

EXPAREL: a non-opioid approach to postsurgical pain management

Key considerations for health system implementation

INDICATION

EXPAREL® (bupivacaine liposome injectable suspension) is indicated to produce postsurgical local analgesia via infiltration in patients aged 6 years and older and regional analgesia in adults via an interscalene brachial plexus nerve block, sciatic nerve block in the popliteal fossa, and an adductor canal block. 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 in adults with an incidence greater than or equal to 10% following EXPAREL administration via infiltration were nausea, constipation, and vomiting; adverse reactions reported in adults with an incidence greater than or equal to 10% following EXPAREL administration via nerve block were nausea, pyrexia, headache, and constipation

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IMPORTANT SAFETY INFORMATION (cont'd)

- Adverse reactions with an incidence greater than or equal to 10% following EXPAREL administration via infiltration in pediatric patients six to less than 17 years of age were nausea, vomiting, constipation, hypotension, anemia, muscle twitching, vision blurred, pruritus, and tachycardia
- Do not admix lidocaine or other non-bupivacaine local anesthetics with EXPAREL. EXPAREL may be administered at least 20 minutes or more following local administration of lidocaine

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Considerations for multimodal pain management

The negative impact of opioids

Although opioids have a well-established adverse risk profile

UP TO **95%** OF SURGICAL PATIENTS RECEIVE OPIOIDS

This pain management approach may result in poor outcomes and may lead to opioid^{1,2}:

- Dependency
- Misuse
- Persistent use

Almost **1** OUT OF **10** patients



who received postsurgical opioids had potential ORAEs, which were associated with^{3*}:

- Higher hospitalization costs
- Longer LOS
- Increased risk of mortality

Reducing opioid reliance through multimodal therapy



- Opioid-minimizing and multimodal postsurgical pain management strategies may enhance recovery through ERAS protocols⁴⁻⁹:
 - **Reducing** pain, minimizing opioid consumption and ORAEs
 - **Shortening** discharge time for faster recovery
 - **Decreasing** costs through more efficient care delivery
- Opioid-minimizing strategies that improve recovery are supported by a range of professional society guidelines.¹⁰⁻¹⁴

The NOPAIN Act supports non-opioid options such as EXPAREL through increased Medicare reimbursement in the outpatient setting^{15,16}

*Data represent 9.1% of patients. A retrospective, observational cohort study was conducted using administrative, billing, clinical, and medication administration data from two hospitals. Data were collected for all adult patients who were opioid-free at admission, underwent surgery between October 1, 2015, and September 30, 2016, and received postsurgical opioids.³ ERAS, Enhanced Recovery After Surgery; LOS, length of stay; ORAE, opioid-related adverse event; NOPAIN, Non-Opioids Prevent Addiction in the Nation.

IMPORTANT SAFETY INFORMATION (cont'd)

- EXPAREL is not recommended to be used in the following patient populations: patients <6 years old for infiltration, patients younger than 18 years old for nerve blocks, 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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Regional analgesia: targeted pain management

Unlike systemic approaches that impact the entire body, regional approaches such as nerve blocks can deliver effective analgesic results in specific sites of the body

Neuraxial blocks:

Epidural and spinal anesthesia

Frequently used for surgeries of the lower abdomen, pelvis, and lower extremities

Peripheral nerve blocks:

Injection of anesthetic near nerves or muscle planes

Provide targeted pain control in specific parts of the body during surgical procedures

Local infiltration¹⁷:

Injection into surgical wounds

Provide site-specific pain relief when injected directly into the wound at the operating site, with long-acting options



Types of peripheral nerve blocks

Peripheral nerve blocks can be used in a wide range of areas, depending on the needs of the surgical procedure. There are many different types of nerve blocks in this category, including:

- Upper extremity (interscalene, suprascapular, infraclavicular, axillary, intercostobrachial, wrist, and digital nerve)
- Lower extremity (adductor canal, lumbar plexus, femoral nerve block, fascia iliaca, obturator nerve, popliteal, saphenous, ankle, and digital nerve)
- Scalp
- Head and neck (cervical plexus)
- Thoracic nerve (intercostal, paravertebral, interfascial plane)
- Abdominal nerve (transversus abdominis plane, subcostal, rectus, ilioinguinal and iliohypogastric, transversalis fascia plane, and quadratus lumborum)
- Pudendal and paracervical

IMPORTANT SAFETY INFORMATION (cont'd)

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, sciatic nerve block in the popliteal fossa, and adductor canal block**, or intravascular or intra-articular use

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Evaluating the use of EXPAREL in your health system

When assessing the inclusion of EXPAREL into your system's surgical protocols, some best practices can be kept in mind.



