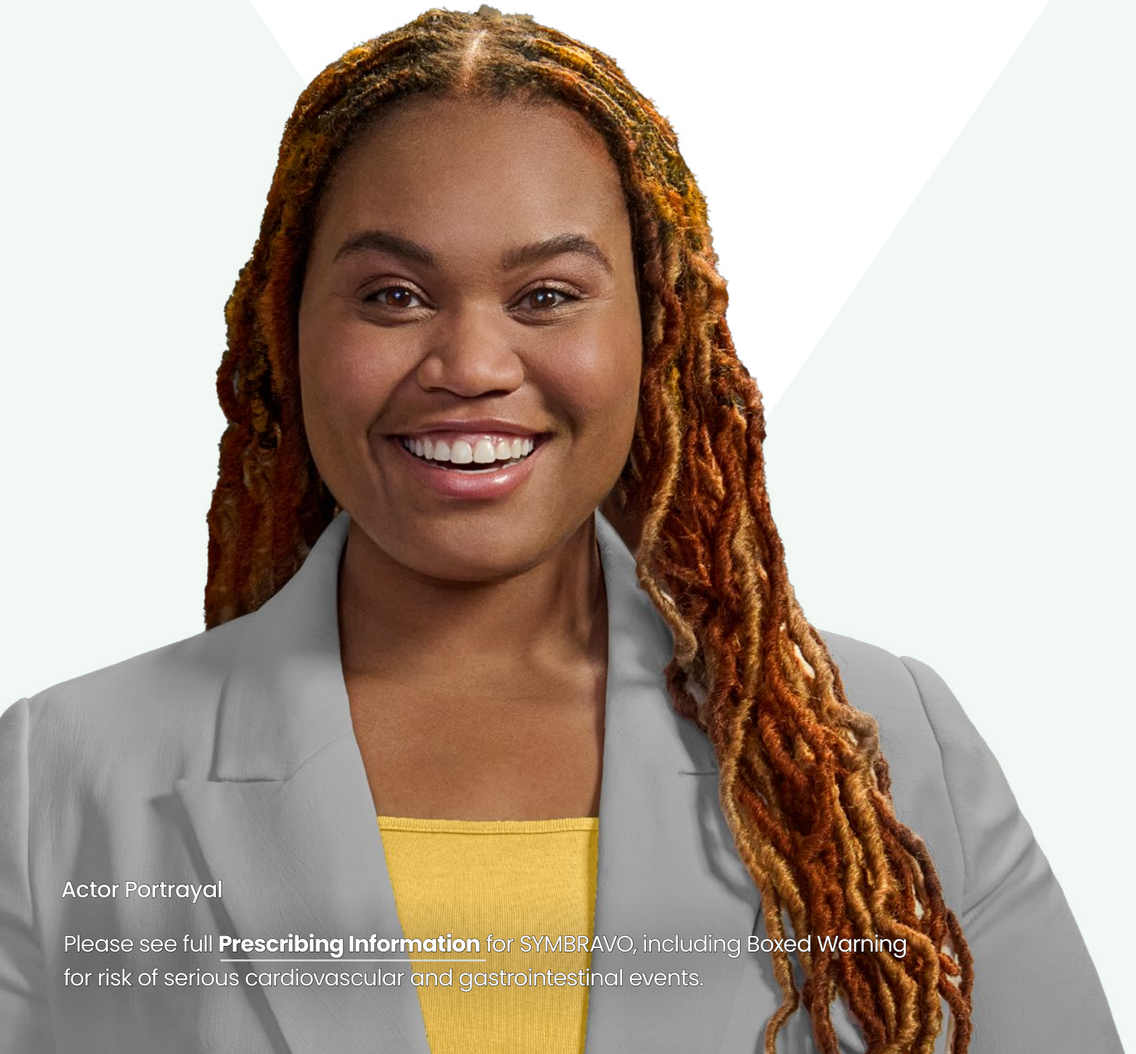
SYMBRAVO®
(meloxicam and rizatriptan)
**20 mg/10 mg** tablets



Actor Portrayal

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

# Quick Start Guide

**Things you need to know about the SYMBRAVO Coverage Process.**

axsome®

**Click Here** to learn more about Axsome

# Prior Authorization: Reference Information

This section outlines potential PA submission or Step Edit requirements for patients starting on Symbravo. A Medical Necessity Letter may also be required during formulary placement review or if Symbravo is not covered.

