GENERAL SURGERY CLINICAL CONNECTIONS

CASE STUDIES IN POSTOPERATIVE PAIN MANAGEMENT

ZYNRELEF® (bupivacaine and meloxicam) extended-release solution, for instillation use
29.25 mg/mL and 0.88 mg/mL

LEFT OPEN INGUINAL HERNIA REPAIR

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CASE PRESENTATION

- **Gender**: Female
- **Chronic pain**: Yes
- **Prior opioid use**: Yes
- **Age**: 62 years old
- **Weight**: 123 lbs
- **Height**: 5'3"
- **BMI**: 21.8

TEST RESULTS

- **Physical exam revealed**: Obvious Left Inguinal Hernia (LIH)
- **Preoperative labs included**: Normal CBC and BMP

HISTORY AND PHYSICAL

- **Patient present for:** Left open inguinal hernia
- Patient presents with pain and a bulge in the left inguinal area. She does not remember doing anything specifically to cause the pain. She is now able to see a bulge in the left inguinal area. She chronically takes opioid pain medications for a back injury suffered in a motor vehicle accident 10 years ago.
- **Existing medications**: Oxycodone 5 mg po tid, lisinopril 10 mg po qd

DIAGNOSIS

- **Presenting diagnosis:** LIH
- **Primary diagnosis:** LIH

RECOMMENDED PROCEDURE

- **Recommended procedure**: Open repair of a LIH

PATIENT'S PERIOPERATIVE ANALGESIC PROTOCOL

Anesthesia: General anesthesia with laryngeal mask airway

MEDICATION	Pre-Op	Intra-Op	PACU	Post-Op Day 0	Post-Op Day 1	Post-Op Day 2	Post-Op Days 3 to 7
ZYNRELEF (bupivacaine/meloxicam)		10.5 ml (300 mg/ 9 mg)*					
ACETAMINOPHEN (ORAL)	1 g				1 g tid	1 g tid	
IBUPROFEN			600 mg		600 mg tid	600 mg tid	
OXYCODONE				5 mg bid†	5 mg tid†	5 mg tid†	5 mg tid†

*400 mg vial of ZYNRELEF used.
†This is the same dose the patient came in on.
Do not exceed the recommended maximum daily limits of bupivacaine by all routes.
Do not exceed the recommended maximum daily limits of acetaminophen (4 g max daily dose).

APPLICATION

With a 5-8 cm incision for the LIH, utilize up to 10.5 mL of product but do not use more than needed to coat tissue. Apply ~5 mLs to deep tissues working around perimeter and above mesh, especially medially. Suture the external oblique fascia with a Vicryl suture and apply ~5 mLs to superficial tissues prior to closing the scarpa fascia with Vicryl and the dermal layer with Monocryl.

bid: two times a day; **BMP**: basic metabolic panel; **CBC**: complete blood count; **po**: taken by mouth; **qd**: once a day; **tid**: three times a day.

INDICATION

ZYNRELEF is indicated in adults for instillation to produce postsurgical analgesia for up to 72 hours after soft tissue and orthopedic procedures including foot and ankle, and other procedures in which direct exposure to articular cartilage is avoided.

Limitations of Use: Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large 4 or more level spinal, and head and neck procedures.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

- **Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use.**
- **ZYNRELEF is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.**
- **NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events.**

Please see additional Important Safety Information on next page and full Prescribing Information, including Boxed Warning and updated Warnings and Precautions for serious skin reactions caused by nonsteroidal anti-inflammatory drugs (NSAIDs).

This case study is intended only to provide healthcare professionals with an example of the use of ZYNRELEF in the treatment of one specific patient. The outcomes described may not be representative of, and may differ significantly from, outcomes that may be obtained in treating other patients. This case study is not intended to provide specific treatment advice, recommendations, or opinions, and should not replace a clinician's judgment with respect to the treatment of any particular patient.

OUTCOMES

PAIN ASSESSMENT*	OPIOID CONSUMPTION
PACU: 5/10	**INTRA-OP**: 0 MMEs
POD 0†: 4/10	**POD 0**: 15 MMEs
POD 1: 4/10 at hour 8 and 24	**POD 1**: 22.5 MMEs
POD 2: 3/10 at hour 48	**POD 2**: 22.5 MMEs
POD 3: 3/10 at hour 72	**POD 3-7**: 22.5 MMEs

Office call back after discharge for pain management: None

PATIENT SATISFACTION

- **Patient satisfaction:** Extremely satisfied

DISCHARGE

- **Time to discharge:** PACU discharge time - 60 minutes
- **Facility length of stay after surgery:** 60 minutes

FOLLOW-UP

- **Follow-up visit:** 2 weeks
- **Pain level:** Back to her baseline pain. No pain from her hernia repair.

