hours postsurgery. Rescue opioids for pain were available upon patient request. Rates and types of AEs were similar between treatment groups. The most common AEs in the EXPAREL group were nausea, muscle spasms, and vomiting.

EXPAREL vs placebo in hemorrhoidectomy^{26,27}

45% FEWER OPIOIDS

Overall opioid consumption over 72 hours

P=0.0006[†]

SIGNIFICANTLY BETTER PAIN CONTROL

Cumulative pain scores over 72 hours

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 EXPAREL 300 mg (30 mL) (n=95) and placebo (n=94) in subjects undergoing 2- or 3-column excisional hemorrhoidectomy. Primary end point: cumulative pain score reflected in AUC 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. Rates of AEs were comparable between groups. The most common AEs were gastrointestinal.

EXPAREL vs bupivacaine HCl in TAP block for C-section²⁸

52% FEWER OPIOIDS

Postsurgical opioid consumption at 72 hours

P=0.0117

72 hrs PAIN CONTROL

Comparable pain control compared to bupivacaine

Results from a randomized, active-controlled, double-blind investigation using a multimodal protocol with EXPAREL in a TAP block vs standard bupivacaine in patients undergoing elective C-section and given spinal anesthesia. Primary end point: total postsurgical opioid consumption (mg) in oral morphine-equivalent dosing through 72 hours. Patients were randomized in a blinded 1:1 ratio to receive TAP infiltration with EXPAREL 266 mg (20 mL) plus bupivacaine HCl (n=97) or active bupivacaine HCl alone (n=89). Rescue opioids for pain were available upon patient request. The safety profile was similar between groups, with the most common AEs being pruritus, nausea, vomiting, and headache.

AEs=adverse events; TKA=total knee arthroplasty.

*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.

Important Safety Information (continued)

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.

Please refer to the full Prescribing Information for complete Dosage and Administration information before using EXPAREL.

EXPAREL Demonstrates Statistically Significant Opioid Reduction*

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EXPAREL vs placebo in ISBP nerve block for total shoulder arthroplasty and rotator cuff repair²⁴

>1 OUT OF 10 PATIENTS WHO RECEIVED EXPAREL WAS OPIOID FREE THROUGH DAY 2



EXPAREL vs bupivacaine HCl in TKA²⁵

1 OUT OF 10 PATIENTS WHO RECEIVED EXPAREL WAS OPIOID FREE THROUGH DAYS 2 & 3



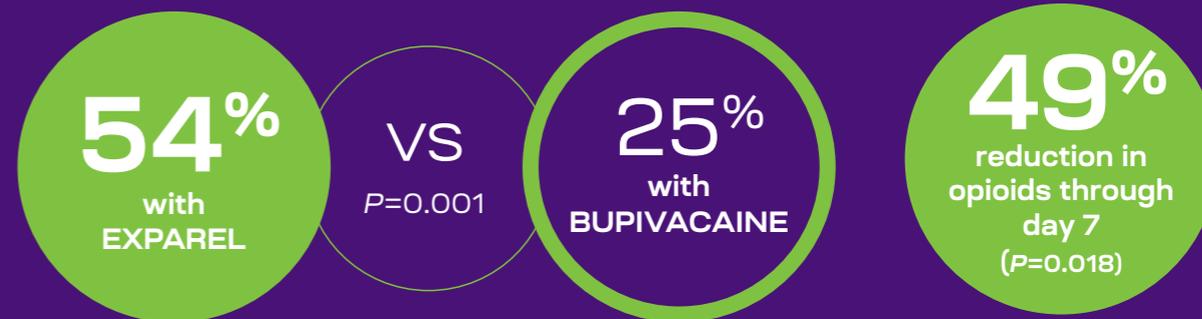
EXPAREL vs placebo in hemorrhoidectomy^{26,27}

3 OUT OF 10 PATIENTS WHO RECEIVED EXPAREL WERE OPIOID FREE THROUGH DAY 3



EXPAREL vs bupivacaine HCl in TAP block for C-section²⁸

>5 OUT OF 10 PATIENTS WHO RECEIVED EXPAREL WERE OPIOID SPARED THROUGH DAY 3[†]



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

†"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.

