# Frequently asked questions

Find information on the efficacy and safety of EXPAREL, including results from the Infiltration Trial in Third Molar Extraction Observing the Analgesic Effect of EXPAREL (INNOVATE) trial in oral surgery, as well as guidance on administration.

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What is EXPAREL?</strong></td>
<td><strong>Answer</strong></td>
</tr>
<tr>
<td>Has EXPAREL been studied in oral surgery?</td>
<td><strong>Answer</strong></td>
</tr>
<tr>
<td>Which oral surgery procedures are appropriate for EXPAREL?</td>
<td><strong>Answer</strong></td>
</tr>
<tr>
<td>How is EXPAREL administered?</td>
<td><strong>Answer</strong></td>
</tr>
<tr>
<td>Can I split a vial of EXPAREL?</td>
<td><strong>Answer</strong></td>
</tr>
<tr>
<td>Can I use bupivacaine with EXPAREL?</td>
<td><strong>Answer</strong></td>
</tr>
<tr>
<td>How much bupivacaine is available to the body immediately?</td>
<td><strong>Answer</strong></td>
</tr>
<tr>
<td>Are there potential concerns with toxicity when administering EXPAREL with bupivacaine HCl?</td>
<td><strong>Answer</strong></td>
</tr>
<tr>
<td>Is EXPAREL available in a cartridge?</td>
<td><strong>Answer</strong></td>
</tr>
<tr>
<td>How much volume is appropriate?</td>
<td><strong>Answer</strong></td>
</tr>
<tr>
<td>How is EXPAREL covered?</td>
<td><strong>Answer</strong></td>
</tr>
<tr>
<td>Where is EXPAREL infiltrated?</td>
<td><strong>Answer</strong></td>
</tr>
</tbody>
</table>

Please refer to Important Safety Information on page 12. For more information, please visit [www.EXPAREL.com](http://www.EXPAREL.com) or call 1-855-RX-EXPAREL (793-9727).
What is EXPAREL?

EXPAREL is an FDA-approved, long-lasting, non-opioid analgesic that, as part of a multimodal approach to pain management, provides effective postsurgical pain relief and helps reduce the need for opioids after surgery.\(^1,2\) 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. EXPAREL works locally at the surgical site and uses the DepoFoam\(^\circledR\) drug delivery technology, which encapsulates bupivacaine in multivesicular liposomes. Following injection, DepoFoam particles gradually release bupivacaine over time as the lipid membranes are absorbed, prolonging the duration of action of bupivacaine.\(^3,4\) More than 4.5 million patients have received EXPAREL since 2012.\(^5\)

**EXPAREL has a robust clinical trial program**

In multiple clinical trials, EXPAREL demonstrated significant, long-lasting pain control while reducing opioid use.\(^*\)

**Study 1:** A phase 3, multicenter, parallel-group, placebo-controlled, randomized, double-blind study comparing EXPAREL vs placebo for the management of postsurgical pain following bunionectomy.\(^6\)

- A **14.7% reduction** in cumulative pain scores was demonstrated \((P=0.0005)\)
- A **19.1% reduction** was shown in overall opioid consumption \((P=0.0077)\)
  - A significant delay in time to first opioid rescue was also demonstrated \((7.2 \text{ vs } 4.3 \text{ hours}; P<0.0001)\)

**Study 2:** A phase 3, multicenter, parallel-group, randomized, double-blind study comparing EXPAREL vs placebo for postsurgical pain relief in patients undergoing hemorrhoidectomy.\(^1\)

- A **30% reduction** in cumulative pain scores was achieved \((P<0.0001)\)
- A **45.7% reduction** was shown in overall opioid consumption \((P<0.0006)\)\(^1,7\)
  - In the EXPAREL group, 28% of patients did not require rescue medication vs 10% of patients in the placebo group \((P<0.0008)\)
  - A significant 13-hour difference in median time to first opioid rescue between treatment groups was also demonstrated

\(^*\)The clinical benefit of the decrease in opioid consumption was not demonstrated in the pivotal trials.
What is EXPAREL? (continued)

Study 3: A phase 3, multicenter, randomized, double-blind study comparing EXPAREL vs placebo for brachial plexus nerve block following total shoulder arthroplasty (TSA) or rotator cuff repair (RCR).  
- A 46% reduction in mean AUC and VAS pain intensity was achieved ($P<0.0001$)  
- A 77% reduction was shown in postsurgical opioid consumption ($P<0.0001$)  
  - EXPAREL also increased the portion of patients who were opioid free (9 patients vs 1 patient; $P=0.008$)  
  - Median time to first opioid rescue was significantly prolonged (4.2 vs 0.6 hours; $P<0.0001$)

Phase 4 clinical study—PILLAR: A parallel-group, randomized, double-blind, active-controlled study comparing local infiltration analgesia (LIA) with EXPAREL vs LIA with bupivacaine HCl in patients undergoing total knee arthroplasty (TKA).  
- A 13.6% reduction in mean AUC and VAS pain intensity (180.8 vs 209.3; $P=0.0381$) was demonstrated  
- A 77.9% reduction was shown in postsurgical opioid consumption (18.7 mg vs 84.9 mg; $P=0.0048$)  
- Time to first opioid rescue ranged from 0.25 to 48 hours with EXPAREL vs 0.27 to 33 hours without EXPAREL  
  - Time to rescue of 50% of patients was 4.1 and 2.9 hours, respectively, with a significant difference between the survival curves ($P=0.0230$)

EXPAREL significantly increased the proportion of opioid-free patients and significantly delayed time to first opioid rescue compared with placebo. The percentage of opioid-free patients through 48 and 72 hours (or discharge) was significantly greater ($P<0.01$) with EXPAREL compared with placebo.

