ZYNRELEF®
(bupivacaine and meloxicam)
extended-release solution,
for instillation use
29.25 mg/mL and 0.88 mg/mL

J0668

- ☑ Updated Product-Specific Code (J0668) Effective October 1, 2025
- ☑ HOPD, ASC: Separate Payment Through 2027 (Medicare)

EFFECTIVE OCTOBER 1, 2025

Bill J0668 when using ZYNRELEF across all settings of care

REIMBURSEMENT AND BILLING GUIDE

For billing and coding questions, call **Heron Connect®** at **1-844-HERON11 (1-844-437-6611)** 8 AM to 5 PM ET, Monday through Friday.

ZYNRELEF is the first and only extended-release dual-acting local anesthetic.

INDICATION

ZYNRELEF is indicated in adults for instillation to produce postsurgical analgesia for up to 72 hours after soft tissue and orthopedic procedures including foot and ankle, and other procedures in which direct exposure to articular cartilage is avoided.

Limitations of Use: Safety and efficacy have not been established in highly vascular surgeries, such as intrathoracic, large 4 or more level 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 Important Safety Information throughout and full Prescribing Information, including Boxed Warning and updated Warnings and Precautions for serious skin reactions caused by nonsteroidal anti-inflammatory drugs (NSAIDs).

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INTRODUCTION

Heron Therapeutics, Inc, is pleased to provide this reference guide to support patient access to ZYNRELEF.

The coding information contained herein is for informative purposes only and is not a guarantee of coverage or reimbursement for any product or service. This information is not intended to substitute for the physician's independent diagnosis or treatment of each patient.

Coding, coverage, and reimbursement for ZYNRELEF will vary based on the patient's health insurance and the reimbursement status per site of care.

HERON CONNECT

Dedicated Heron Connect Reimbursement Counselors offer customized support for ZYNRELEF billing and coding questions. Reimbursement Counselors are available at **1-844-HERON11 (1-844-437-6611)** from 8 AM to 5 PM ET, Monday through Friday.

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

HERON CONNECT®

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.

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ZYNRELEF REIMBURSEMENT AND BILLING SUMMARY

ZYNRELEF should be billed using J0668. The billable unit for J0668 is 1 mg/0.03 mg. (ex: 400 mg Vial = 400 Billable Units)

Medicare Billing and Separate Payment

- ZYNRELEF is available for separate payment outside the surgical bundle at ASP + 6% in HOPDs and ASCs under the Non-Opioid Policy for Pain Relief*

The Policy provides separate payments for qualifying non-opioid treatments for pain relief in both the hospital outpatient department and ambulatory surgical center settings. The goal of this policy is to remove financial barriers to use non-opioids and ensure the use of opioids is not financially incentivized.

*The key inclusion criteria are the following:
- A label indication approved by the Food and Drug Administration to reduce postoperative pain, or produce postsurgical or regional analgesia, without acting upon the body's opioid receptors.
- Demonstrated the ability to replace, reduce, or avoid intraoperative or postoperative opioid use or the quantity of opioids prescribed in a clinical trial or through data published in a peer-reviewed journal.

Commercial Billing and Reimbursement

To determine if ZYNRELEF is separately reimbursed by a specific payer, practices can do any of the following:

- **Verify ZYNRELEF Fee Schedule Inclusion:** Check if HCPCS code J0668 is listed in the payer's fee schedule by accessing the payer-specific provider portal.
- **Confirm Separate Payment Eligibility:** Conduct a Benefit Investigation (BI) or Separate Payment Investigation (SPI) directly with the payer or through Heron Connect.
- **Confirm Separate Payment Based on Contracting Terms:** Review the payer's contracting strategy, particularly if contracts are structured as a percentage of the Medicare allowable rate.