Review relevant procedural data

Collect and review any relevant literature and information on how EXPAREL utilization may benefit postsurgical pain management.

- Indications and key clinical benefits of EXPAREL (page 6)
- EXPAREL in multimodal protocols and impact on your patient and case mix
- Outcomes from major health systems that have used EXPAREL (page 7)
- Refer to the clinical trial evaluation checklist (page 10)



Map out the approach

- Evaluate how appropriate use of EXPAREL would be operationalized and tracked.
- The addition of EXPAREL into key service lines and its impact on your patients
- Establishment of a cross-functional team to map out usage and protocol
- Primary stakeholders who will help support multidisciplinary team readiness
- Prioritization of select procedures for initial EXPAREL adoption to ensure appropriate use
- Identification of usage limitations based on providers and care settings



Develop an implementation plan

Consider what system updates or training will be necessary for successful implementation.

- Team training in the appropriate use of EXPAREL (eg, administration technique)
- Updates to processes and EHR to ensure optimal billing, coding, and reimbursement of EXPAREL
- Revisions of order sets to help support the clinical decision-making process



Analyze cost benefits and clinical outcomes

Ensure that procedural improvements from EXPAREL use are tracked to support continued utilization

- Measurement of improvement in clinical, economic, and patient-reported outcomes (pages 10, 11)
- Assessment of other areas that may align to identified outcomes

EHR, electronic health record.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS SPECIFIC TO EXPAREL (cont'd)

- 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

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EXPAREL: non-opioid postsurgical pain management

EXPAREL delivers effective postsurgical pain management with lasting results¹⁸:



Uses pMVL technology to control postsurgical pain for up to 96 hours¹⁸⁻²⁴



Proven to decrease opioid use^{18,20,25*}



Established reductions in the need for rescue pain medications, supporting a faster and more comfortable recovery^{18,20,25}



Demonstrated superiority vs bupivacaine HCl in 2 LENB pivotal trials and a phase 4 local infiltration study in TKA^{18,20,22†}

EXPAREL is FDA approved for²⁶:

- Broad indication for local infiltration and fascial plane blocks (eg, TAP, ESP)
- Upper-extremity nerve block: interscalene brachial plexus nerve block
- Lower-extremity nerve blocks: sciatic nerve block in the popliteal fossa and adductor canal block
- The only FDA-approved, long-lasting, local analgesic for patients 6 years of age and older

EXPAREL provides a powerful non-opioid alternative for effective pain management during the critical initial days after surgery.¹⁸⁻²⁴

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

†EXPAREL showed superiority to bupivacaine in the adductor canal nerve block pivotal trial and the sciatic nerve block in the popliteal fossa pivotal trial.^{18,20,22} ESP, erector spinae plane block; FDA, US Food and Drug Administration; HCl, hydrochloride; LENB, lower extremity nerve block; pMVL, proprietary multivesicular liposome; TAP, transversus abdominis plane; TKA, total knee arthroplasty.

IMPORTANT SAFETY INFORMATION (cont'd)

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

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EXPAREL has demonstrated improved outcomes in real-world studies



Total shoulder arthroplasty

Source: CMS database²⁷

Comparators: Patients received EXPAREL or non-EXPAREL

Outcomes: For patients with opioid use after surgery, significantly fewer opioids were consumed in the first week by patients receiving EXPAREL (an average of 165 vs 183 MMEs; $P=0.01$)

Study Design and Methodology:

The retrospective cohort study assessed adults who underwent total shoulder arthroplasty in an HOPD between January 2019 and December 2021 using deidentified patient data from 20% of the Medicare beneficiaries in the CMS database.

- Patients were required to have continuous enrollment at least 6 months prior to surgery and 12 months following the surgery date
- Propensity score matching (1:1 ratio) was conducted between the EXPAREL and non-EXPAREL cohorts based on age, sex, race, comorbidities, procedure year, and region

- Baseline characteristics were similar between groups after propensity score matching
- The final cohort was composed of 2,050 EXPAREL patients and 2,050 non-EXPAREL patients.
 - Patients were an average age of 74, most were female (56%), and the majority had osteoarthritis ($\geq 94\%$).
 - Patients did not have substance use disorder at baseline
- Primary outcomes of interest were the day-of-surgery cost in addition to 12-month period post-discharge outcomes, including opioid use and cost



Colorectal procedures

Source: Houston Methodist Research Institute, Houston, TX (Tran AT, et. al. 2022)²⁸

Comparators: Patients received EXPAREL or non-EXPAREL

Outcomes: EXPAREL use in colorectal surgery was associated with a significant reduction in total cost of care driven by reduced costs for hospital stay and postsurgical management

Study Design and Methodology:

This was a retrospective, single-center, pharmacoeconomic evaluation using electronic medical records conducted at a large academic medical center from May 2016 until February 2018.