Has EXPAREL been studied in oral surgery?

The safety, efficacy, and pharmacokinetics of EXPAREL were evaluated in a multicenter, phase 4, randomized, double-blind, placebo-controlled study of local administration of EXPAREL for prolonged postsurgical analgesia in patients undergoing bilateral third-molar extraction. EXPAREL was shown to be safe in the safety population (EXPAREL, n=105; placebo, n=57).

Back to questions
Which oral surgery procedures are appropriate for EXPAREL?

In December 2015, the FDA confirmed that EXPAREL has a broad indication for infiltration into the surgical site to produce postsurgical analgesia. The indication encompasses use for postsurgical analgesia when administered as local infiltration at the site of oral surgery procedures, including tooth extraction. The indication also includes use as a local anesthetic deposited near a terminal branch of the maxillary or mandibular branch of the trigeminal nerve (periapical injections). EXPAREL is also indicated as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia. Safety and efficacy have not been established in other nerve blocks.

For more information on the reaffirmation of the broad indication for EXPAREL by the FDA, learn more at [www.pacira.com](http://www.pacira.com).

How is EXPAREL administered?

EXPAREL should be injected with a 25-gauge or a larger bore needle. It is best administered using a frequent and consistent injection technique throughout the surgical site. EXPAREL readily diffuses into surrounding tissues and spreads throughout the site. It requires fewer injections for adequate pain-receptor coverage.

For more details on administration and injection into the maxilla and mandible, see this [case report](http://www.pacira.com) in which EXPAREL was used in a third-molar extraction.

Can I split a vial of EXPAREL?

EXPAREL is intended for single-dose administration only and is available in single-use vials for infiltration. A vial of EXPAREL should not be used for more than one patient.
Can I use bupivacaine with EXPAREL?

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. See Administering EXPAREL for more information.

Back to questions

How much bupivacaine is available to the body immediately?

EXPAREL contains a small amount of extra-liposomal bupivacaine (about 3%), with 150 ng/mL available in the plasma serum soon after administration.¹¹

**Plasma levels of bupivacaine released from EXPAREL over 96 hours**¹²

![Graph showing plasma levels of bupivacaine over time](chart.png)

*Data from a total knee arthroplasty study.

Systemic plasma levels of bupivacaine following administration of EXPAREL are not correlated with local efficacy.

Back to questions
Are there potential concerns with toxicity when administering EXPAREL with bupivacaine HCl?

Please note that the rate of systemic absorption of bupivacaine is dependent on total dose, the route of administration, and the vascularity of the administration site. Also, the toxic effects of these drugs are additive and their administration should be used with caution, including monitoring for neurologic and cardiovascular effects related to local anesthetic systemic toxicity. Please see the full Prescribing Information for more details.

Is EXPAREL available in cartridge?

No. EXPAREL is only available in 133 mg/10 mL and 266 mg/20 mL single-use vials.

How much volume is appropriate?

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 of 266 mg (20 mL)

Volume may be expanded to accommodate larger surgical sites. A 20 mL vial of EXPAREL can be administered unexpanded or expanded up to a total of 300 mL with normal (0.9%) saline or lactated Ringer’s solution.

Proper injection technique of EXPAREL is critical to ensure optimal delivery for your patients. EXPAREL is intended for single-dose administration only.

Different formulations of bupivacaine are not bioequivalent, even if the milligram strength is the same; therefore, it is not possible to convert dosing from any other formulations of bupivacaine to EXPAREL.

EXPAREL should be injected slowly and deeply (generally 1-2 mL per injection) into soft tissues using a moving needle technique, which involves injecting while simultaneously withdrawing the needle.

Please refer to Important Safety Information on page 12. For more information, please visit www.EXPAREL.com or call 1-855-RX-EXPAREL (793-9727).
How is EXPAREL covered?

It is important to inform patients that EXPAREL may not be covered by insurance or that coverage may be limited.

Beginning January 1, 2019, oral surgeons can use D9613 for the following*:

- Infiltration of a sustained-release therapeutic drug—single or multiple sites
- Infiltration of a sustained-release pharmacologic agent for long-acting surgical site pain control (not for local anesthesia purposes)

*Actual coverage will vary based on each individual’s insurance plan.

Back to questions

Where is EXPAREL infiltrated?

Infiltration with EXPAREL following an infiltration of 2% lidocaine with 1:100,000 epinephrine into the buccal aspect and into the palatal aspect:

1. A total of 4 mL of EXPAREL infiltrated along the lateral aspect of the mandible bilaterally as 4 separate 0.5-mL injections to ensure maximum analgesic coverage

2. 1 mL of EXPAREL infiltrated into the buccal aspect of the upper third molars bilaterally

Back to questions
**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 the full Prescribing Information.

References