Important Safety Information (continued)

Warnings and Precautions for Bupivacaine-Containing Products

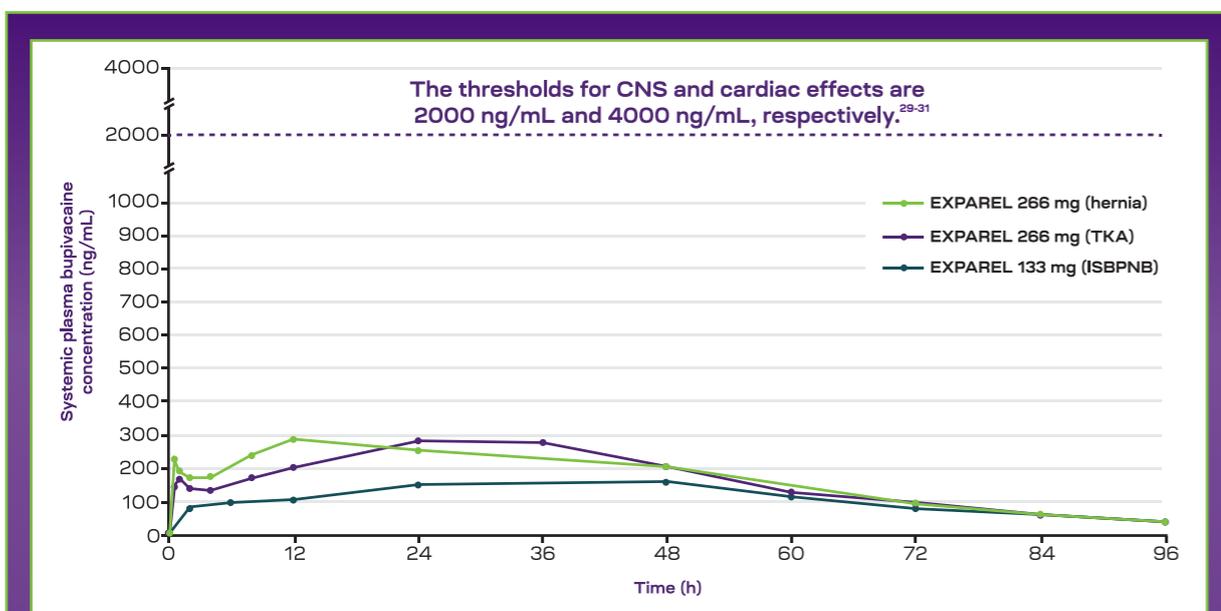
Cardiovascular System Reactions: Toxic blood concentrations depress cardiac conductivity and excitability which may lead to dysrhythmias, sometimes leading to death.

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.

Please refer to the full Prescribing Information for complete Dosage and Administration information before using EXPAREL.