ZYNRELEF Coding Information

HCPCS Code	Description	Billable Unit
J0668	Instillation, bupivacaine and meloxicam	1 mg/0.03 mg

NDC[a]	Bupivacaine/Meloxicam	Billable Units[b]
47426-501-02 (VAN)	400 mg/12 mg	400
47426-503-01 (VAN)	200 mg/6 mg	200

[a]11-digit NDCs for billing ZYNRELEF include a 0 before the 3 of the product code.
[b]Use the JZ modifier if there are no discarded amounts. Use the JW modifier to separately bill unused and discarded drug amounts.
Note: ZYNRELEF is supplied as a kit consisting of a single-dose nonsterile glass vial (containing sterile active ingredients) and the following sterile components: Luer lock syringe(s), a Vial Access Needle, Luer lock cone-shaped applicator(s), and syringe tip cap(s). ZYNRELEF should only be prepared and administered with the components provided in the ZYNRELEF kit.

Modifier	Description
JZ	Zero drug amount discarded/not administered to any patient
JW	Drug amount discarded/not administered to any patient (indicate quantity discarded)
JG	Modifier for drug or biological acquired with 340B drug pricing program discount, reported for informational purposes
TB	Modifier for drug or biological acquired with 340B drug pricing program discount; reported for informational purposes for select entities

Note: For dates of service on or after July 1, 2023, the JZ modifier is required on claims for single-dose containers when no amount was discarded.

IMPORTANT SAFETY INFORMATION (CONT)

Warnings and Precautions (cont)

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.

Please see Important Safety Information throughout and full Prescribing Information, including Boxed Warning and updated Warnings and Precautions for serious skin reactions caused by nonsteroidal anti-inflammatory drugs (NSAIDs).

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ASC COVERAGE AND BILLING FOR ZYNRELEF

Coverage for ZYNRELEF varies by health insurance plan and site of care. The table below summarizes the coverage and payment type for ASCs.

ZYNRELEF Coverage and Reimbursement Policy in ASCs

Medicare	ZYNRELEF is available for separate payment outside the surgical bundle at ASP + 6% in HOPDs and ASCs under the Non-Opioid Policy for Pain Relief.
Medicaid	Each State Medicaid Agency sets its own coverage policies and payment rates.
Private Commercial Payer	Separate payment for ZYNRELEF is available for many commercial patients. Commercial reimbursement varies by payer and site of care; contact payers to verify coverage.

IMPORTANT SAFETY INFORMATION (CONT)

Warnings and Precautions (cont)

Anaphylactic Reactions: Seek emergency help if an anaphylactic reaction occurs.

Risk of Joint Cartilage Necrosis and Degeneration with Unapproved Intra-articular Use: Animal studies evaluating the effects of ZYNRELEF following intra-articular administration in the knee joint demonstrated cartilage necrosis and degeneration.

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. NSAIDs can also cause fixed drug eruption (FDE). FDE may present as a more severe variant known as generalized bullous fixed drug eruption (GBFDE), which can be life-threatening. 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 effects.

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ACUTE CARE (HOSPITAL INPATIENT DEPARTMENT, ED[a], AND HOPD) COVERAGE AND BILLING FOR ZYNRELEF

Coverage for ZYNRELEF varies by health insurance plan and site of care. Reimbursement of ZYNRELEF in a surgical procedure occurring during a hospital inpatient admission would be included in the diagnosis-related group (DRG) payment.

The table below summarizes the coverage and payment type for HOPDs.

ZYNRELEF Coverage and Reimbursement Policy in HOPDs

Medicare	ZYNRELEF is available for separate payment outside the surgical bundle at ASP + 6% in HOPDs and ASCs under the Non-Opioid Policy for Pain Relief.
Medicaid	Each State Medicaid Agency sets its own coverage policies and payment rates.
Private Commercial Payer	Separate payment for ZYNRELEF is available for many commercial patients. Commercial reimbursement varies by payer and site of care; contact payers to verify coverage.

[a]For patients covered by Medicare, when the surgery occurs in the ED, reimbursement is the same as in a HOPD; however, if a patient is admitted, inpatient reimbursement rules apply.

