

## RIGHT TOTAL KNEE ARTHROPLASTY

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### CASE PRESENTATION

- **Gender:** Male
- **Chronic pain:** No
- **Prior opioid use:** No
- **Age:** 65 years old
- **Weight:** 226 lbs
- **Height:** 6'4"
- **BMI:** 27.6

### TEST RESULTS

- **X-ray revealed:** Medial compartment joint space narrowing, medial compartment osteophytes, lateral compartment bone on bone, joint space loss worse on PA view, lateral compartment osteophytes and subchondral sclerosis, right knee. Kellgren and Lawrence Grade 4 findings present.
- **Preoperative labs included:** BMP – normal, CBC – normal

### DIAGNOSIS

- **Presenting diagnosis:** Right knee end-stage arthritis
- **Primary diagnosis:** Osteoarthritis

### RECOMMENDED PROCEDURE

- **Recommended procedure:** Right total knee arthroplasty (medial pivot)

### HISTORY AND PHYSICAL

- **Patient present for:** 65-year-old male undergoing right total knee arthroplasty with same day discharge.
- This 65-year-old male has a several (>10) year history of right knee pain. On a pain scale, the knee is rated an 8/10 and is constant. The pain is particularly bad with standing, standing for long periods, walking, walking long distances, going down stairs, rising from a chair, getting out of bed and at night. The pain is located essentially throughout the knee. The pain is described as sharp, throbbing, dull and achy. He complains of instability. He has used or is currently using acetaminophen, ibuprofen and naproxen for pain. Other conservative treatment to date has included activity modification, physical therapy, knee bracing, intraarticular steroids, weight reduction and NSAIDs. He had a skiing accident in 2007. He had a lateral meniscus tear followed by an arthroscopy in 2007. He relies heavily on his left knee for skiing and activities. He does not trust his right knee for stability. He can't walk the 5-6 miles he used to, he can't ski anymore, and he can't go down hills because of his knee.
- **Existing medications:** amlodipine, acetaminophen, ibuprofen, naproxen

### PATIENT'S PERIOPERATIVE ANALGESIC PROTOCOL

- **Anesthesia:** Spinal (chloroprocaine 1%) and adductor canal block (ropivacaine 0.5%)
- **Tourniquet(s) used during surgery:** Yes, released at 70 minutes

MEDICATION	Pre-Op	Intra-Op	PACU	Post-Op Day 0	Post-Op Day 1	Post-Op Day 2	Post-Op Days 3 to 7
<b>ZYNRELEF (bupivacaine/meloxicam)</b>		14 ml (400 mg/12 mg)					
<b>CELECOXIB</b>	200 mg			200 mg	200 mg bid	200 mg bid	200 mg bid
<b>IV ACETAMINOPHEN</b>		1 mg					
<b>IV KETOROLAC</b>				15 mg			
<b>HYDROCODONE/ACETAMINOPHEN</b>				10 mg prn			10 mg prn
<b>ORAL ACETAMINOPHEN</b>				500 mg	1000 mg q8hr	1000 mg q8hr	1000 mg q8hr
<b>CHLOROPROCAINE 1%</b>		6 ml					
<b>ROPIVACAINE 0.5%</b>		10 ml					

Do not exceed the recommended maximum daily limits of bupivacaine by all routes.

Do not exceed 4 g for Apap by all routes

**bid:** two times a day; **NSAIDs:** Non-steroidal anti-inflammatory drugs. **prn:** as needed; **q8hr:** every 8 hours.

### INDICATION

ZYNRELEF is indicated in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after foot and ankle, small-to-medium open abdominal, and lower extremity total joint arthroplasty surgical procedures.

**Limitations of Use:** Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large multilevel 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 reverse and full Prescribing Information, including Boxed Warning.**

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: 2/10	INTRA-OP: [0] MMEs
POD 0: 0/10	POD 0: [10] MMEs
POD 1: 0/10 at hour 8 and 24	POD 1: [0] MMEs
POD 2: 0/10 at hour 48	POD 2: [0] MMEs
POD 3: 1/10 at hour 72	POD 3-7: rare Hydrocodone use

Office call back after discharge for pain management: None

## FUNCTIONAL OUTCOMES

- **Weight bearing:** as tolerated
- **Ambulation:** yes
- **Time of first ambulation:** Within 3 hours of surgery patient walking in hallway
- **Distance of first ambulation:** 25 ft x 2
- **Assistance needed in first ambulation (eg, boot):** walker used
- **Range of motion:** 0-100 degrees prior to discharge
- **Physical therapy participation:** yes

## PATIENT SATISFACTION

- Very satisfied†

\*Based on a 10-point visual analog scale (VAS).

†Based on 5 point Likert scale.

pod: post operative day

## 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.

**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. If symptoms present, evaluate clinically.

## DISCHARGE

- **Time to discharge:** PACU Discharge Time: 40 minutes
- **Facility length of stay after surgery:** 3.5 hours after surgery
- **"Other" Outcomes:** Reports "No pain at all, period, for the first 3 days!"

## FOLLOW-UP

- **Follow-up visit:** rare opioid use in first week
- **Pain level:** minimal pain

*"Large, young, athletic males can be some of our most challenging knee replacement patients. It is great to have locally applied, non-opioid medication options which can reduce pain and speed recovery in these types of patients." – Alexander Sah, MD*

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  $\geq 10\%$ ) in controlled clinical trials with ZYNRELEF are constipation, vomiting, 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](http://www.fda.gov/medwatch).

**Please see full Prescribing Information, including Boxed Warning.**