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 refer to the accompanying full Prescribing Information.
PILLAR
STUDY DESIGN¹
(NCT02713490)

16 study sites in the United States enrolled 139 patients

All patients were required to stay in the hospital for 48 hours post-op to capture all data required to assess primary endpoints

All surgeons were trained on and required to follow a standard infiltration technique and protocol as described in the published administration protocol for TKAs

RANDOMIZATION 1:1

139 adult patients underwent a primary unilateral TKA

EXPAREL
Local infiltration with:
266 mg/20 mL EXPAREL
+ 20 mL 0.5% bupivacaine HCl
+ 80 mL saline
= 120 mL TOTAL volume

CONTROL GROUP
Local infiltration with:
20 mL 0.5% bupivacaine HCl
+ 100 mL saline
= 120 mL TOTAL volume

PHASE IV
Double-blind

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.

Important Safety Information

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.

Please see Important Safety Information and accompanying full Prescribing Information.

Area under the curve (AUC) of visual analog scale (VAS) pain intensity scores 12 to 48 hours post-op

Total opioid consumption 0 to 48 hours post-op

AUC VAS pain scores through 72 hours

Opioid consumption through 72 hours

% of patients opioid free through 72 hours

Time to first opioid rescue through 72 hours
RESULTS

EXPAREL® (bupivacaine liposome injectable suspension) compared with bupivacaine HCl

**TOTAL OPIOID CONSUMPTION**

0 to 48 hours

<table>
<thead>
<tr>
<th></th>
<th>EXPAREL</th>
<th>Bupivacaine HCl</th>
</tr>
</thead>
<tbody>
<tr>
<td>%FEWER OPIOIDS</td>
<td>78%</td>
<td>78%</td>
</tr>
<tr>
<td>P</td>
<td>0.0048</td>
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</table>

**PAIN INTENSITY SCORES**

AUC of VAS pain intensity scores

12 to 48 hours

<table>
<thead>
<tr>
<th></th>
<th>EXPAREL</th>
<th>Bupivacaine HCl</th>
</tr>
</thead>
<tbody>
<tr>
<td>%LESS PAIN</td>
<td>13.6%</td>
<td>13.6%</td>
</tr>
<tr>
<td>P</td>
<td>0.0381</td>
<td></td>
</tr>
</tbody>
</table>

**FEWER OPIOIDS**

in EXPAREL group*

**LESS PAIN**

in EXPAREL group

of patients in the EXPAREL group were opioid free through the first 72 hours following surgery compared with 0% of patients who received bupivacaine HCl alone

(\(P=0.01\))

Rates and types of adverse events were similar between treatment groups. The most common adverse events in the EXPAREL group were nausea, muscle spasms, and vomiting.

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

**POSTOPERATIVE MEDICATIONS AIDED OPIOID MINIMIZATION IN THE PILLAR STUDY**

**PREOPERATIVE & POSTOPERATIVE MEDICATIONS AIDED OPIOID MINIMIZATION IN THE PILLAR STUDY**

**Important Safety Information, continued**

**Warnings and Precautions for Bupivacaine-Containing Products, continued**

**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.

Important Safety Information, continued
The PILLAR protocol highlights an appropriate infiltration technique, optimal targeting of tissue sites, and adequate volume expansion in TKA. 

PILLAR PROTOCOL AND TECHNIQUE

Preoperative
- Patients receive acetaminophen (e.g., TYLENOL®) 1000 mg + celecoxib 200 mg + pregabalin 300 mg and IV tranexamic acid 1 g within 4 hours of surgery

Intraoperative
- **20 mL** EXPAREL Bupivacaine HCl 0.5% + **20 mL** EXPAREL Bupivacaine HCl 0.5% + **80 mL** Normal Saline = **120 mL** Total

Postoperative
- Patients receive oral acetaminophen (e.g., TYLENOL®) 975 to 1000 mg as needed every 8 hours + celecoxib 200 mg as needed every 12 hours until discharge
- All participants have access to rescue opioids as needed, including oral oxycodone ≤10 mg every 4 hours or IV morphine every 4 hours

To achieve optimal analgesia, it is suggested to administer EXPAREL using:

- **Consistent volume** (120 mL) mixed with free bupivacaine HCl
- **Consistent infiltration** protocol at anatomical sites with high nerve density
- **Consistent infiltration** technique (1 to 1.5 mL volume spaced 1 to 1.5 cm apart)
- **Opioid-minimizing** multimodal pain management protocol following surgery

Prior to Cementation
- **Syringe #1**
  - Posterior capsule (8-10 sticks medial and 8-10 sticks lateral)
- **Syringe #2**
  - Femur – medial and lateral periosteum, posterior periosteum, suprapatellar/quadriceps tendon
- **Syringe #3**
  - Tibia – fat pad (5 sticks)
  - Pes anserinus, medial collateral ligament, and gutter (15 sticks)
- **Syringe #4**
  - Circumferential periosteum (15-20 sticks)

After Cementation
- **Syringe #5**
  - Midline quadriceps tendon (10 sticks)
  - Retinaculum, medial gutter, femoral to tibial (10 sticks)
- **Syringe #6**
  - Lateral gutter, femoral to tibial (10 sticks)
  - Subcutaneous/closure (10 sticks)

EXPAREL® (bupivacaine liposome injectable suspension) DEMONSTRATED

- **78% reduced opioid consumption**
- **13.6% lower pain intensity scores**
- **10% of patients opioid-free through 72 hours**

Demonstrated in Phase IV TKA PILLAR Clinical Trial compared to bupivacaine HCl

Long-lasting pain control

Broad indication for infiltration

Unique multivesicular formulation
Important Safety Information

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Warnings and Precautions Specific to EXPAREL

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Warnings and Precautions for Bupivacaine-Containing Products

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Please refer to accompanying full Prescribing Information.

References


Please contact your DePuy Synthes Sales Consultant for more information.

For complete information related to EXPAREL, call 1-855-RX-EXPAREL (793-9729) or visit www.EXPAREL.com.

NON-OPIOID EXPAREL® (bupivacaine liposome injectable suspension)