once-daily ZEPOSIA® (ozanimod) | 0.92 mg capsules

ZEPOSIA—FOCUSED ON WHAT COUNTS

Based on the full Prescribing Information, ZEPOSIA Is the First and Only S1P With No First-Dose Observation Required

A Different S1P That Lets Patients Start as Soon as Today[1-3]

✗ **NO** First-Dose Observation Required ✗ **NO** Genetic Testing Required ✗ **NO** Ophthalmic Testing Required for Most Patients[4a]

Required Assessments Prior to Initiating ZEPOSIA[1]

- Obtain a **CBC** (within 6 months or after discontinuation of prior MS therapy), including lymphocyte count
- Obtain an **ECG** to determine whether preexisting conduction abnormalities are present
- Obtain **transaminase and bilirubin levels** (within 6 months)
- Evaluate **current and prior medications**
- Patients without a confirmed history of VZV or without documented VZV vaccination should be tested for antibodies. If VZV or other live attenuated **immunizations** are required, administer at least 1 month prior to initiation

An up-titration schedule should be used to reach the maintenance dose, as a transient decrease in heart rate and AV conduction delays may occur[1]

- **Single maintenance dose** of 0.92 mg for all patients
- **If a dose is missed within the first 2 weeks** of treatment, re-initiate with the titration regimen
- If a dose is missed **after the first 2 weeks** of treatment, continue with the treatment as planned

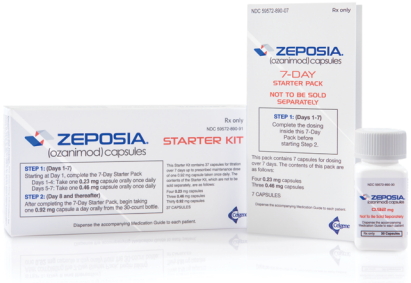
The mean (CV%) plasma half-life ($t_{1/2}$) of ZEPOSIA was approximately 21 hours (15%).[1]

The mean (CV%) effective half-life ($t_{1/2}$) of the active metabolite CC112273 was approximately 11 days.[1]

One Capsule, Once a Day, From the Start[1]

ZEPOSIA 7-DAY TITRATION SCHEDULE

DAYS 1-4	DAYS 5-7	DAY 8
0.23 mg	0.46 mg	0.92 mg



Learn more at **ZEPOSIAhcp.com**

[a]Diabetes mellitus and uveitis increase the risk of macular edema; patients with a history of these conditions should have an ophthalmic evaluation of the fundus, including the macula, prior to treatment initiation. A prompt ophthalmic evaluation is recommended if there is any change in vision while taking ZEPOSIA.[1]

AV=atrioventricular; CBC=complete blood count; ECG=electrocardiogram; S1P=sphingosine-1-phosphate; VZV=varicella-zoster virus.

INDICATION

ZEPOSIA is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

IMPORTANT SAFETY INFORMATION

Contraindications:

- Patients who in the last 6 months, experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III/IV heart failure or have a presence of Mobitz type II second or third-degree atrioventricular (AV) block, sick sinus syndrome, or sino-atrial, unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients taking a monoamine oxidase (MAO) inhibitor

Infections: ZEPOSIA may increase the susceptibility to infections. Life-threatening and rare fatal infections have occurred in patients receiving ZEPOSIA. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS therapy) complete blood count (CBC) including lymphocyte count before initiation of ZEPOSIA. Delay initiation of ZEPOSIA in patients with an active infection until the infection is resolved. Consider interruption of treatment with ZEPOSIA if a patient develops a serious infection. Continue monitoring for infections up to 3 months after discontinuing ZEPOSIA

Please see Important Safety Information throughout and full Prescribing Information and Medication Guide.

Support for Your Patients Every Step of the Way

ZEPOSIA 360 Support™ Can Help Appropriate Patients Start and Stay on Therapy

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ZEPOSIA 360 Support™ Program—Services for Patients

Pre-Initiation Support

- **Pre-Initiation Testing Assistance**—includes comprehensive baseline testing[a]

Access Support

- **Access Assistance**—help with Benefits Investigation, Prior Authorization (PA), and Appeals

Financial Support

- **Third-Party Referrals**—suggestions for independent third-party foundations that may be able to assist with treatment costs

Dedicated **Nurse Navigators** provide a consistent point of contact for your patients taking ZEPOSIA

ZEPOSIA Bridge Program

a free supply of ZEPOSIA for up to 24 months to qualified, commercially insured patients who are at risk of an interruption in therapy[b]

- Up to **24 months of ZEPOSIA for $0**, as long as program eligibility rules are being met