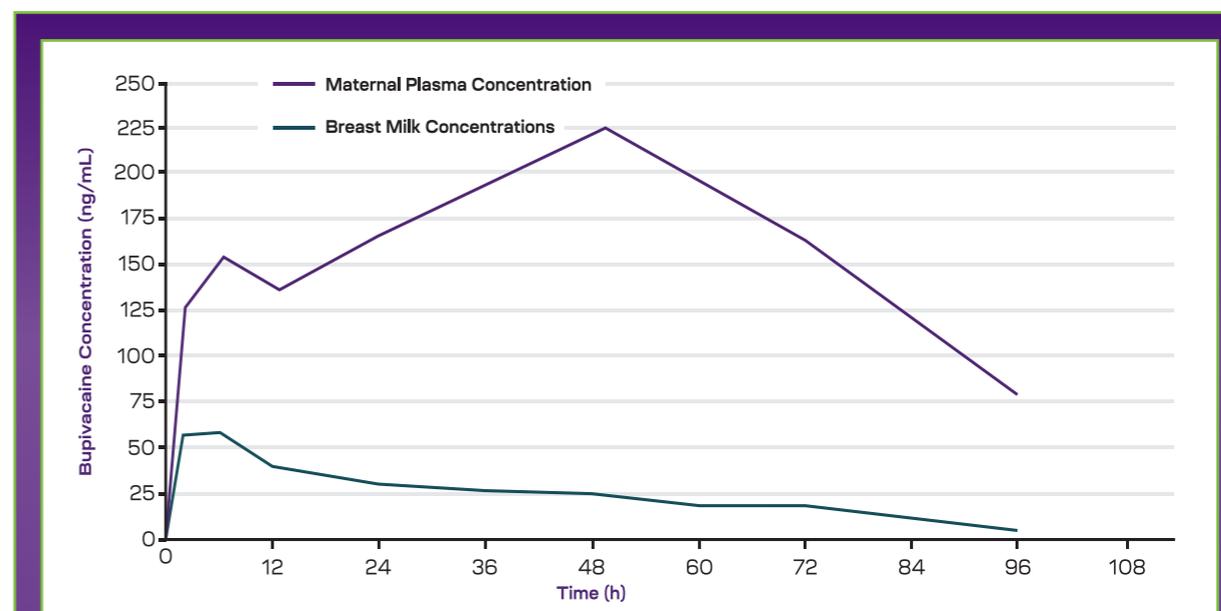
EXPAREL Has a Proven Safety Profile

At both doses of EXPAREL (266 mg and 133 mg), the plasma levels of bupivacaine remain below toxicity thresholds^{10,24,29,30}



EXPAREL Has a Unique Pharmacokinetic Profile

- Pharmacokinetics demonstrate plasma levels of bupivacaine that can persist for 96 hours^{10,24,31,32}
- At all doses studied, plasma bupivacaine levels are maintained well below toxic thresholds^{10,24,31,32}
- 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
- Avoid additional use of local anesthetics within 96 hours
- Systemic plasma levels of bupivacaine following administration of EXPAREL are not correlated with local efficacy



Transfer Into Breast Milk After C-section Supports Safety of EXPAREL³³

- Plasma and milk AUC_{0-t} ratios indicate that very little plasma bupivacaine was transferred into breast milk and bupivacaine did not accumulate in breast milk
- Concentrations of bupivacaine in breast milk peaked at 6 hours, followed by a steady decline to undetectable levels at 96 hours
- Maternal plasma concentrations had 2 peaks, first at 6 hours and then at 48 hours, followed by a steady decline
- A relative neonatal dose <10% of the maternal dose is considered acceptable —At all time intervals, the relative neonatal dosage was <1%

ISBPNB=interscalene brachial plexus nerve block; CNS=central nervous system.

Important Safety Information (continued)

Warnings and Precautions for Bupivacaine-Containing Products

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 or call 1-855-793-9727.

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

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 Bariatric Sleeve gastrectomy Roux-en-Y gastric bypass	 Orthopedic TKA, THA, ACL	 Urologic Nephrectomy
 Breast Mastectomy, reconstruction	 Obstetric/Gynecologic Hysterectomy, myomectomy, cesarean delivery	 Shoulder Total shoulder arthroplasty, rotator cuff repair
 Colorectal/General Colectomy, hernia	 Oral/Maxillofacial Third-molar extraction, temporomandibular joint, orthognathic	 Spine Percutaneous lumbar fusion, awake TLIF

EXPAREL is reimbursed for procedures performed in ASCs using code C9290 and for dental procedures using code D9613.*



THA=total hip arthroplasty; ACL=anterior cruciate ligament; TLIF=transforaminal lumbar interbody fusion; ASC=ambulatory surgery center.
*Pricing subject to Centers for Medicare and Medicaid Services updates.

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.

Please refer to the full Prescribing Information for complete Dosage and Administration information before using EXPAREL.