## 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.

## IMPORTANT SAFETY INFORMATION

**WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS**

- **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.**
- **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.**

## ICD-10 codes for Migraine:

| | |
|---|---|
| G43 | Migraine |
| G43.0 | Migraine without aura |
| G43.1 | Migraine with aura |

ICD-10=International Classification of Diseases, Tenth Revision

*Please refer to the Important Safety Information on page 10.

**Disclaimer:** These codes are presented for informational purposes only. They represent no statement, promise, or guarantee by Axsome concerning coverage and/or levels of reimbursement, payment, or charge and are not intended to increase or maximize reimbursement by any payer. It is the responsibility of the healthcare providers to determine the appropriate code(s) for service provided to their patients. Laws, regulations, and policies concerning reimbursement are complex and updated frequently. Although we have made an effort to be current as of May 2025, the information may not be current or comprehensive when you view it. Please consult the applicable payer organization with regard to local or actual coverage, reimbursement policies, and determination process.

# Steps in the PA Process

## Is a PA required? Here's what to do.

### Step 1

#### Complete PA Request

- **Obtain the proper PA form for the specific health plan.**
  - *You may start a PA request through CoverMyMeds.*
- **It is important to fill out the form completely.**
- **Missing information can lead to a PA rejection.**
- **Prepare supplemental documents to justify the use of Symbravo.**

Documents required are unique to each health plan but may include:

- **Patient clinical notes**
- **Clinical studies or peer-reviewed journal articles stating medical effectiveness**

### Step 2

#### Submit the PA Request

Choose to submit all information, including supplemental documents, by phone, fax, email, CoverMyMeds, or the health plan's website (see form for this info).

- **Keep a copy of everything you submit with the request for reference.**

### Step 3

#### Track the Status of the Request

Keep a detailed log of all PA submissions and denials for each patient.

### Step 4

#### Follow Up as Needed

Submit any additional documentation requested as soon as possible.

**Remember:**
Upon PA approval, reauthorization may be required after 6-12 months.

This information is provided for reference only.
HCP is solely responsible for the completion, accuracy, and submission of PA request.

covermymeds®

**Questions? CoverMyMeds can help.**
**Live support available:**
1-866-452-5017 or chat at covermymeds.com
**Resources:**
go.covermymeds.com/help

#### Prior Authorization Support

- Offers a streamlined process for submitting PA requests
- Available at no cost to providers and their staff
- Receive faster PA determinations, often in real time*
- Submit requests for any medication and all plans

*compared to phone and fax

**Need more information?**
Visit **www.symbravohcp.com/samples-support** for resources, such as:

**Digital Version of This Quick Reference Guide**
**PA Appeals Letter Template**
**Letter of Medical Necessity Template**
**Formulary Exception Letter Template**



Need full Symbravo prescribing information? Visit: www.axsome.com/symbravo-prescribing-information.pdf
Please see Important Safety Information for SYMBRAVO at the end of this document and full Prescribing Information, including Boxed Warning for risk of serious cardiovascular and gastrointestinal events.

# The minimum information required for most PAs

## Step 1

### Provide the appropriate medical and dosing information

Below is the usual dosing for Symbravo. Check the patient's prescription and medical history to determine necessary modifications.