IMPORTANT SAFETY INFORMATION (CONT)

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 ≥5%) in controlled clinical trials with ZYNRELEF are soft tissue procedures: vomiting and orthopedic procedures: constipation 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 Important Safety Information throughout and full Prescribing Information, including Boxed Warning and updated Warnings and Precautions for serious skin reactions caused by nonsteroidal anti-inflammatory drugs (NSAIDs).

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SAMPLE CLAIM FORM CMS-1450 (UB-04): HOPD, ASC (NON-MEDICARE PAYERS; CONFIRM WITH PAYER)

Complete the information needed to bill for the procedure. **ZYNRELEF must be billed using a separate line**.

Field 42:
Include revenue code 0636.

Field 43:
Include the required additional information (eg, product name and NDC).

Example:

- **For 400 mg/12 mg (14-mL) VAN kit:** ZYNRELEF, 47426-501-02
- **For 200 mg/6 mg (7-mL) VAN kit:** ZYNRELEF, 47426-503-01

Payer NDC requirements and placement may vary; confirm with payer or Heron Connect.

Field 44:
Specify HCPCS Code for ZYNRELEF, **J0668**.

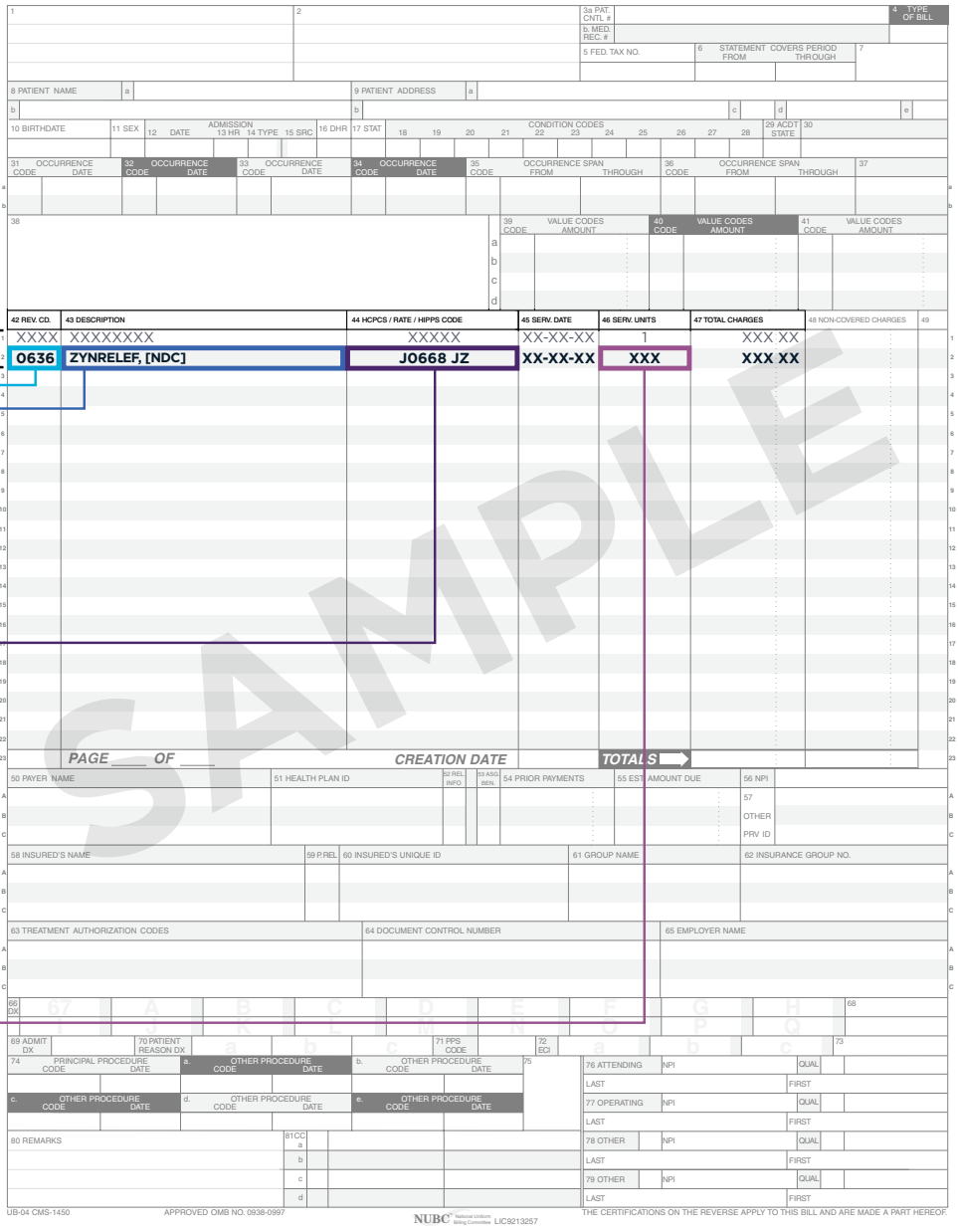
To indicate that the complete single-dose vial was administered, use the HCPCS modifier JZ.[a]