EXPAREL Key Dosing Considerations

EXPAREL is available in 2 single-dose vials: 266 mg (20 mL) and 133 mg (10 mL)

For local infiltration and field blocks

Up to a maximum dose of 266 mg (20 mL), 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
- **For infiltration and field blocks in larger procedures**, such as abdominal, colorectal, general, breast, gynecologic, orthopedic, and spine, the 266 mg (20 mL) dose is appropriate
- **When infiltrating small surgical sites**, such as hand/foot, facial, plastic, and oral/maxillofacial, the 133 mg (10 mL) dose can be used

For interscalene brachial plexus nerve blocks

The approved dose is 133 mg (10 mL) and is based on a study of patients undergoing either total shoulder arthroplasty or rotator cuff repair.

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
- RCR/TSA



The 266 mg (20 mL) dose is appropriate for procedures such as*:

- Abdominal/Colorectal/General
- Breast
- Gynecologic
- Orthopedic
- Spine

RCR=rotator cuff repair.

*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.

Important Safety Information (continued)

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.

Please refer to the full Prescribing Information for complete Dosage and Administration information before using EXPAREL.

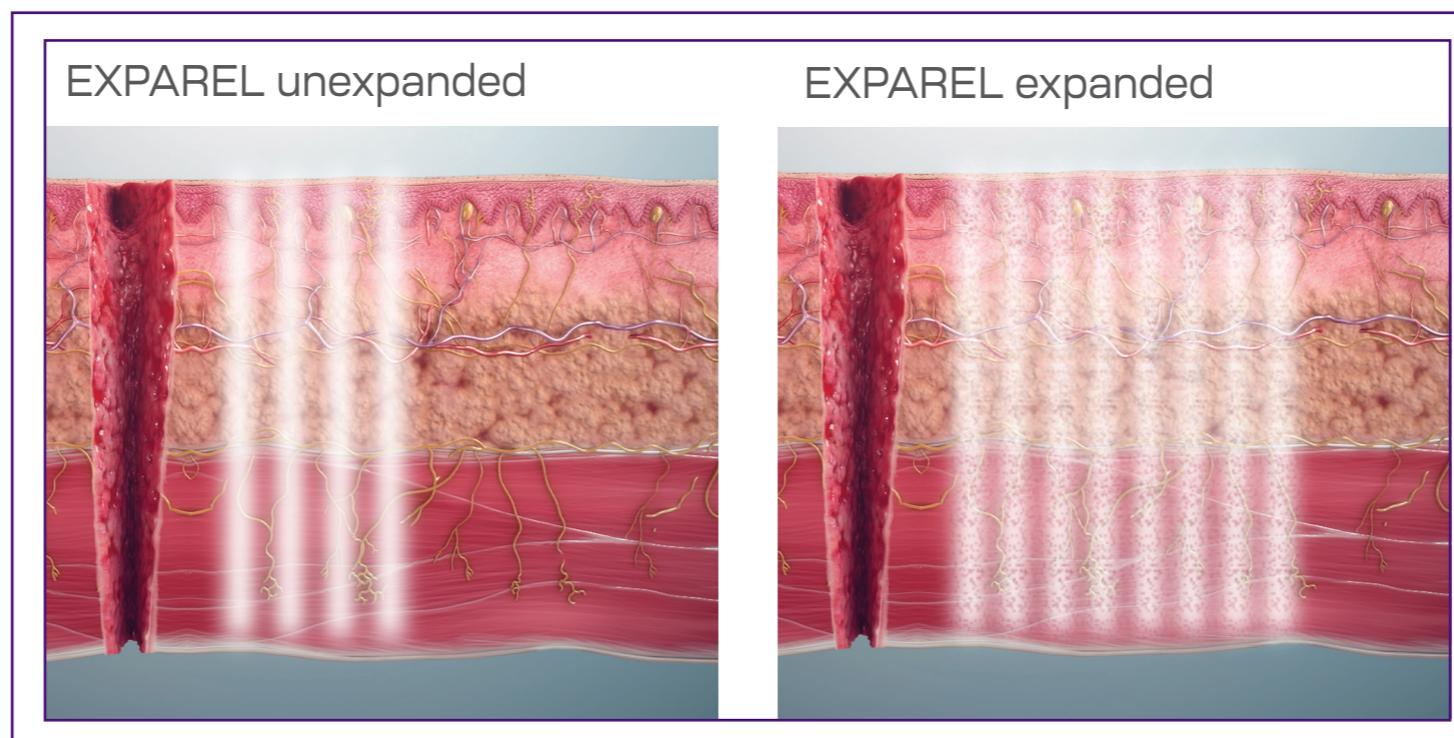
How to Administer EXPAREL for Optimal Analgesia: EXPAREL Can Be Expanded to Ensure Pain Receptor Coverage