**Indication:**
See page 2 for indication and ICD-related information.

**National Drug Code (NDC):**
81968-020-09

**Medication and Strength:**
Symbravo (meloxicam and rizatriptan) 20mg/10mg

**Frequency/Directions for Use:**
1 tablet PO daily as needed

**Quantity:** 9

PO=by mouth

## Step 2

### Check history of patient's previous therapies

Below are the most commonly prescribed generics that may satisfy Step Edit requirements:

- **Sumatriptan**
- **Rizatriptan**
- **Zolmitriptan**
- **Naratriptan**
- **Eletriptan**
- **Almotriptan**
- **Frovatriptan**
- **sumatriptan/naproxen**

Refer to patient notes for additional information, such as specific dates within the "lookback period" that the patient was on the medication and reasons why the patient switched therapies.

## Step 3

### Common mistakes during initial PA submission

- Incorrect or missing diagnosis information
- Incomplete PA fields or missing information, such as prior treatment failures
- Incomplete list of all prior therapies and any appropriate chart notes

**Disclaimer:** The completion, accuracy, and submission of this form is the sole responsibility of the healthcare provider.

# Receive a PA Denial?

## This could be why:

- Incomplete or inaccurate information on the PA form. (this is the #1 reason, so check this carefully!)
- Clinical reasons regarding medical necessity of Symbravo, which may require additional information.
- Patients have not fulfilled the step therapy requirement of trying and failing a required medication.

## Proving Medical Necessity

Visit **www.symbravohcp.com/samples-support** for the following resources:

**Letter of Medical Necessity Template for Symbravo**

## Next steps if the PA is denied

- Appeal the decision by contacting the health plan directly to have a peer-to-peer discussion regarding the patient, clinical issues, and reasons for requesting Symbravo.
- If a phone call isn't possible, you may submit an appeal. Visit **www.symbravohcp.com/samples-support** for the following resources:

**PA Appeals Letter Template**

**Formulary Exception Letter Template**

*CoverMyMeds may also provide possible next steps for a denied PA.*

Actor Portrayal

This information is provided for reference only.
HCP is solely responsible for the completion, accuracy, and submission of PA request.

# Guidance for Insurance Letters

## Tips for Developing a Letter of Appeal

**Summarize the background and status of your patient's condition**

- Cite diagnostic evidence of migraine, including baseline functional exam results
- List their current and prior treatment(s) and reasons why it is not sufficient, including any side effects, lack of response, or disease progression

**Review the health plan's denial and justify why you believe Symbravo is the appropriate treatment for your patient**

- Address the details of the denial and provide clinical justification that supports its repeal, citing any relevant literature and documentation

**If denied due to incomplete information, review the health plan's criteria to ensure everything is provided**

**If denied due to absence of plan's preferred formulary agents** (including completion of step therapy or formulary exclusions), provide clinical rationale for why these agents aren't appropriate for the patient

- Address each specific preferred agent in the denial
- Include documentation of any prior trial/failures with required formulary alternatives
- Provide relevant medical notes supporting clinical rationale for not prescribing preferred alternatives

### When submitting the appeal, follow these steps:

**Step 1**
Populate the template as medically appropiate

**Step 2**
Delete any specific instructions for completion, disclaimers, trademarks, and document numbers

**Step 3**
Submit the letter of appeal with the appropiate appeal form and any supplemental documents

The content in this document is not an attempt to provide specific guidance. It is merely for your consideration and review. Please make all changes that you believe to be appropriate or disregard as needed. The medical professional is ultimately responsible for the accuracy and completeness of all claims submitted to third-party payers. Please see the FDA-approved label for information relevant to any prescribing decisions.

Fields required for customization are in blue text in brackets.

Please place template on official letterhead (if applicable).

<Date>
**ATTENTION:** <Medical Director Name and/or Medical Review/Appeals>
<Payer/Health Plan Name>
<Payer Address>

Ensure health plan information is correct. This can be found on the appeal form or the health plan's website.

**REGARDING:** Denied Claim for Symbravo® (meloxicam and rizatriptan)
**PATIENT NAME:** <Patient Name>
**DATE OF BIRTH:** <Patient Date of Birth>
**POLICY ID NUMBER:** <Patient Policy ID Number>
**PROVIDER ID NUMBER:** <Provider ID Number>
<Optional: Claim rejection number>

Fill out the patient information completely and accurately. Ensure the policy ID number matches the patient's insurance card.

