THE OBJECTIVE OF THE PILLAR STUDY WAS TO ASSESS THE SAFETY & EFFICACY of EXPAREL vs bupivacaine HCl in Total Knee Arthroplasty using STANDARDIZED volume, technique, and protocol in both the study and control groups.

EXPAREL is indicated for administration into the surgical site to produce postsurgical analgesia.

Please refer to the accompanying full Prescribing Information.
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

**PRIMARY ENDPOINTS**

- 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

**SECONDARY ENDPOINTS**

- 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

**Important Safety Information Continued**

- In clinical trials, the most common adverse reactions (incidence 10%) following EXPAREL administration were nausea, constipation, and vomiting
- 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. Patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally, are at a greater risk of developing toxic plasma concentrations

**Warnings and Precautions Specific to EXPAREL**

- EXPAREL is not recommended for the following types or routes of administration: epidural, intrathecal, regional nerveblocks, or intravascular or intra-articular use
- Non-bupivacaine-based local anesthetics, including lidocaine, may cause an immediate release of bupivacaine from EXPAREL if administered together locally. The administration of EXPAREL may follow the administration of lidocaine after a delay of 20 minutes or more. Formulations of bupivacaine other than EXPAREL should not be administered within 96 hours following administration of EXPAREL
Using the PILLAR protocol and administration technique, surgeons were able to achieve consistently favorable outcomes\(^1\)

**RESULTS**\(^1\)

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

### Scheduled preoperative medications:
- Oral acetaminophen 1000 mg
- Oral celecoxib 200 mg
- Oral pregabalin 300 mg
- IV tranexamic acid 1 g

**EXPAREL®**
(bupivacaine liposome injectable suspension)
266 mg/20 mL
+ 20 mL 0.5% bupivacaine HCl
+ 80 mL saline

**Bupivacaine HCl**
20 mL 0.5%
bupivacaine HCl
+ 100 mL saline

### Rescue opioids permitted for breakthrough pain postoperatively, including:
- Oral oxycodone <10 mg every 4 hours as needed
- IV morphine 2.5 to 5.0 mg every 4 hours as needed
- Hydromorphone 0.5 to 1.0 mg every 4 hours as needed

**TOTAL OPIOID CONSUMPTION**
0 to 48 hours

78%
P\(=0.0048\)

**PAIN INTENSITY SCORES**
AUC of VAS pain intensity scores
12 to 48 hours

13.6%
P\(=0.0381\)

**FEWER OPIOIDS**
in EXPAREL group

**LESS PAIN**
in EXPAREL group

### 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 paresthesias. 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
- EXPAREL is contraindicated in obstetrical paracervical block anesthesia

10% of patients in the EXPAREL group were opioids free
(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.

### Important Safety Information Continued

**Warnings and Precautions for Bupivacaine-Containing Products Continued**
- In clinical trials, the most common adverse reactions (incidence 10%) following EXPAREL administration were nausea, constipation, and vomiting

Please see full Important Safety Information and accompanying full Prescribing Information.
The PILLAR protocol highlights an appropriate infiltration technique, optimal targeting of tissue sites, and adequate volume expansion in TKA\(^1\)

**PILLAR PROTOCOL AND TECHNIQUE\(^1\)**

**Preoperative**
- Patients receive oral acetaminophen 1000 mg + celecoxib 200 mg + pregabalin 300 mg and IV tranexamic acid 1 g within 4 hours of surgery

**Intraoperative:**

\[
\begin{align*}
20 \text{ mL} & \quad + \quad 20 \text{ mL} & \quad + \quad 80 \text{ mL} & \quad = \quad 120 \text{ mL}
\end{align*}
\]

**EXPAREL** Bupivacaine HCl 0.5% Normal Saline Total

**Postoperative:**
- Patients receive oral acetaminophen 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\(^1\)
- **Consistent infiltration** protocol at anatomical sites with high nerve density\(^1\)
- **Consistent infiltration** technique (1 to 1.5 mL volume spaced 1 to 1.5 cm apart)\(^1\)
- **Opioid-minimizing** multimodal pain management protocol following surgery\(^1\)

**EXPAREL\(^\circledR\)** (bupivacaine liposome injectable suspension) PROVIDES

- 78% reduced opioid consumption\(^1\)
- 13.6% lower pain intensity scores\(^1\)
- 10% of patients opioid-free at 72 hours\(^1\)
- Long-lasting pain control\(^2\)
- Broad indication for use
- Unique multivesicular formulation

**Prior to Cementsation**
- Syringe #1
  - Posterior capsule (8-10 sticks medial and 8-10 sticks lateral)
  - 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, ligament, and gutter (15 sticks)
- Syringe #4
  - Circumferential periosteum (15-20 sticks)

**After Cementsation**
- 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)

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

Please see full Important Safety Information and accompanying full Prescribing Information.
EXPAREL® (bupivacaine liposome injectable suspension)

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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.