EXPAREL 266 mg (20 mL) can be expanded up to 300 mL for large sites

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

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 for long-lasting analgesia



Important Safety Information (*continued*)

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.

Please refer to the full Prescribing Information for complete Dosage and Administration information before using EXPAREL.

How to Administer EXPAREL for Optimal Analgesia: Infiltration Technique

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

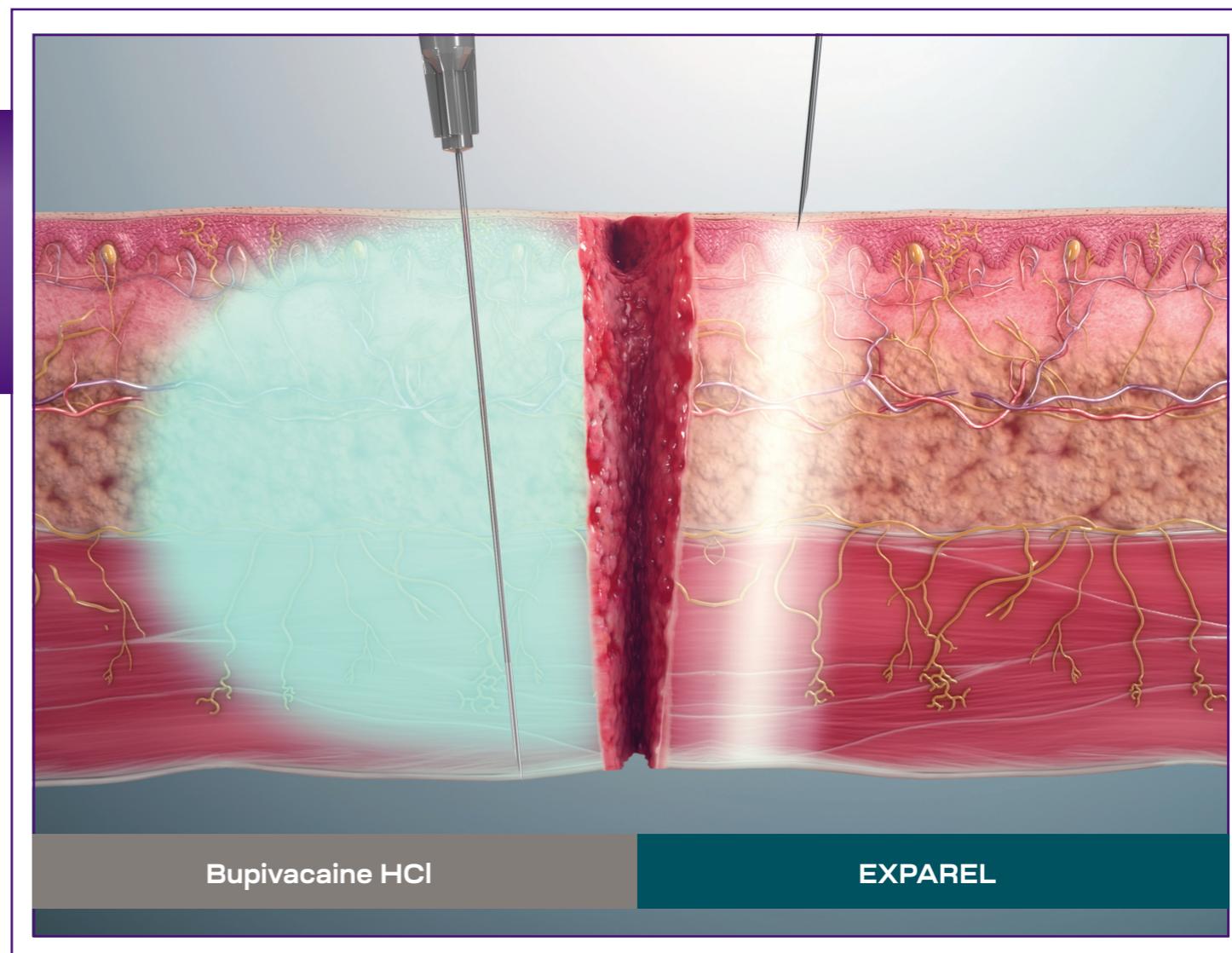
When infiltrating, use a frequent and consistent injection technique throughout the surgical site

