SYMBRAVO®
(meloxicam and rizatriptan)
20 mg/10 mg tablets

YOU ARE CORDIALLY INVITED TO ATTEND

SYMBRAVO: A Multi-Mechanistic Approach for the Acute Treatment of Migraine

Objectives:

- **Review current unmet needs & challenges faced with treating acute migraine today**
- **Discuss the time courses & implications of key mediators of acute migraine pain**
- **Examine how a multi-mechanistic treatment approach may help address central sensitization**

Date:
Thursday, November 12, 2026

Time:
6:30 PM CT
Meeting duration: 60 minutes

Meeting Information:
Charles Anthony Restaurant "The Pub"
10044 Chantilly Parkway
Montgomery, AL 36117

Presented by:
Christopher Rhyne, MD
Headache Medicine Physician
Emory Comprehensive Headache Center

Faculty are paid speakers presenting on behalf of Axsome Therapeutics, Inc.

To reserve your spot, please contact LaPearl Wright at lwright@axsome.com or

INDICATION:
SYMBRAVO is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use:
- SYMBRAVO should only be used where a clear diagnosis of migraine has been established. If a patient has no response for the first migraine attack treated with SYMBRAVO, the diagnosis of migraine should be reconsidered before SYMBRAVO is administered to treat any subsequent attacks.
- SYMBRAVO is not indicated for the preventive treatment of migraine attacks.
- SYMBRAVO is not indicated for the treatment of cluster headache.

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

Cardiovascular Risk
- Non-steroidal 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.
- SYMBRAVO is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.

Gastrointestinal Risk
- 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.

IMPORTANT SAFETY INFORMATION

DOSAGE AND ADMINISTRATION
The recommended dose of SYMBRAVO is one tablet as needed for the acute treatment of migraine. The maximum daily dose should not exceed one tablet. The safety and effectiveness of a second dose for the same migraine attack have not been established. The safety of treating, on average, more than 7 headaches in a 30-day period has not been established. Use for the shortest duration consistent with individual patient treatment goals.

CONTRAINDICATIONS
Ischemic coronary artery disease (CAD), coronary artery vasospasm including Prinzmetal's angina, or other significant underlying cardiovascular disease

In the setting of CABG surgery

History of stroke or transient ischemic attack (TIA)

Hemiplegic or basilar migraine

Peripheral vascular disease

Ischemic bowel disease

Uncontrolled hypertension

Concomitant use of propranolol

Recent (within 24 hours) use of another triptan, ergotamine containing medication, or ergot-type medication

Concurrent administration, or recent discontinuation (within 2 weeks), of a MAO-A inhibitor

Known hypersensitivity to meloxicam, rizatriptan, NSAIDs, SYMBRAVO, or any of its excipients

History of asthma, urticaria, or other allergic-type reactions after taking aspirin or NSAIDs: Severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported

Patients with moderate to severe renal insufficiency at risk for renal failure due to volume depletion or who are on dialysis

Please note that there are no certified continuing medical education credits approved for this program.
Axsome Therapeutics, Inc. is committed to the principles of the Pharmaceutical Research and Manufacturers of America (PhRMA) Code on Interactions with Healthcare Professionals. As part of our commitment to that Code, we cannot pay for any costs incurred for travel or food of spouses or guests of any program participants, and any such spouses or guests may not attend any portion of a program's meeting or event. We appreciate your understanding in this regard.
Prescribers in Minnesota are limited to $50 per year for meals, Vermont prescribers can't receive meals, and in New Jersey, limits are $17 for breakfast and lunch and $35 for dinner. Meal reporting depends on state and federal laws.

Please see additional Important Safety Information and accompanying full Prescribing Information, including **Boxed Warning**, for risk of serious cardiovascular and gastrointestinal events.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

Cardiovascular Thrombotic Events and Myocardial Infarction: Avoid the use of SYMBRAVO in patients with a recent MI unless the benefits are expected to outweigh the risk of recurrent CV thrombotic events. If SYMBRAVO is used in patients with a recent MI, monitor patients for signs of cardiac ischemia. Perform a cardiovascular evaluation in triptan-naive patients with multiple cardiovascular risk factors and if satisfactory, consider administering the first dose in a medically supervised setting.

GI Bleeding, Ulceration, & Perforation: NSAIDs, including meloxicam, a component of SYMBRAVO, can cause serious GI adverse events including inflammation, bleeding, ulceration, and perforation of the esophagus, stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with meloxicam.

Arrhythmias: Life-threatening arrhythmias, including ventricular tachycardia and ventricular fibrillation leading to death, have been reported within a few hours following the administration of 5-HT1 agonists. Discontinue SYMBRAVO if these arrhythmias occur.

Cerebrovascular Events: Cerebral hemorrhage, subarachnoid hemorrhage, and stroke have occurred in patients treated with 5-HT1 agonists, some resulting in fatalities. Discontinue SYMBRAVO if any of these events occur.

Before treating headaches in patients not previously diagnosed with migraine, and in patients with migraine who present with atypical symptoms, care should be taken to exclude other potentially serious neurological conditions.

Anaphylactic Reactions: SYMBRAVO can cause anaphylactic reactions in patients with and without known hypersensitivity to meloxicam and in patients with aspirin-sensitive asthma. Hypersensitivity reactions, including angioedema and anaphylaxis, have also occurred in patients receiving rizatriptan. Seek emergency help if an anaphylactic reaction occurs.

Chest/Throat/Neck/Jaw Pain/Tightness, Pressure, or Heaviness: Sensations of tightness, pain, pressure in the chest, and heaviness in the precordium, throat, neck, and jaw commonly occur after treatment with SYMBRAVO and are usually non-cardiac in origin. Perform a cardiac evaluation if a cardiac origin is suspected.