- The patient population included adults undergoing open or minimally invasive colorectal resection or excision
- Patients were excluded if they were younger than 18 years of age, had surgery performed after the second calendar day of admission, underwent creation or reversal of colostomies or ileostomies, had colostomies or ileostomies retained after surgery, and were allergic to acetaminophen, opioids, or bupivacaine
- The final cohort included 286 EXPAREL patients and 200 non-EXPAREL patients

- A key outcome of interest was total cost of care, which included analgesic administration

Limitations:

The study was conducted at a single hospital, limiting generalizability. Many medical comorbidities were not considered, and results may have been confounded by a potential imbalance in unmeasured covariates as well as nonstandard patient selection for EXPAREL and variations in surgeon practices and dosing of EXPAREL. Patients with an ostomy were excluded, and study results may not be generalizable to these patients. Total cost did not include patient-controlled analgesia delivery pumps and catheter placement. The analysis used public cost figures derived from estimates of charges, which are generally larger than actual costs, although this was addressed in a sensitivity analysis

CMS, Centers for Medicare & Medicaid Services; HOPD, hospital outpatient department; MME, morphine milligram equivalent.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS FOR BUPIVACAINE-CONTAINING PRODUCTS (cont'd)

- **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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Expanded reimbursement for EXPAREL is available for Medicare and top commercial plans

Separate reimbursement for both Medicare patients and major national commercial plans is available outside of the bundled procedure cost¹⁵



The cost of EXPAREL is reimbursed for Medicare patients when used in outpatient settings (eg, ASCs, HOPDs) with code J0666^{15,16,29*}



EXPAREL is the only covered single-dose therapy approved for both local and regional analgesia across surgeries **qualifying for reimbursement under the NOPAIN Act**^{15,16,30}



Top commercial plans also cover and separately reimburse EXPAREL

Initiatives to Support Access and Reimbursement for EXPAREL

- **On contract** with all major GPOs
- **340B pricing** available
- **Two single-dose vial sizes for more flexibility** in dosing and administration, minimizing cost impact to your system^{4-9,19†}

Pacira can help you take advantage of this additional reimbursement. Visit [EXPARELpro.com/reimbursement](https://www.exparelpro.com/reimbursement)

*Reimbursement is provided as ASP+6%, meaning an additional 6% above the average sales price of EXPAREL.^{15,16}

†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, available at www.exparelpro.com, before using.

ASC, ambulatory surgery center; ASP, average selling price; GPO, group purchasing organization; NOPAIN, Non-Opioids Prevent Addiction in the Nation.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS FOR BUPIVACAINE-CONTAINING PRODUCTS (cont'd)

- **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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Assessing clinical postsurgical outcome studies

Since it received FDA approval in 2011, EXPAREL has demonstrated improved clinical and economic outcomes in numerous surgical procedures.^{18,20,31-38}

Evaluation of the most relevant and rigorous data is key to supporting the adoption of EXPAREL.

Clinical trial evaluation checklist

- ✓ Appropriate study design and methodology
- ✓ Relevant comparators
- ✓ Adequate sample size
- ✓ Clinically relevant endpoints on patient and economic outcomes (eg, pain, opioid use)
- ✓ FDA-approved label-aligned administration techniques

If you have any questions about studies related to EXPAREL, reach out to your Pacira representative.

FDA, US Food and Drug Administration.

INDICATION

EXPAREL® (bupivacaine liposome injectable suspension) is indicated to produce postsurgical local analgesia via infiltration in patients aged 6 years and older and regional analgesia in adults via an interscalene brachial plexus nerve block, sciatic nerve block in the popliteal fossa, and an adductor canal block. Safety and efficacy have not been established in other nerve blocks.