Please provide claim rejection number (if applicable).

Dear <Health Plan Contact Name>:

I am writing to appeal the denied claim for SYMBRAVO for my patient, <Patient Name>, for which the reason for denial was <quote the specific reason for denial in denial letter>. As a <board-certified medical specialty> (<NPI>), I have prescribed SYMBRAVO due to my patient being diagnosed with <migraine> <migraine without aura> <migraine with aura> <migraine with typical aura> and consider this choice of treatment as the appropriate option for my patient.

It's important to understand and state the reason for denial specifically. If it's unclear, you can call and speak to the health plan directly.

Attached to this request are clinical notes regarding this patient's disease state and the SYMBRAVO package insert.

SYMBRAVO is indicated for the acute treatment of migraine with or without aura in adults. The following is the medical history of <Patient Name> and the rationale for treatment with SYMBRAVO.

| | |
|---|---|
| **Date of Diagnosis** | <MM/DD/YY> |
| **Diagnosis** | <ICD-10 code> |
| **Summary of clinical symptoms** | • <Patient's current condition, including an overview of symptoms and quality of life or functional impairment as applicable><br>• <Test information & results><br>• <Prognosis without treatment> |
| **Previous and current treatment regimens** | <If applicable, include previous and current pharmacologic treatments for migraine, including drug name, dates of use, and reasons for stopping> |

Fill out the table with objective, patient-specific information.

<Restate the denial reason and your clinical rationale for why the denial should be overturned and why SYMBRAVO is medically necessary for this patient.>

Only include rationale addressing the specific denial reason. Excess information may influence payer to deny coverage again.

Thank you for taking the time to read this letter. I believe treatment with SYMBRAVO is appropriate for this patient. Please feel free to contact me for any additional information you may require. I look forward to your prompt review of this request.

Best regards,

<Physician Signature>
<Physician Name>
<Physician's NPI>
<Physician Contact Information>
<Phone #>
<Fax #>

Include your office/clinic's phone number, fax number, and email.

**ATTACHMENTS:**
• SYMBRAVO package insert/prescribing information
• Patient clinical notes and other relevant supporting documentation

Update the list of attachments to only include documents being sent with the request.

Visit **www.symbravohcp.com/samples-support** to download this sample letter.

# Tips for Developing a Letter of Medical Necessity

**Summarize the background and status of your patient's condition**

- Cite diagnostic evidence of migraine, including baseline functional exam results
- List their current and prior treatments and provide reasons why it is not sufficient, including any side effects, lack of response, or disease progression

**Justify why you believe Symbravo is the appropriate treatment for your patient**

- Provide clinical justification supporting Symbravo treatment for your patient, citing any relevant literature
- State any patient-specific reasons for the treatment choice, such as expected effect of treatment
- Review the health plan's criteria. Point out the specific criteria your patient meets and reasons for exclusion from those they don't

**Provide additional documentation that supports your decision**

- Review the health plan's requirements to ensure that all requested information is incorporated. This may include:
  - Patient clinical notes, such as relevant medical records and treatment history
  - Clinical studies or peer-reviewed journal articles documenting the medical effectiveness of Symbravo

## When submitting the letter, follow these steps:

**Step 1**
Populate the template as medically appropiate

**Step 2**
Delete any specific instructions for completion, disclaimers, trademarks, and document numbers

**Step 3**
Submit the letter of medical necessity with the appropiate form for the PA request and any supplemental documents

For independent consideration and review, please make all changes that you believe to be appropriate or disregard these suggestions in their entirety. The medical professional is ultimately responsible for the accuracy and completeness of all claims submitted to third-party payers. Please see the FDA-approved label for information relevant to any prescribing decisions.

All bracketed blue text is a required customization field.

Please place template on official letterhead (if applicable).

<Date>
**ATTENTION:** <Medical Director Name and/or Medical Review/Appeals>
<Payer/Health Plan Name>
<Payer Address>

Reference the health plan's appeal form or website to ensure all information is correct.