Co-Pay Assistance Program

Pay as little as $0

helps patients with co-pay costs, including prescription and medical assessment/initiation costs[c]

- **Prescription Benefits**—eligible patients pay as little as $0 in out-of-pocket costs for their ZEPOSIA prescription
- **Medical Benefits**—commercially insured patients can be fully reimbursed for any out-of-pocket costs associated with medical assessments (required pre-initiation testing, such as blood tests and baseline heart tests)

IMPORTANT SAFETY INFORMATION (CONTINUED)

Infections (Continued):

- Herpes zoster was reported as an adverse reaction in ZEPOSIA-treated patients. Herpes simplex encephalitis and varicella zoster meningitis have been reported with sphingosine 1-phosphate (S1P) receptor modulators. Patients without a healthcare professional-confirmed history of varicella (chickenpox), or without documentation of a full course of vaccination against varicella zoster virus (VZV), should be tested for antibodies to VZV before initiating ZEPOSIA. A full course of vaccination for antibody-negative patients with varicella vaccine is recommended prior to commencing treatment with ZEPOSIA
- Cases of fatal cryptococcal meningitis (CM) were reported in patients treated with another S1P receptor modulator. If CM is suspected, ZEPOSIA should be suspended until cryptococcal infection has been excluded. If CM is diagnosed, appropriate treatment should be initiated.
- Progressive Multifocal Leukoencephalopathy (PML) is an opportunistic viral infection of the brain that typically occurs in patients who are immunocompromised, and that usually leads to death or severe disability. No cases of PML were identified in active-controlled MS clinical trials with ZEPOSIA. PML has been reported in patients treated with S1P receptor modulators and other MS therapies and has been associated with some risk factors. If PML is suspected, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued

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Additional Services for Your Patients

ZEPOSIA 360 Support™ Can Help You Keep Appropriate Patients on Therapy

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ZEPOSIA 360 Support™ Program—Additional Services

Ongoing Support

- Payer Policy Research
- Ongoing Reverification of Benefits
- Shipment Coordination/Tracking

Support Coordinators

- Insurance Information and Support
- Regionally Assigned Points of Contact

AssistRx

AssistRx is a third-party service that simplifies patient access, provides resources, and accelerates time to therapy. Services are offered through a provider portal.

covermymeds®

CoverMyMeds offers electronic Prior Authorization (ePA) support.
A prescriber-facing ePA is available for locating, submitting, and tracking PAs and pre-certifications.

[a]For patients with commercial coverage in all states except MA, MN, and RI.

[b]The Bridge Program is available at no cost for eligible commercially insured, on-label diagnosed patients if there is a delay in determining whether commercial prescription coverage is available, and is not contingent on any purchase requirement. The Bridge Program is not available to patients who have prescription insurance coverage through Medicare, Medicaid, or any other federal or state program, or MA or MI residents, and is available for no more than 6 months (180 days) to patients in MN and RI. Appeal of any prior authorization denial must be made within 90 days or as per payer guidelines, to remain in the Program. Eligibility will be re-verified in January for patients continuing into the following year, and may be at other times during Program participation. Up to 12 additional refills may be provided if needed. Offer is not health insurance, and may be modified or discontinued at any time without notice. Other limitations may apply.

[c]Depending on insurance coverage and where the full cost is not covered by patient's insurance, eligible patients may receive a prescription benefit offer for out-of-pocket drug costs and pay as little as $0 per prescription, as well as a medical assessment benefit offer for out-of-pocket costs for the initial blood tests and ECG screening. Maximum savings limit applies; patient out-of-pocket expenses may vary. This program is not health insurance. Offer not valid for patients enrolled in Medicare, Medicaid, or other federal or state health care programs. Please visit ZEPOSIA.com/copayterms for Program Terms, Conditions, and Eligibility Criteria. Medical co-pay benefit not available for residents of MA, MI, MN, and RI.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Infections (Continued)**:**

- In clinical studies, patients who received ZEPOSIA were not to receive concomitant treatment with antineoplastic, non-corticosteroid immunosuppressive, or immune-modulating therapies used for treatment of MS. Concomitant use of ZEPOSIA with any of these therapies would be expected to increase the risk of immunosuppression. When switching to ZEPOSIA from immunosuppressive medications, consider the duration of their effects and their mode of action to avoid unintended additive immunosuppressive effects
- Use of live *attenuated* vaccines should be avoided during and for 3 months after treatment with ZEPOSIA. If live *attenuated* vaccine immunizations are required, administer at least 1 month prior to initiation of ZEPOSIA

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IMPORTANT SAFETY INFORMATION (CONTINUED)

