ZYNRELEF is a new foundation for postoperative pain management, providing superior pain relief for up to 72 hours, with fewer patients experiencing severe pain, and reducing or eliminating the need for opioids in many patients following surgery versus standard-of-care bupivacaine HCl solution.1-3

**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 the following page and full Prescribing Information, including Boxed Warning.

*Synergistic increases in analgesia compared with meloxicam or bupivacaine alone were shown in preclinical and Phase 2 studies.1,5

*Clinical findings were demonstrated in Phase 3 trials for bunionectomy with osteotomy and open inguinal herniorrhaphy comparing ZYNRELEF to both placebo and bupivacaine HCl solution.1,3

*The HOPE Project collected data on opioid elimination protocols in a real-world setting. In HOPE Hernia 1, ZYNRELEF was used as the foundation of 2 different non-opioid multimodal postoperative regimens for patients undergoing open inguinal herniorrhaphy.6
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.

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.

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 ≥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.

Please see full Prescribing Information, including Boxed Warning.

Additional resources and product information, including clinical trial results, an explanation of the product’s mechanism of action, and pricing, can be found online at ZYNRELEF.com

For general information, contact 844-HERON11 (844-437-6611)

To report an adverse event or product complaint, contact 844-HERON11 (844-437-6611)

MEDINFO@HERONTX.COM

Heron Connect® provides support programs that meet the needs of patients and providers. Visit HERONCONNECT.COM

References:

SKU: stock-keeping unit. GPO: group purchasing organization. WAC: wholesale acquisition cost.