**REGARDING:** Request for Medical Necessity for Symbravo® (meloxicam and rizatriptan) tablets
**PATIENT NAME:** <Patient Name>
**DATE OF BIRTH:** <Patient Date of Birth>
**POLICY ID NUMBER:** <Patient Policy ID Number>
**PROVIDER ID NUMBER:** <Provider ID Number>
<Optional: Claim rejection number>

Fill out the patient information completely and accurately. Ensure the policy ID number matches the patient's insurance card.

Please provide claim rejection number (if applicable).

Dear <Health Plan Contact Name>:

I am writing this letter of medical necessity in support of my request to treat <Patient Name> with SYMBRAVO for the treatment of <migraine> <migraine without aura> <migraine with aura> <migraine with typical aura> in adults.

As a <board-certified> <Field of Certification> with <##> years caring for patients with acute migraine, I believe that treatment with SYMBRAVO is warranted, appropriate, and medically necessary for this patient based on my clinical judgment and expertise.

It's important to understand and state the reason for denial specifically. If it's unclear, you can call and speak to the health plan directly.

The following is the medical history of <Patient Name> and the rationale for treatment with SYMBRAVO. I have also attached to this letter the clinical findings that summarize my patient's current medical condition and the SYMBRAVO package insert/prescribing information.

| | |
|---|---|
| **Date of Diagnosis** | <MM/DD/YY> |
| **Diagnosis** | <ICD-10 code> |
| **Summary of clinical symptoms** | • <Patient's current condition, including an overview of symptoms and quality of life or functional impairment as applicable><br>• <Test information & results><br>• <Prognosis without treatment> |
| **Previous and current treatment regimens** | <If applicable, include previous and current pharmacologic treatments for migraine, including drug name, dates of use, and reasons for stopping> |

Fill out the table with objective, patient-specific information.

I would like to prescribe SYMBRAVO for <Patient Name> because I have concluded that it is a medically appropriate and necessary therapeutic option for the following reason(s):

<Rationale for treating the patient with SYMBRAVO. In this rationale, include a description of the patient's disease state, treatment history, comorbid health issues, and any other factors that have influenced your treatment decision.>

Only include rationale addressing the specific denial reason. Excess information may influence payer to deny coverage again.

<You may wish to include relevant background or clinical trial information about SYMBRAVO in the letter. For additional information, please refer to the SYMBRAVO Prescribing Information.>

Strengthen your request by including clinical trial information about Symbravo, specifically in similar patient populations.

Given the patient's history, <his/her/their> current condition, and the data of the effects of SYMBRAVO in patients with migraine, I believe that treatment of <Patient Name> with this product is warranted, appropriate, and medically necessary. The totality of the data available to date supports the potential benefit of <treatment/continuing treatment> with SYMBRAVO.

Please feel free to contact me at my office at <telephone number> if I can provide you with any additional information you may require. I look forward to receiving your timely response.

Choose the correct language based on whether your patient is initiating or continuing treatment with Symbravo.

Best regards,

<Physician Signature>
<Physician Name>
<Physician's NPI>
<Physician Contact Information>
<Phone #>
<Fax #>

Include your office/clinic's phone number, fax number, and email.

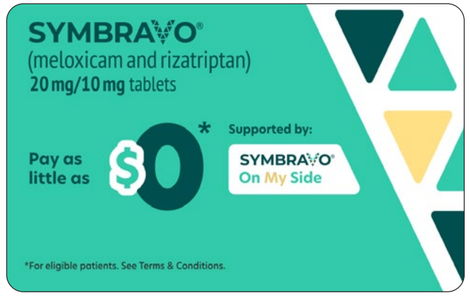
**ATTACHMENTS:**
- SYMBRAVO package insert/prescribing information
- Patient clinical notes and other relevant supporting documentation

Please update the list of attachments to only include documents being sent with the request.

Visit **www.symbravohcp.com/samples-support** to download this sample letter.

# Symbravo On My Side Program

Symbravo On My Side is a comprehensive patient support program designed to help patients get the most out of their treatment.