Bupivacaine is an aqueous solution

- Readily diffuses into surrounding tissue throughout the 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



Important Safety Information (*continued*)

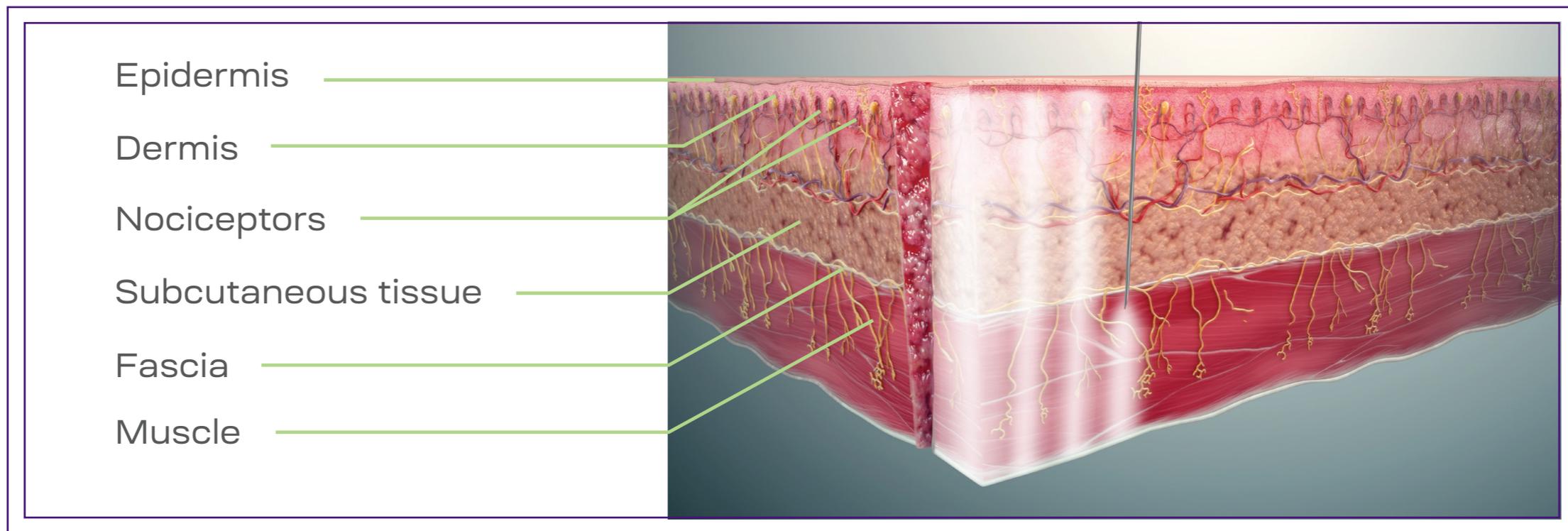
Warnings and Precautions Specific to EXPAREL

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.

