ZYNRELEF™
(bupivacaine and meloxicam)
extended-release solution
29.25 mg/mL and 0.88 mg/mL

REIMBURSEMENT AND CODING OVERVIEW

Medicare: ZYNRELEF Is Reimbursed Separately in Hospital Outpatient Departments and ASCs[a]

Setting of Care	ZYNRELEF at Launch *C9399*	ZYNRELEF 3-Year Pass-Through[a] *Product-specific C-code/J-code*	Exparel®[b] (Pass-Through Expired) *C9290; no J-code*
Inpatient	Diagnosis-Related Group (DRG) Payment		DRG Payment
HOPD	95% of AWP	ASP + 6%[c]	Packaged
HOPD (340B)	95% of AWP	ASP + 6%[c]	N/A
ASC	95% of AWP	ASP + 6%[c]	ASP + 6%

Pumps, generic local anesthetics like bupivacaine HCl solution, and other non-opioid postoperative pain products are packaged across all settings of care (except for Exparel in ASCs).[d]

Commercial Reimbursement Varies by Payer and Site of Care

- Heron is applying for a J-code to facilitate separate reimbursement
- Like all new products, until CMS assigns a permanent code, commercial payers will require a miscellaneous code (J3490 or C9399) for ZYNRELEF
- Heron is working with commercial payers to enable separate reimbursement of innovative non-opioids
- Heron helps customers navigate coding and reimbursement for ZYNRELEF
- Heron offers extended dating through selected distributors

ZYNRELEF Coding Information

HCPCS Code[e] (effective at launch)	Care Setting	Description
C9399	HOPD, ASC[f]	Unclassified drugs and biologicals
J3490	Physician Office	Unclassified drugs

HERON CONNECT

Heron Connect offers customized support for ZYNRELEF billing and coding questions. Reimbursement Counselors are available at **1-844-HERON11 (1-844-437-6611)** from 8 AM to 8 PM ET, Monday through Friday.

For more information, visit **HeronConnect.com**

HERON CONNECT®

[a] Heron expects to receive transitional pass-through status for ZYNRELEF. Pass-through status is for 3 years once granted.

[b] Exparel (bupivacaine liposome injectable suspension) is a trademark of Pacira Pharmaceuticals, Inc.

[c] ZYNRELEF will be reimbursed at WAC plus 3% until ASP is established.

[d] Reimbursement comparisons do not imply safety or efficacy.

[e] When billing ZYNRELEF with either C9399 or J3490, the NDC, drug name, dose, and method of administration should be included on the claim form.

[f] Some commercial payers may require J3490 for claims in the HOPD or ASC.

ASC: ambulatory surgical center. **HOPD:** hospital outpatient department. **AWP:** average wholesale price. **ASP:** average selling price.
CMS: Centers for Medicare & Medicaid Services. **HCPCS:** healthcare common procedure coding system. **WAC:** wholesale acquisition cost.

Please see Indication and Important Safety Information on the following page and full Prescribing Information, including Boxed Warning.

ZYNRELEF™
(bupivacaine and meloxicam)
extended-release solution
29.25 mg/mL and 0.88 mg/mL

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.**

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 ≥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.

4242 CAMPUS POINT COURT, SUITE 200 • SAN DIEGO, CA 92121 • 858-251-4400