Other Vasospasm Reactions: SYMBRAVO may cause non-coronary vasospastic reactions, such as peripheral vascular ischemia, gastrointestinal vascular ischemia and infarction, splenic infarction, and Raynaud's syndrome. Discontinue SYMBRAVO if any of these events occur.

Reports of transient and permanent blindness and significant partial vision loss have been reported with the use of 5-HT1 agonists.

Hepatotoxicity: Elevations of ALT or AST have been reported in patients taking NSAIDs. Rare, sometimes fatal cases of severe hepatic injury, including fulminant hepatitis, liver necrosis, and hepatic failure have been reported. Inform patients of the warning signs and symptoms of hepatotoxicity. Discontinue immediately if clinical signs and symptoms consistent with liver disease develop and perform a clinical evaluation.

Hypertension/Increase in Blood Pressure (BP): NSAIDs, including meloxicam, a component of SYMBRAVO, can lead to new onset of hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking angiotensin converting enzyme (ACE) inhibitors, thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs.

Significant elevation in BP, including hypertensive crisis with acute impairment of organ systems, has been reported on rare occasions in patients with and without a history of hypertension receiving 5-HT1 agonists, including rizatriptan, a component of SYMBRAVO.

Monitor BP during the initiation of the treatment and throughout the course of therapy.

Heart Failure and Edema: Avoid the use of SYMBRAVO in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If SYMBRAVO is used in patients with severe heart failure, monitor patients for signs of worsening heart failure.

Renal Toxicity and Hyperkalemia:

Renal Toxicity - Long-term administration of NSAIDs has resulted in serious renal injury, including acute renal failure. SYMBRAVO is not recommended in patients with moderate to severe renal insufficiency and is contraindicated in patients with moderate to severe renal insufficiency who are at risk for renal failure due to volume depletion. The renal effects may hasten the progression of renal dysfunction in patients with pre-existing renal disease.

Correct volume status in dehydrated or hypovolemic patients prior to initiating SYMBRAVO. Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia during use. Avoid the use in patients with advanced renal disease unless the benefits are expected to outweigh the risk of worsening renal function. If SYMBRAVO is used in patients with advanced renal disease, monitor patients for signs of worsening renal function.

Hyperkalemia - Increases in serum potassium concentration, including hyperkalemia, have been reported with use of NSAIDs, even in some patients without renal impairment.

Serious Skin Reactions: NSAIDs, including SYMBRAVO, can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. 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. These serious events may occur without warning. Discontinue SYMBRAVO at the first appearance of skin rash or any other sign of hypersensitivity.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS): DRESS has been reported in patients taking NSAIDs, such as SYMBRAVO. Some of these events have been fatal or life-threatening. If signs or symptoms of DRESS are present, discontinue SYMBRAVO and evaluate the patient immediately.

Fetal Toxicity: Limit use of NSAIDs, including SYMBRAVO, between about 20 to 30 weeks in pregnancy due to the risk of oligohydramnios/fetal renal dysfunction. Avoid use of NSAIDs in women at about 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/fetal renal dysfunction and premature closure of the fetal ductus arteriosus.

Hematologic Toxicity: Anemia has occurred in NSAID-treated patients. Monitor hemoglobin or hematocrit in patients with any signs or symptoms of anemia. NSAIDs, including SYMBRAVO, may increase the risk of bleeding events. Monitor patients for signs of bleeding.

Exacerbation of Asthma Related to Aspirin Sensitivity: In patients with preexisting asthma (without known aspirin sensitivity), monitor patients for changes in the signs and symptoms of asthma.

Medication Overuse Headache: Overuse of acute migraine drugs may lead to exacerbation of headache. Detoxification and treatment of withdrawal may be necessary.

Serotonin Syndrome: Serotonin syndrome may occur with triptans, including SYMBRAVO, particularly during co-administration with selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, and MAOIs. Discontinue SYMBRAVO if serotonin syndrome is suspected.

Masking of Inflammation and Fever: The pharmacological activity of SYMBRAVO in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infections.

Laboratory Monitoring: Because serious GI bleeding, hepatotoxicity, and renal injury can occur without warning symptoms or signs, consider monitoring patients on long-term NSAID treatment with a CBC and a chemistry profile periodically.

DRUG INTERACTIONS

- Monitor patients for bleeding who are concomitantly taking drugs that interfere with hemostasis. Analgesic doses of aspirin are not recommended.
- Monitor blood pressure in patients taking ACE inhibitors, ARBs, or beta-blockers due to decreased antihypertensive effects.
- Monitor for deterioration of renal function in elderly patients with renal impairment or volume depletion taking ACE inhibitors or ARBs.
- Monitor for reduced diuretic efficacy in patients taking furosemide or thiazide diuretics.
- Monitor lithium levels.
- Monitor methotrexate levels.

USE IN SPECIFIC POPULATIONS: NSAIDs are associated with reversible infertility. Consider withdrawal of SYMBRAVO in women who have difficulties conceiving or who are undergoing investigation of infertility.

ADVERSE REACTIONS

Most common (≥1% and greater than placebo) adverse reactions after a single dose pooled from 2 studies were somnolence (2%) and dizziness (2%).

SYM HCP ISI 03/2025

Please see accompanying full Prescribing Information, including **Boxed Warning** for risk of serious cardiovascular and gastrointestinal events.

REFERENCE: SYMBRAVO [prescribing information]. New York, NY: Axsome Therapeutics, Inc.; 2025.

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