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ZYNRELEF.com/bunion

# ADMINISTRATION OF ZYNRELEF

ZYNRELEF is administered via a needle-free syringe directly to affected tissue.<sup>1</sup>

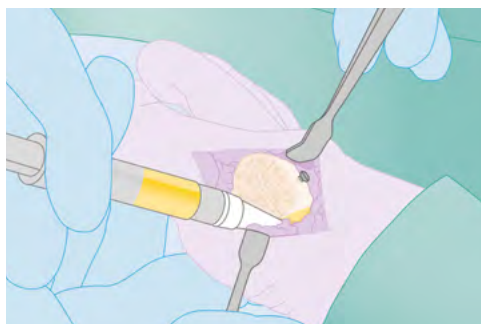
## Important Information

- Recommended dose for a bunionectomy: up to 60 mg/1.8 mg (withdraw 2.3 mL)<sup>1</sup>
- Diluting and/or mixing ZYNRELEF with bupivacaine is not necessary to achieve efficacy. ZYNRELEF cannot be mixed with water, saline, or other local anesthetics as the product will become difficult to administer.<sup>1</sup>
- Only administer with syringe and Luer lock cone-shaped applicator provided in kit<sup>2</sup>
- If any of the kit components are damaged or become unusable, use replacement components, which are individually supplied separate from the kit<sup>2</sup>
- Only apply to tissue layer below the skin, after final irrigation and suction, before closing<sup>1</sup>
- When ZYNRELEF comes in contact with moisture in the tissues, it becomes more viscous, allowing it to stay in place<sup>1</sup>
- You may use other local anesthetics before application of ZYNRELEF without causing release of the active ingredients all at once. The toxic effects of local anesthetics are additive. Avoid additional use of local anesthetics within 96 hours following administration of ZYNRELEF.<sup>1</sup>
- ZYNRELEF does not degrade sutures. If using monofilament sutures, use 3 or more knots as contact with ZYNRELEF may cause a single knot to loosen or untie.<sup>1</sup>

Please see additional information in [Instructions for Use](#).

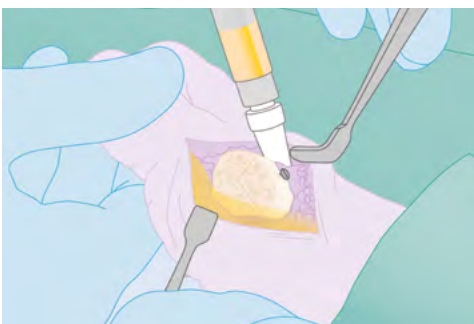
APPLY ZYNRELEF AFTER FINAL IRRIGATION AND SUCTION OF EACH LAYER, BEFORE CLOSING.

### 1 APPLY TO PLANTAR SIDE OF METATARSAL HEAD.<sup>3</sup>



- Insert applicator beneath first metatarsal head and apply a sufficient amount to coat tissues

### 2 APPLY TO JOINT CAPSULE AND OSTEOTOMY.<sup>4</sup>



- Apply majority of ZYNRELEF around capsule, including plantar side, as well as around osteotomy

### 3 APPLY DISTALLY AND PROXIMALLY AROUND FIRST METATARSAL HEAD.<sup>3</sup>



- Apply remaining ZYNRELEF in a ring pattern around both proximal and distal ends of metatarsal
- Use applicator to spread the remainder of the material wherever there may be nerve endings
- Do not add ZYNRELEF to dermal or subdermal layers; if excess does express from site, clean skin surface after suturing

Do not use more than is needed to coat tissues to prevent excess from being expressed from site during closure.

Please see additional information in [Instructions for Use](#).

## INDICATION

ZYNRELEF is indicated in adults for soft tissue or periarticular instillation to produce postsurgical analgesia for up to 72 hours after bunionectomy, open inguinal herniorrhaphy and total knee arthroplasty.

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](#).



## IMPORTANT SAFETY INFORMATION (CONT)

### Contraindications

ZYNRELEF is contraindicated in patients with 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 coronary artery bypass graft (CABG) surgery.

### 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.

**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.

### 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 effect.

### 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.**

**References:** **1.** ZYNRELEF [package insert]. San Diego, CA: Heron Therapeutics Inc; 2021. **2.** ZYNRELEF [instructions for use]. San Diego, CA: Heron Therapeutics Inc; 2021. **3.** Data on file. Pharmacy/study manual for clinical study protocol: HTX-011-301. San Diego, CA: Heron Therapeutics Inc; 2017. **4.** Data on file. HTX-034 administration (updates by Pollak RA). San Diego, CA: Heron Therapeutics Inc; 2020.

For preparation steps, please refer to the Instructions for Use in your ZYNRELEF Kit, or visit [ZYNRELEF.com/admin](http://ZYNRELEF.com/admin)