*Based on a 10-point visual analog scale (VAS).
†POD 0 = day of surgery.
POD: post operative day.

"We were super excited because most patients are difficult to operate on if they are already on a lot of opioid pain medicine. The fact we were able to get her through her surgery without additional pain medication is a win for everyone." – Timothy L. Beard, MD, FACS

FPO

Use camera app to scan and view resources

IMPORTANT SAFETY INFORMATION (CONT)

Contraindications

ZYNRELEF is contraindicated in patients with a known hypersensitivity (eg, anaphylactic reactions and serious skin reactions) to any amide local anesthetic, NSAIDs, or other components of ZYNRELEF; with history of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs (severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported in such patients); undergoing obstetrical paracervical block anesthesia; or undergoing CABG.

Warnings and Precautions

Dose-Related Toxicity: Monitor cardiovascular and respiratory vital signs and patient's state of consciousness after application of ZYNRELEF. When using ZYNRELEF with other local anesthetics, overall local anesthetic exposure must be considered through 72 hours.

Hepatotoxicity: If abnormal liver tests persist or worsen, perform a clinical evaluation of the patient.

Hypertension: Patients taking some antihypertensive medication may have impaired response to these therapies when taking NSAIDs. Monitor blood pressure.

Heart Failure and Edema: Avoid use of ZYNRELEF in patients with severe heart failure unless benefits are expected to outweigh risk of worsening heart failure.

Renal Toxicity: Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia. Avoid use of ZYNRELEF in patients with advanced renal disease unless benefits are expected to outweigh risk of worsening renal failure.

Anaphylactic Reactions: Seek emergency help if an anaphylactic reaction occurs.

Risk of Joint Cartilage Necrosis and Degeneration with Unapproved Intra-articular Use: Animal studies evaluating the effects of ZYNRELEF following intra-articular administration in the knee joint demonstrated cartilage necrosis and degeneration.

Chondrolysis: Limit exposure to articular cartilage due to the potential risk of chondrolysis.

Methemoglobinemia: Cases have been reported with local anesthetic use.

Serious Skin Reactions: NSAIDs, including meloxicam, can cause serious skin adverse reactions. NSAIDs can also cause fixed drug eruption (FDE). FDE may present as a more severe variant known as generalized bullous fixed drug eruption (GBFDE), which can be life-threatening. If symptoms present, evaluate clinically.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS): If symptoms are present, evaluate clinically.

Fetal Toxicity: Due to the risk of oligohydramnios/fetal renal dysfunction and premature closure of the ductus arteriosus with NSAIDs, limit use of ZYNRELEF between about 20 to 30 weeks gestation, and avoid use after about 30 weeks.

Hematologic Toxicity: Monitor hemoglobin and hematocrit in patients with any signs or symptoms of anemia.

Drug Interactions

Drugs That Interfere with Hemostasis: Monitor patients for bleeding who are using ZYNRELEF with drugs that interfere with hemostasis (eg, warfarin, aspirin, SSRIs/SNRIs).

ACE Inhibitors, Angiotensin Receptor Blockers (ARBs), or Beta-Blockers: Use with ZYNRELEF may diminish the antihypertensive effect of these drugs. Monitor blood pressure.

ACE Inhibitors and ARBs: Use with ZYNRELEF in elderly, volume-depleted, or those with renal impairment may result in deterioration of renal function. In such high-risk patients, monitor for signs of worsening renal function.

Diuretics: NSAIDs can reduce natriuretic effect of furosemide and thiazide diuretics. Monitor patients to assure diuretic efficacy including antihypertensive effects.

Use in Specific Populations

Infertility: NSAIDs are associated with reversible infertility. Consider avoidance of ZYNRELEF in women who have difficulties conceiving.

Severe Hepatic Impairment: Only use if benefits are expected to outweigh risks; monitor for signs of worsening liver function.

Severe Renal Impairment: Not recommended.

Adverse Reactions

Most common adverse reactions (incidence ≥5%) in controlled clinical trials with ZYNRELEF are soft tissue procedures: vomiting and orthopedic procedures: constipation and headache.

Report side effects to Heron at 1-844-437-6611 or to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information, including Boxed Warning and updated Warnings and Precautions for serious skin reactions caused by nonsteroidal anti-inflammatory drugs (NSAIDs).

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