How to Administer EXPAREL for Optimal Analgesia: Infiltration Technique (*continued*)

Infiltrate into all tissue layers to ensure complete analgesic coverage

- Inject EXPAREL slowly and deeply (generally 1 mL to 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 cm to 1.5 cm apart)

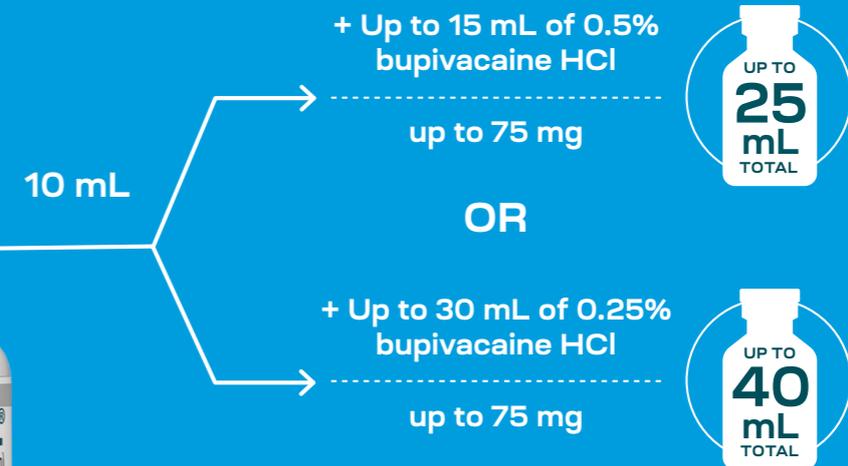
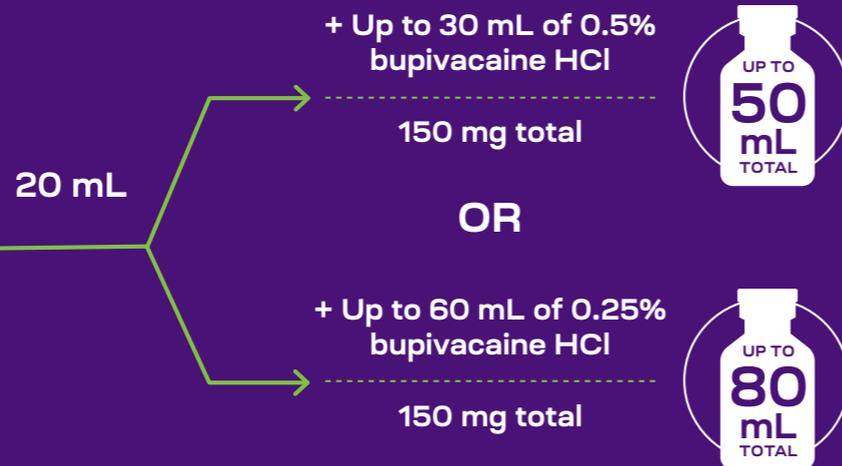


EXPAREL is a local anesthetic that produces postsurgical analgesia. It is administered via single-dose infiltration. When infiltrated into the surgical site, it produces local analgesia. It may also be infiltrated in the fascial plane to produce regional analgesia as a regional field block. Regional anesthetic techniques to produce regional analgesia include, but are not limited to, transversus abdominis plane (TAP) block, pectoralis (PEC) and serratus anterior plane (SAP) blocks, erector spinae plane (ESP) block, thoraco-lumbar interfascial plane (TLIP) block, interspace between the popliteal artery and capsule of the posterior knee (iPACK), and quadratus lumborum (QL) block. EXPAREL may also be administered as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia in total shoulder arthroplasty (TSA) and rotator cuff repair (RCR) procedures.