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Measuring the clinical and economic impacts of EXPAREL in your health system

Tracking the impact of implementing EXPAREL within your health system is critical to support further use. The following metrics can help when assessing the impact:



Patient outcomes

Tracking patient outcomes is key in supporting the clinical efficacy of EXPAREL through the management of:

- Pain levels
- Opioid consumption rates
- Patient satisfaction



Economic outcomes

The economic benefits of EXPAREL can be assessed through reviews of improvements in:

- LOS
- Readmission rates
- Post-discharge ER visits
- Post-discharge outpatient visits
- Net reimbursement



Additional considerations

It is important to ensure that the use of EXPAREL is in accordance with P&T Committee guidance. When EXPAREL is used, it should be in line with protocols in relation to use:

- Appropriate HCPs
- Relevant service lines
- Right setting of care

ER, emergency room; HCP, healthcare professional; LOS, length of stay; P&T, Pharmacy and Therapeutics.

IMPORTANT SAFETY INFORMATION

- EXPAREL is contraindicated in obstetrical paracervical block anesthesia
- Adverse reactions reported in adults with an incidence greater than or equal to 10% following EXPAREL administration via infiltration were nausea, constipation, and vomiting; adverse reactions reported in adults with an incidence greater than or equal to 10% following EXPAREL administration via nerve block were nausea, pyrexia, headache, and constipation

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EXPAREL implementation in health systems

These case studies, developed from stakeholder interviews, showcase successful EXPAREL integration and NOPAIN Act protocol implementation within three health systems, resulting in positive clinical and economic impacts.

The Pharmacist Perspective

A hospital outpatient department re-added EXPAREL to their formulary and saw reduced opioid use in their community

The Anesthesiologist Perspective

A major integrated health system included EXPAREL in their formulary as a non-opioid option and saw clinical improvements

The Chief Pharmacy Officer Perspective

A mid-sized regional non-profit health system implemented and expanded EXPAREL, resulting in lower opioid use and cost of care

Disclaimer: These case studies represent the individual experiences of these US health systems and are intended to demonstrate their experiences navigating formulary and operationalization of EXPAREL. Other health systems' experience may vary based on, but are not limited to, population, location, reimbursement structure, and surgery types.

Pacira BioSciences, Inc. recognizes that there are alternative methodologies for identifying appropriate indications, patient populations, management approaches, and data tracking, and approaches vary by health system.

NOPAIN, Non-Opioids Prevent Addiction in the Nation.

IMPORTANT SAFETY INFORMATION (cont'd)

- Adverse reactions with an incidence greater than or equal to 10% following EXPAREL administration via infiltration in pediatric patients six to less than 17 years of age were nausea, vomiting, constipation, hypotension, anemia, muscle twitching, vision blurred, pruritus, and tachycardia
- Do not admix lidocaine or other non-bupivacaine local anesthetics with EXPAREL. EXPAREL may be administered at least 20 minutes or more following local administration of lidocaine

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EXPAREL implementation in health systems (cont'd)

Re-adding EXPAREL to Formulary: The Pharmacist Perspective

System Overview: Small, physician-owned surgical center, operating as a hospital outpatient department, that had removed EXPAREL from its formulary for approximately 5 years based on cost concerns

Strategic Goal: Leverage separate Medicare reimbursement for EXPAREL (NOPAIN Act) to create an opportunity for adding EXPAREL back onto formulary in order to reduce opioid use in the community surrounding the health system

Approach

- 1 Established positive rapport with cross-functional partners:** The Director of Pharmacy engaged physicians and surgeons who had experience with EXPAREL at other facilities to understand their perspectives and kickstart the conversation
- 2 Engaged leadership:** Key members of system leadership—including the medical executive team—were educated on the potential benefits of EXPAREL prior to presenting the full plan to the Pharmacy & Therapeutics committee
- 3 Started with few indications to monitor closely:** EXPAREL usage was initially granted to only two indications, interscalene and adductor canal blocks, based on high usage in orthopedic procedures and provided on a case-by-case basis, requiring the anesthesiologists to prove that the patient use case met preidentified criteria to gain approval
- 4 Ensured appropriate implementation:** Surgeons and anesthesiologists were trained to ensure that EXPAREL was tracked and charted appropriately (in milligrams), and office managers were engaged to ensure that the J-code was used for billing
- 5 Regularly analyzed cost benefits and clinical outcomes:** Leadership met quarterly to review the economic benefits and clinical outcomes, including postoperative pain scores and opioid use compared with patients not receiving EXPAREL

IMPORTANT SAFETY INFORMATION (cont'd)

