

ZYNRELEF is approved for use in adults to reduce pain for up to 3 days after removal of bunions, groin hernia repair, and total knee replacement. ZYNRELEF is applied into the wound at the time of surgery.¹

ZYNRELEF is a non-opioid that reduces or eliminates the need for opioids in many patients following surgery compared to standard-of-care bupivacaine solution without sacrificing pain relief.²⁻³

ZYNRELEF is redefining postoperative pain management:



Synergistic mechanism of action

Synergistic formulation of local anesthetic bupivacaine with low-dose meloxicam (a nonsteroidal anti-inflammatory drug, NSAID), to overcome the challenges of pain and inflammation at the surgical site.^{4,5}



Fewer patients require opioids after surgery

Non-opioid that demonstrated significantly less opioid use in the 72 hours following surgery versus standard-of-care bupivacaine HCl solution in Phase 3 studies.^{2,3}



Superior postoperative pain management

First postoperative pain medication to demonstrate superior reduction in pain up to 72 hours versus the standard-of-care bupivacaine HCl solution in Phase 3 studies.^{2,3,5}



Needle-free administration

Administered as a single-dose needle-free application that directly coats the affected tissue within the surgical site following final irrigation and suction and prior to suturing.⁵



Maximized access and customer value

Pricing, distribution, and reimbursement and 2 dosing options designed to maximize broader access and customer value.

Next generation dual-acting local anesthetic (DALA)

ZYNRELEF is the first and only postoperative pain medication intended to address both pain and inflammation at the surgical site.^{4,5}



Meloxicam normalizes pH

ZYNRELEF works by reducing local inflammation, thereby normalizing pH at the surgical site and enabling more bupivacaine to penetrate the nerve cells.⁴



Bupivacaine blocks pain

ZYNRELEF contains bupivacaine, an amide-type local anesthetic that penetrates nerve cells to block pain signals to the brain.⁴

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IMPORTANT SAFETY INFORMATION

ZYNRELEF contains an NSAID (non-steroidal anti-inflammatory drug), a type of medicine which:

- Can increase the risk of a heart attack or stroke that can lead to death. This risk increases with higher doses and longer use of an NSAID.
- Cannot be used during heart bypass surgery.
- Can increase the risk of gastrointestinal bleeding, ulcers, and tears.

ZYNRELEF demonstrated statistically significant reductions in both pain intensity and the use of postoperative opioids through 72 hours following surgery when compared to standard-of-care bupivacaine HCl solution.^{2,4,5}



46%

of bunionectomy patients
did not experience severe pain^{2a}



51%

of herniorrhaphy patients
did not experience severe pain^{3a}



29%

of bunionectomy patients
required no postoperative
opioids for 72 hours postsurgery²



51%

of herniorrhaphy patients
required no postoperative
opioids for 72 hours postsurgery³

a) Significance of this analysis not controlled for multiple hypothesis testing.

IMPORTANT SAFETY INFORMATION (CONT.)

ZYNRELEF should also not be used:

- If you are allergic to any components of ZYNRELEF, aspirin or other NSAIDs (such as ibuprofen or naproxen), or have had an asthma attack, hives, or other allergic reaction after taking any of these medicines.
- As a paracervical block, during childbirth.

The most common side effects of ZYNRELEF are constipation, vomiting, and headache.

The medicines in ZYNRELEF (a local anesthetic and an NSAID) can affect the nervous and cardiovascular system; may cause liver or kidney problems; may reduce the effects of some blood pressure medicines; should be avoided if you have severe heart failure; may cause a rare blood disorder, or life-threatening skin or allergic reactions; may harm your unborn baby if received at 20 weeks of pregnancy or later; and may cause low red blood cells (anemia).

Tell your healthcare provider about all your medical conditions and about all the medicines you take including prescription or over-the-counter medicines, vitamins or herbal supplements to discuss if ZYNRELEF is right for you.

Talk to your healthcare provider for medical advice about side effects. Report side effects to Heron at 1-844-437-6611 or to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

The information provided here is not comprehensive. Please see full Prescribing Information, including Boxed Warning.

References:

1. ZYNRELEF [Summary of Product Characteristics]. Heron Therapeutics. Available at: HYPERLINK "http://www.ZYNRELEF.com" www.ZYNRELEF.com.
2. Viscusi et al. HTX-011 reduced pain intensity and opioid consumption versus bupivacaine HCl in bunionectomy: phase III results from the randomized EPOCH 1 study. *Reg Anesth Pain Med.* 2019;44(7):700-706. doi:10.1136/rapm-2019-100531.
3. Viscusi et al. HTX-011 reduced pain intensity and opioid consumption versus bupivacaine HCl in herniorrhaphy: results from the phase 3 EPOCH 2 study. *Hernia.* 2019;23(6):1071-1080. doi:10.1007/s10029-019-02023-6.
4. ZYNRELEF [package insert]. San Diego, CA: Heron Therapeutics Inc; 2021.
5. Ottoboni et al. Mechanism of action of HTX-011: a novel, extended-release, dual-acting local anesthetic formulation for postoperative pain. *Reg Anesth Pain Med.* 2020;45(2):117-123. doi:10.1136/rapm-2019-100714.



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05/2021 PP-HTX011-0285