If a portion of the single-use vial was discarded, document it on a separate line using the HCPCS modifier JW.

Commercial: Confirm coding with payers or by contacting Heron Connect.

Field 46:
Specify the number of units administered. **The billable unit for J0668 is 1 mg/0.03 mg.** For example, 400 mg/12 mg (14-mL) corresponds to 400 billable units.

[a]For dates of service on or after July 1, 2023, the JZ modifier is required on claims for single-dose containers when no amount was discarded.



This document is provided for your guidance only. Coding requirements may vary by payer; please consult the payer to determine which codes are required.

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SAMPLE CLAIM FORM CMS-1500: ASC (MEDICARE) AND PHYSICIAN OFFICE

CMS requires ASCs to submit a CMS-1500 claim form when billing a Medicare Administrative Contractor (MAC). Most commercial plans require a CMS-1450 (UB-04) claim form (see page 6 for an example). Please use the claim form that you are currently utilizing when submitting to a commercial plan. Physician office billing requires the submission of the CMS-1500 claim form for all plans.

Complete the information needed to bill for the procedure. ***ZYNRELEF must be billed using a separate line.***

Field 24 (Shaded Area):
Include the required additional information (eg, product name and NDC).

Example:

- **For 400 mg/12 mg (14-mL) VAN kit:** ZYNRELEF, 47426-501-02
- **For 200 mg/6 mg (7-mL) VAN kit:** ZYNRELEF, 47426-503-01

Payer NDC requirements and placement may vary; confirm with payer or Heron Connect.

Field 24D:
Specify HCPCS Code for ZYNRELEF, **J0668**.