## How Your Patients Can Get a Savings Card

The easiest way for a patient to receive a savings card is by visiting **Symbravo.com/Savings** to download the Symbravo On My Side savings card.

**SYMBRAVO®(meloxicam and rizatriptan) Co-Pay Terms and Conditions**

This SYMBRAVO Co-Pay Assistance Program is designed to assist eligible commercially insured patients who have been prescribed an Axsome medicine for an FDA-approved indication.

**Patient Benefit:**

- Eligible patients will pay as little as $0 with a valid prescription for an FDA-approved indication; monthly, annual, and/or per-claim maximum program benefits may apply and vary depending on the patients specific terms of their prescription drug plan and to ensure that the funds are used for the benefit of the patient, based on factors determined by Axsome.

**Program Eligibility Requirements and Benefits:**

- Patients must have commercial (private) health insurance. This program is not valid where the entire cost of the medication is reimbursed by insurance or where insurance does not cover the medication.
- Offer not valid for patients with prescription insurance through federal or state healthcare programs, including but not limited to, Medicaid, Medicare drug benefit plan, Tricare, or other federal or state health programs (such as medical assistance programs).
- Some prescription drug plans have implemented programs commonly known as "co-pay maximizer" or "accumulator" programs. These programs adjust the patient's out-of-pocket cost to reflect the availability of financial support received from a co-pay support program, so that out-of-pocket payments that are subsidized by a manufacturer's co-pay program are not treated as a patient's out-of-pocket payments. Patients enrolled in these types of programs may receive benefits from the Axsome Co-Pay Savings Program that vary over time to ensure funds are used for the benefit of the patient.
- Cash-paying patients are not eligible for co-pay assistance.
- This offer may not be redeemed for cash.
- Patient must be a resident of the United States or U.S. territories.
- Patient or patient's guardian must be 18 years of age or older.
- Patients with questions about the SYMBRAVO On My Side Savings Offer should please call 1-800-805-8621.

**Additional Terms & Conditions of Program:**

- By using this offer, the patient and pharmacist certify that the patient meets the eligibility criteria and will comply with all the terms and conditions.
- Cash Discount Cards and other non-insurance plans are not valid as primary insurer under this offer. If the patient is eligible for drug benefits under any such program, the patient cannot use this offer.
- This offer is not transferable and is limited to one offer per patient. This co-pay offer cannot be combined with any other savings, free trial, or similar offer(s) for the specified prescription.
- Void where prohibited by law. Not valid if reproduced.
- **This program is not insurance.**
- Axsome Therapeutics reserves the right to rescind, revoke, or amend this offer without notice at any time.

**To the Pharmacist:**

- When you apply this offer, you are certifying that you have not submitted a claim for reimbursement under any federal, state, or other governmental programs for this prescription.
- Participation in this program must comply with all applicable laws and regulations as a pharmacy provider. You are certifying that you will comply with the terms and conditions described in the Restrictions section.
- **For commercially insured/covered claims: 1.** Submit the claim to the primary Third-Party Payer first. **2.** Submit the balance due to McKesson as a secondary claim with Other Coverage Code 08.
- **For commercially insured/not covered claims: 1.** Submit the claim to the primary Third-Party Payer first. **2. If the primary claim response shows a prior authorization is required, please initiate the appropriate prior authorization process before proceeding with processing. 3.** If the claim is not covered by the primary Third-Party Payer, submit a secondary claim to McKesson with Other Coverage Code 03.
- For any questions regarding McKesson online processing, please call the Help Desk at 1-888-215-8370.

**By using this card, you and your pharmacist understand and agree to comply with these eligibility requirements and terms of use.**

Please see **Important Safety Information** for SYMBRAVO at the end of this document and **full Prescribing Information**, including Boxed Warning for risk of serious cardiovascular and gastrointestinal events.