- EXPAREL is not recommended to be used in the following patient populations: patients <6 years old for infiltration, patients younger than 18 years old for nerve blocks, 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 implementation in health systems (cont'd)

Re-adding EXPAREL to Formulary: The Pharmacist Perspective

Key Considerations:

- **Start small with clear criteria:** Establishing the benefit in select indications can help gain a controlled assessment of the potential for EXPAREL
- **Have a vision:** Mapping out the proposed plan and the potential impact can help gain buy-in from colleagues and leadership
- **Collect and assess data:** Using health system data and patient feedback is critical to determining success and guiding future decisions
- **Leverage manufacturer support:** Maintaining a strong relationship with the Pacira representative helped connect the system with medical science liaisons and nurse educators

Reported Impact at This Health System:

- By adding EXPAREL back onto formulary with clear controls and a controlled population, **the system was able to see reductions** in spending compared with their original experience 5 years prior
- The Director of Pharmacy and their team were **able to elevate the standard of care for the health system while helping to reduce opioid use** and providing greater overall patient satisfaction
- The success of the initial rollout has allowed **the facility to expand the use of EXPAREL to more indications** while maintaining control and minimizing the financial impact
- The Director of Pharmacy was able to establish **strong lines of communication between clinicians and pharmacy** to support future collaborations in advancing patient care

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS SPECIFIC TO EXPAREL

- Avoid additional use of local anesthetics within 96 hours following administration of EXPAREL

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EXPAREL implementation in health systems (cont'd)

Evidence Generation for EXPAREL Formulary Inclusion: The Anesthesiologist Perspective

System Overview: Major integrated health system operating across seven states in the western United States

Strategy Goal: Generate clinical and economic data to support EXPAREL formulary inclusion in a hospital system in an effort to expand non-opioid options

Approach

- 1 Conducted internal quality improvement study with multidisciplinary support:** Clinicians evaluated the cost-benefit profile of non-formulary use of EXPAREL in peripheral nerve blocks in the health system, analyzing opioid use, pain scores, and length-of-stay data pulled from the EMR
- 2 Recommended EXPAREL be added to formulary:** The P&T committee added EXPAREL to formulary for procedures that saw benefits in the internal study (eg, brachial plexus blocks for upper-extremity surgeries, anterior thigh and knee blocks). Exceptions for off-formulary procedures were allowed with appropriate clinical justification
- 3 Established system-wide use protocols:** Anesthesiologists added EXPAREL into the pre-existing, opioid-sparing, multimodal order sets for the approved procedures, to promote safe, efficient, and outcome-driven use
- 4 Monitored patient-reported outcomes:** The team collected data about opioid use, pain scores, block effectiveness, and patient satisfaction post-discharge daily through day 5 via nurse calls and digital tools
- 5 Checked compliance of EXPAREL use:** The team conducted quarterly compliance checks to ensure that EXPAREL was used mostly for approved formulary procedures

EMR, electronic medical record; P&T, Pharmacy and Therapeutics.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS SPECIFIC TO EXPAREL (cont'd)

- EXPAREL is not recommended for the following types or routes of administration: epidural, intrathecal, regional nerve blocks **other than interscalene brachial plexus nerve block, sciatic nerve block in the popliteal fossa, and adductor canal block**, or intravascular or intra-articular use

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EXPAREL implementation in health systems (cont'd)

Evidence Generation for EXPAREL Formulary Inclusion: The Anesthesiologist Perspective

Key Considerations:

- **Plan approach for data capture:** Preparing data collection before formulary implementation can support appropriate use, identify new use cases, and improve outcomes
- **Build consensus among key stakeholders:** Aligning clinicians, pharmacists, and health system leadership promotes successful formulary addition and proper documentation
- **Use internal data to drive decisions:** Leveraging your health system's data can help identify the most suitable procedure for introducing EXPAREL. Analyze the potential impact on your specific patient population, clinical teams, and system costs, including the effects on opioid use and length of stay

Reported Impact at This Health System:

- Decreased postoperative opioid use, decreased pain scores, shortened length of stay, decreased system cost, and increased sensory block time with the use of EXPAREL*
- Expanded formulary approval for EXPAREL across many procedure types, including new nerve blocks, based on strong outcomes data and high formulary compliance
- Ongoing stakeholder partnerships supported continued data generation

*Based on data reported by the anesthesiologist interviewed for this case study. These results reflect the experiences of one health system; results at other health systems may vary.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS SPECIFIC TO EXPAREL (cont'd)