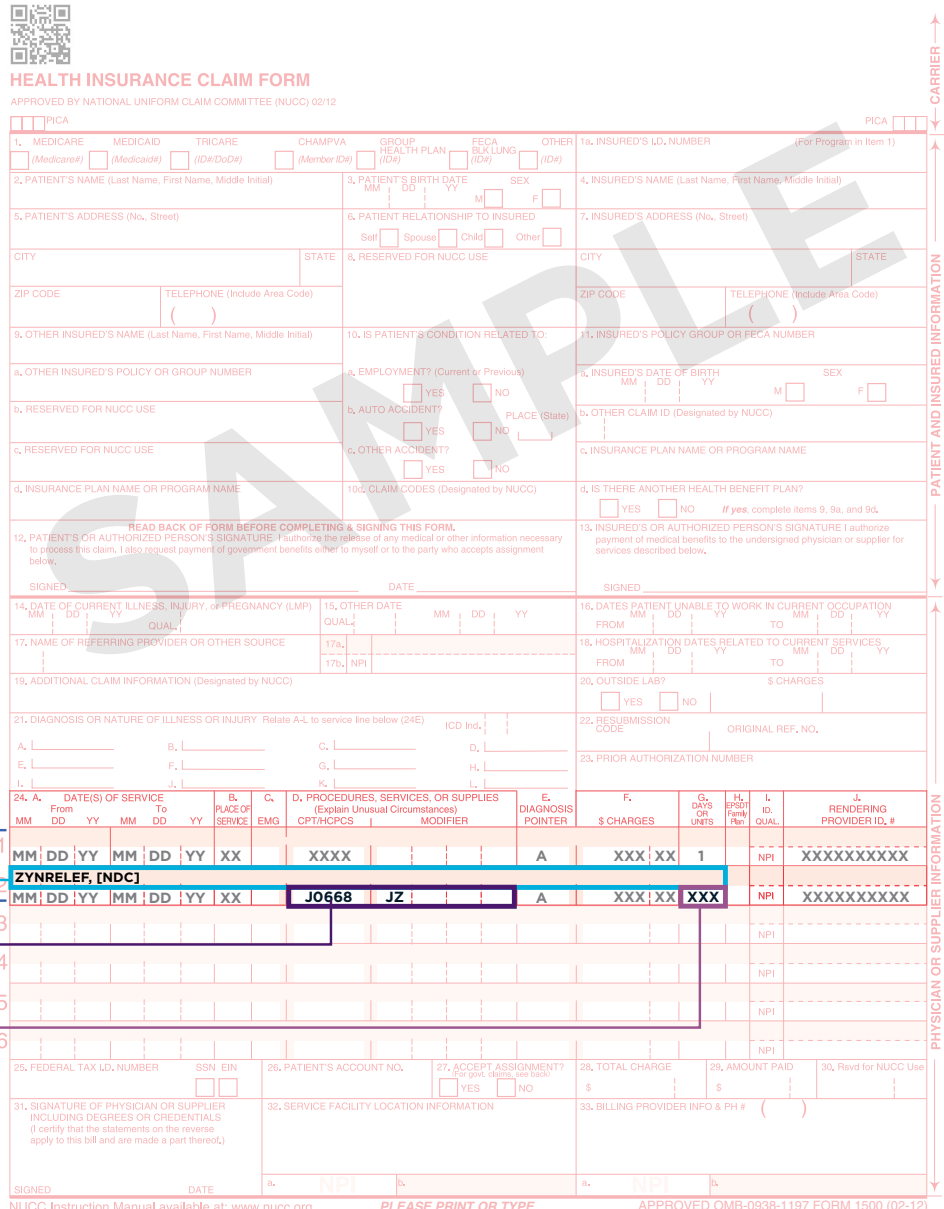
To indicate that the complete single-dose vial was administered, use the HCPCS modifier JZ.[a]

If a portion of the single-use vial was discarded, document it on a separate line using the HCPCS modifier JW.

Additional modifiers may be required, please confirm with commercial plans.

Field 24G:
Specify the number of units administered. **The billable unit for J0668 is 1 mg/0.03 mg.** For example, 400 mg/12 mg (14-mL) corresponds to 400 billable units.

[a]For dates of service on or after July 1, 2023, the JZ modifier is required on claims for single-dose containers when no amount was discarded.



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J0668 **Effective October 1, 2025, use J0668 when billing for ZYNRELEF**

CLAIM SUBMISSION CHECKLIST

Have you included the HCPCS code for ZYNRELEF?

☐ J0668

Have you included the following information to support utilization of J0668?

☐ Drug name ☐ NDC

Have you utilized the appropriate modifier to document use of the complete single-dose vial (JZ) or to document that a portion of the vial was discarded (JW)?

☐ Yes

Have you included other modifiers as applicable, such as TB or JG for drugs acquired through the 340B Program?

☐ Yes

Have you billed ZYNRELEF as per mg used? (ex: 400 mg Vial = 400 Billable Units)

☐ Yes

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Please see full Prescribing Information, including Boxed Warning and updated Warnings and Precautions for serious skin reactions caused by nonsteroidal anti-inflammatory drugs (NSAIDs).

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