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

# Learn More

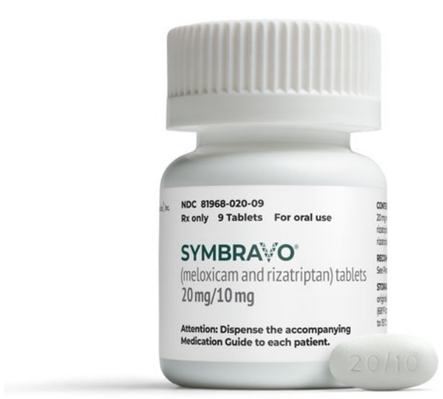
## Symbravo® (meloxicam and rizatriptan) tablets

Symbravo is a combination of meloxicam (an NSAID) and rizatriptan (a serotonin [5-HT] 1B/1D receptor agonist [triptan]), indicated for the acute treatment of migraine with or without aura in adults.

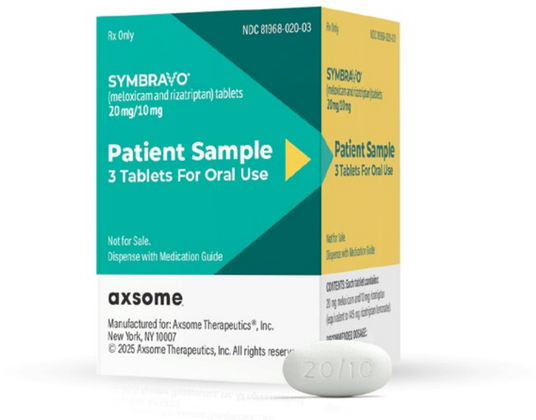
### How Is Symbravo Supplied?

Symbravo tablets are white, modified capsule-shaped, film-coated, and debossed with "MXRZ" on one side and "20/10" on the other. Symbravo is supplied in the following package configuration: Meloxicam 20 mg and rizatriptan 10 mg bottles of 9 tablets.

NDC Number (9-count bottle)
NDC 10: 81968-020-09
NDC 11: 81968-0020-09




Example of a 9-count bottle




Example of a sample package

### Need to order samples?

**Two Ways to Request Symbravo Samples**
(if regulations in your state allow the use of samples)

**1. If you're not registered**

**Contact your sales representative.**

**2. If you're already registered**

Log in to the ordering portal at **axsomehcpsamples.qpharmacorp.com/** to place your order.

Have questions or need to register for access?

Please contact Axsome@qpharmacorp.com or call 973-644-2378.

### Pharmacy Ordering Questions:

If your pharmacy needs to order Symbravo stock, it may contact its preferred distributor below to order.

- **Anda Inc.**
  [www.andanet.com] 1-800-647-0575
- **Cencora**
  [www.cencora.com] 1-877-679-8835
- **Cardinal Health**
  [www.cardinalhealth.com] 1-800-926-3161
- **Dakota Drug Inc.**
  [www.dakdrug.com] 1-866-210-5887
- **Louisiana Wholesale Drug Co.**
  [www.lwdrx.com] 1-800-960-3784
- **McKesson**
  [www.mckesson.com]
  - Independent Pharmacies: 1-855-625-7385
  - Retail National Account: 1-855-625-6285
  - Hospitals & Health Systems: 1-855-625-4677
- **Morris & Dickson Co.**
  [www.morrisdickson.com] 1-800-388-3833
- **Mutual Drug**
  [www.mutualdrug.com] 1-800-800-8551
- **Smith Drug Co.**
  [www.smithdrug.com]
  - Spartanburg, SC: 1-800-542-1216
  - Paragould, AR: 1-866-346-9147
  - Carey, OH: 1-833-570-1757
  - Milton, VT: 1-800-338-8703
- **Value Drug Co.**
  [www.valuedrugco.com] 1-800-252-3786





Need full Symbravo prescribing information? Visit: **www.axsome.com/symbravo-prescribing-information.pdf**

Please see **Important Safety Information** for SYMBRAVO at the end of this document and **full Prescribing Information**, including Boxed Warning for risk of serious cardiovascular and gastrointestinal events.

## 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

**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%).

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

SYM HCP ISI 03/2025

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

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