EXPAREL Achieves Statistically Significant Reductions in Opioid Consumption and Pain Scores in Cesarean Section Patients

January 16, 2019

Targeted TAP block with EXPAREL superior to TAP block with bupivacaine HCl

PARSIPPANY, N.J., Jan. 16, 2019 (GLOBE NEWSWIRE) -- Pacira Pharmaceuticals, Inc. (NASDAQ:PCRX) today announced that its Phase 4 study of EXPAREL® (bupivacaine liposome injectable suspension) in patients undergoing Cesarean section (C-section) achieved its primary endpoint with a statistically significant reduction in total postsurgical opioid consumption through 72 hours ($P \leq 0.05$). EXPAREL also achieved statistical significance for reduction in pain intensity scores through 72 hours ($P \leq 0.05$). The full study results will be submitted for publication in the peer-reviewed medical literature later this year.

Importantly, the study also achieved statistical significance ($P \leq 0.05$) for relevant additional endpoints pre-specified in the statistical analysis plan to better characterize the clinical benefit of the opioid reduction, including:

- **Total opioid consumption at one and two weeks** following C-section
- **Percentage of opioid-spared patients**, a composite endpoint, which was defined as patients who took no more than one oxycodone 10 mg tablet (or equivalent) and graded their bother or stress from the following opioid-related adverse events as “not at all”: vomiting, itching, sweating, freezing, or dizziness

“Research shows that inadequately managed postsurgical pain can interfere with a new mother’s ability to care for herself and her infant, and that those mothers experiencing severe pain following cesarean delivery are at increased risk for persistent pain, persistent opioid use, and postpartum depression,” said Ashraf Habib, MD, Chief, Division of Women’s Anesthesia and Professor of Anesthesiology at Duke University and investigator in the study. “TAP blocks have become an increasingly integral part of anesthesiologists’ armamentarium of opioid-sparing pain management approaches, and this study demonstrates that, when added to the standard of care, an EXPAREL TAP block provides a superior long-acting field block that not only adequately controlled patients’ pain following C-section, but also greatly reduced their need for opioids.”

This was a multicenter, randomized, double-blind study including a total of 13 sites and 186 patients. Patients undergoing elective C-section and given spinal anesthesia were randomized to receive EXPAREL or the active comparator bupivacaine HCl. Patients in the EXPAREL arm were administered a transversus abdominis plane (TAP) field block with 10 mL EXPAREL admixed with 10 mL 0.25% bupivacaine HCl and 10 mL normal sterile saline injected bilaterally (for a total volume of 60 mL). Patients in the active comparator arm received a TAP field block with 10 mL 0.25% bupivacaine HCl admixed with 20 mL normal sterile saline injected bilaterally (for a total volume of 60 mL).

In accordance with current medical practice, prior to C-section all patients in this study received an intrathecal injection of 150 mcg preservative-free morphine for spinal injection in conjunction with single-shot spinal anesthesia using 1.4-1.6 mL bupivacaine HCl 0.75% and 15 mcg fentanyl. Following C-section, patients also received 15 mg of intravenous (IV) ketorolac, 1000 mg of IV acetaminophen at the time of skin incision closure, and oral acetaminophen and ibuprofen beginning 6 hours after skin incision closure for up to 72 hours following surgery. Rescue medication was available upon request and postsurgical opioid consumption through 72 hours was collected. Pain intensity was measured using visual analog scale (VAS) pain intensity scores at rest from 6 to 72 hours.

As a follow-on to this study, Pacira will soon begin enrollment in CHOICE, its next-generation C-section trial designed to be completely opioid-free in the EXPAREL arm, including opioid-free spinal anesthesia.

“Effective postsurgical pain control is a critical element in patient recovery following surgery, especially for new mothers who often experience significant pain in the first few days following C-section,” said Richard Scranton, MD, chief medical officer of Pacira. “This study provides clinical evidence that an EXPAREL-based multimodal regimen significantly reduces the need for opioids versus current multimodal approaches that combine bupivacaine, acetaminophen and an NSAID. We look forward to continuing to advance our opioid-free CHOICE study, which we believe will help transform the standard of pain management for Cesarean section patients.”

About Pacira

Pacira Pharmaceuticals, Inc. (NASDAQ: PCRX) is a specialty pharmaceutical company dedicated to advancing and improving postsurgical outcomes for acute care practitioners and their patients. The company’s flagship product, EXPAREL ® (bupivacaine liposome injectable suspension) was commercially launched in the United States in April 2012. EXPAREL utilizes DepoFoam®, a unique and proprietary product delivery technology that encapsulates drugs without altering their molecular structure, and releases them over a desired period of time. To learn more about Pacira, including the corporate mission to reduce overreliance on opioids, visit www.pacira.com.

About EXPAREL®

EXPAREL (bupivacaine liposome injectable suspension) 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. The product combines bupivacaine with DepoFoam®, a proven product delivery technology that delivers medication over a desired time period. EXPAREL represents the first and only multivesicular liposome local anesthetic that can be utilized in the peri- or postsurgical setting. By utilizing the DepoFoam platform, a single dose of EXPAREL delivers bupivacaine over time, providing significant reductions in cumulative pain scores with up to a 78 percent decrease in opioid consumption; the clinical benefit of the opioid reduction was not demonstrated. Additional information is available at www.EXPAREL.com.

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

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