- 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

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EXPAREL implementation in health systems (cont'd)

Multidisciplinary Approach to Integrating EXPAREL: The Chief Pharmacy Officer perspective

System Overview: Mid-sized regional non-profit health system in Texas

Strategy Goal: Implement and expand EXPAREL within a health system using a multidisciplinary approach with multimodal ERAS protocols as the foundation, with consideration given to overall institutional expenses

Approach

- 1 Identified champions:** Clinicians who requested that EXPAREL be added to formulary became key team members in the implementation process, in addition to pharmacists and administrators
- 2 Generated ERAS protocol:** Pharmacists and clinicians worked together to create an ERAS protocol with a multimodal approach that included taking opioids off of their order set
- 3 Targeted high-complication procedures:** EXPAREL was added to formulary first for colorectal procedures because they were high-complication procedures with sufficient surgeon and patient support
- 4 Measured initial outcomes and ensured ERAS protocol use:** A nurse analyzed outcomes (including pain scores, opioid use and side effects, early ambulation, length of stay, and readmissions) compared with those not treated with EXPAREL. The pharmacy team monitored pain management and drug expense data to ensure proper implementation of the ERAS protocol
- 5 Expanded use of EXPAREL:** After its initial use in colorectal procedures showed promising results, EXPAREL was added to other procedures in line with the approved indication one at a time, using ERAS protocols to support appropriate use

ERAS, Enhanced Recovery After Surgery.

IMPORTANT SAFETY INFORMATION (cont'd)

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

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EXPAREL implementation in health systems (cont'd)

Multidisciplinary Approach to Integrating EXPAREL: The Chief Pharmacy Officer Perspective

Key Considerations:

- **Drive cross-discipline collaboration:** Involving key stakeholders early and often is important, including pharmacists, clinicians, and administrators
- **Assess procedures based on clinical and economic impact:** Starting with procedures that have higher opioid use and side effects and longer stays can ease formulary entry
- **Establish ERAS protocols:** Ensuring that ERAS protocols are in place can help build rigorous structure, hold key players accountable, and capture data
- **Reframe the cost discussion:** Building the total cost story of EXPAREL for your health system is critical, rather than focusing only on the immediate costs

Reported Impact at This Health System:

- **Opioid use decreased**, along with opioid-related side effects*
- Early ambulation increased, and **length of stay decreased***
- **ERAS protocol adherence** helped ensure expansion of EXPAREL to additional appropriate procedure types

*Based on data reported by the Chief Pharmacy Officer interviewed for this case study. These results reflect the experiences of one health system; results at other health systems may vary.
ERAS, Enhanced Recovery After Surgery.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS FOR BUPIVACAINE-CONTAINING PRODUCTS

- **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

Please see Important Safety Information throughout and on page 18.
Full Prescribing Information is available at www.EXPARELpro.com.

EXPAREL[®]
BUPIVACAINE LIPOSOME INJECTABLE SUSPENSION

Important Safety Information

INDICATION

EXPAREL® (bupivacaine liposome injectable suspension) is indicated to produce postsurgical local analgesia via infiltration in patients aged 6 years and older and regional analgesia in adults via an interscalene brachial plexus nerve block, sciatic nerve block in the popliteal fossa, and an adductor canal block. 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 in adults with an incidence greater than or equal to 10% following EXPAREL administration via infiltration were nausea, constipation, and vomiting; adverse reactions reported in adults with an incidence greater than or equal to 10% following EXPAREL administration via nerve block were nausea, pyrexia, headache, and constipation
- Adverse reactions with an incidence greater than or equal to 10% following EXPAREL administration via infiltration in pediatric patients six to less than 17 years of age were nausea, vomiting, constipation, hypotension, anemia, muscle twitching, vision blurred, pruritus, and tachycardia
- Do not admix lidocaine or other non-bupivacaine local anesthetics with EXPAREL. EXPAREL may be administered at least 20 minutes or more following local administration of lidocaine
- EXPAREL is not recommended to be used in the following patient populations: patients <6 years old for infiltration, patients younger than 18 years old for nerve blocks, 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, sciatic nerve block in the popliteal fossa, and adductor canal 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.EXPARELpro.com.
For more information, please visit www.EXPARELpro.com
or call 1-855-793-9727.

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reimbursement](http://www.EXPARELpro.com/reimbursement)**

**The EXPAREL Patient Services Team is committed
to ensuring patient access**

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