How to Administer EXPAREL for Optimal Analgesia: Admixing

To ensure early analgesic onset, bupivacaine HCl can be administered immediately before EXPAREL or admixed as part of the total expanded volume

- Admixing may impact the pharmacokinetic/pharmacodynamic properties of EXPAREL; this is concentration dependent
- Ensure ratio of milligram dose of bupivacaine HCl to EXPAREL does not exceed 1:2
- One 20 mL vial contains 266 mg of EXPAREL, which is a molar equivalent to 300 mg of bupivacaine HCl
 - 1:2 ratio allows 150 mg of bupivacaine HCl to 266 mg of EXPAREL
- One 10 mL vial contains 133 mg of EXPAREL, which is a molar equivalent to 150 mg of bupivacaine HCl
 - 1:2 ratio allows 75 mg of bupivacaine HCl to 133 mg of EXPAREL



EXPAREL is a local anesthetic that produces postsurgical analgesia. It is administered via single-dose infiltration. When infiltrated into the surgical site, it produces local analgesia. It may also be infiltrated in the fascial plane to produce regional analgesia as a regional field block. Regional anesthetic techniques to produce regional analgesia include, but are not limited to, transversus abdominis plane (TAP) block, pectoralis (PEC) and serratus anterior plane (SAP) blocks, erector spinae plane (ESP) block, thoraco-lumbar interfascial plane (TLIP) block, interspace between the popliteal artery and capsule of the posterior knee (iPACK), and quadratus lumborum (QL) block. EXPAREL may also be administered as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia in total shoulder arthroplasty (TSA) and rotator cuff repair (RCR) procedures.

How to Administer EXPAREL for Optimal Analgesia: Additional Considerations and Recommendations



Compatibility considerations with EXPAREL:

- EXPAREL should not be admixed with local anesthetics other than bupivacaine prior to administration
- Wait 20 minutes after administering lidocaine or other non-bupivacaine-based local anesthetics before administering EXPAREL into the same surgical site
- Allow topical antiseptics to dry before administering EXPAREL into the same surgical site
- Do not dilute EXPAREL with water for injection or other hypotonic agents as it will result in disruption of the liposomal particles



Storage and handling recommendations for EXPAREL:

- The 133 mg (10 mL) and 266 mg (20 mL) single-dose vials of EXPAREL are available in cartons of 4 and 10 vials
- 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. Vials should not be re-refrigerated
- EXPAREL should not be frozen or exposed to high temperatures (>40°C or 104°F) for an extended period
- Do not administer EXPAREL if it is suspected of having been frozen or exposed to high temperatures. Vials should be visually inspected before use. Do not use the vial if the stopper is bulging
- Open vials of EXPAREL should be used within 4 hours
- Invert vials of EXPAREL multiple times to resuspend the particles immediately prior to withdrawal from the vial
- If pouring EXPAREL into a basin prior to use, stir the suspension in the basin prior to drawing up into the syringe

Important Safety Information (*continued*)

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.

BUILT TO WEATHER POSTSURGICAL PAIN

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Non-opioid EXPAREL, powered by DepoFoam[®] technology, delivers precise pain control for the critical first few days after surgery to enable enhanced recovery.^{6,26}

Use EXPAREL Confidently Across Surgical Procedures

- Long-lasting, significant pain control²⁴⁻²⁸
- Proven opioid reduction^{*24-28}
- Proven safety and tolerability profile^{10,24,31,32}

More than 7 million patients have received non-opioid EXPAREL since 2012³⁴

To learn more about reimbursement for EXPAREL, contact our dedicated reimbursement specialists at reimbursement@pacira.com or call our Reimbursement Helpline at 1-855-793-9727.



Discover more at:
www.EXPAREL.com

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

Important Safety Information (*continued*)

Warnings and Precautions for Bupivacaine-Containing Products

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.

Please refer to the full Prescribing Information for complete Dosage and Administration information before using EXPAREL.

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Important Safety Information (continued)

Warnings and Precautions for Bupivacaine-Containing Products

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 or call 1-855-793-9727.

Indication and Important Safety 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.

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

**NON-OPIOID
EXPAREL®**
(bupivacaine liposome injectable suspension)

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