Bradyarrhythmia and Atrioventricular Conduction Delays: Since initiation of ZEPOSIA may result in a transient decrease in heart rate and atrioventricular conduction delays, dose titration is recommended to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater decreases in heart rate. If treatment with ZEPOSIA is considered, advice from a cardiologist should be sought for those individuals:

- with significant QT prolongation
- with arrhythmias requiring treatment with Class 1a or III anti-arrhythmic drugs
- with ischemic heart disease, heart failure, history of cardiac arrest or myocardial infarction, cerebrovascular disease, and uncontrolled hypertension
- with a history of Mobitz type II second-degree or higher AV block, sick-sinus syndrome, or sinoatrial heart block

Liver Injury: Elevations of aminotransferases may occur in patients receiving ZEPOSIA. Obtain liver function tests, if not recently available (i.e., within 6 months), before initiation of ZEPOSIA. Patients who develop symptoms suggestive of hepatic dysfunction should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Caution should be exercised when using ZEPOSIA in patients with history of significant liver disease

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. Based on animal studies, ZEPOSIA may cause fetal harm. Women of childbearing potential should use effective contraception to avoid pregnancy during treatment and for 3 months after stopping ZEPOSIA

Increased Blood Pressure: Increase in systolic pressure was observed after about 3 months of treatment and persisted throughout treatment. Blood pressure should be monitored during treatment and managed appropriately. Certain foods that may contain very high amounts of tyramine could cause severe hypertension in patients taking ZEPOSIA. Patients should be advised to avoid foods containing a very large amount of tyramine while taking ZEPOSIA

Respiratory Effects: ZEPOSIA may cause a decline in pulmonary function. Spirometric evaluation of respiratory function should be performed during therapy, if clinically indicated

Macular edema: S1P modulators have been associated with an increased risk of macular edema. Patients with a history of uveitis or diabetes mellitus are at increased risk. Patients with a history of these conditions should have an ophthalmic evaluation of the fundus, including the macula, prior to treatment initiation and regular follow-up examinations. An ophthalmic evaluation is recommended in all patients at any time if there is a change in vision. Continued use of ZEPOSIA in patients with macular edema has not been evaluated; potential benefits and risks for the individual patient should be considered if deciding whether ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): Rare cases of PRES have been reported in patients receiving a S1P receptor modulator. If a ZEPOSIA-treated patient develops unexpected neurological or psychiatric symptoms or any symptom/sign suggestive of an increase in intracranial pressure, a complete physical and neurological examination should be conducted. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. Delay in diagnosis and treatment may lead to permanent neurological sequelae. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Unintended Additive Immunosuppressive Effects From Prior Immunosuppressive or Immune-Modulating Drugs: When switching from drugs with prolonged immune effects, the half-life and mode of action of these drugs must be considered to avoid unintended additive immunosuppressive effects while at the same time minimizing risk of disease reactivation. Initiating treatment with ZEPOSIA after treatment with alemtuzumab is not recommended

Severe Increase in Disability After Stopping ZEPOSIA: Severe exacerbation of disease, including disease rebound, has been rarely reported after discontinuation of a S1P receptor modulator. The possibility of severe exacerbation of disease should be considered after stopping ZEPOSIA treatment so patients should be monitored upon discontinuation

Immune System Effects After Stopping ZEPOSIA: After discontinuing ZEPOSIA, the median time for lymphocyte counts to return to the normal range was 30 days with approximately 90% of patients in the normal range within 3 months. Use of immunosuppressants within this period may lead to an additive effect on the immune system, therefore caution should be applied when initiating other drugs 4 weeks after the last dose of ZEPOSIA

Most common Adverse Reactions (≥ 4%): upper respiratory infection, hepatic transaminase elevation, orthostatic hypotension, urinary tract infection, back pain, and hypertension.

Please see Important Safety Information throughout and full Prescribing Information and Medication Guide.

References: 1. ZEPOSIA. Prescribing information. Bristol Myers Squibb; 2020. **2.** Gilenya. Prescribing information. Novartis Pharmaceuticals Corporation; 2019. **3.** Mayzent. Prescribing information. Novartis Pharmaceuticals Corporation; 2019. **4.** Marrie RA. Comorbidity in multiple sclerosis: implications for patient care. *Nat Rev Neurol*. 2017;13(6):375-382. doi:10.1038/nrneurol.2017.33

Bristol Myers Squibb is committed to transparency. For information on the list price of ZEPOSIA as well as information regarding average out-of-pocket costs and assistance programs, please visit our pricing information page at ZEPOSIA.com/cost.

Bristol Myers Squibb™