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

ZEPOSIA INITIATION AND SUPPORT

INDICATIONS

ZEPOSIA® (ozanimod) is indicated for the treatment of:

1. Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
2. Moderately to severely active ulcerative colitis (UC) in adults.

IMPORTANT SAFETY INFORMATION

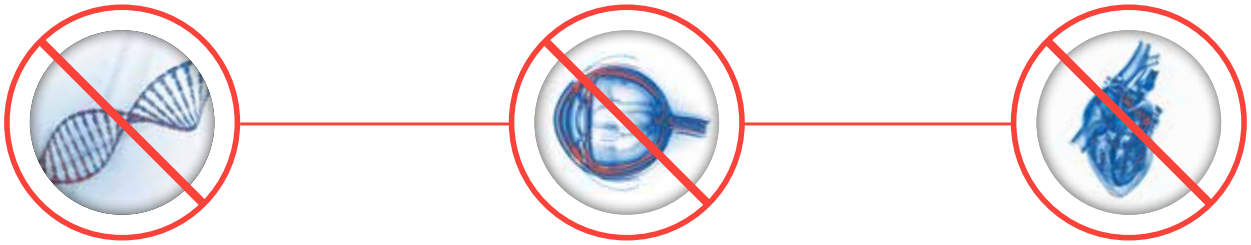
Contraindications:

- 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-degree or third-degree atrioventricular (AV) block, sick sinus syndrome, or sino-atrial block, unless the patient has a functioning pacemaker

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

One Capsule, Once a Day, From the Start With Minimal Pre-Initiation Requirements[1]

Full Prescribing Information for ZEPOSIA Has



NO
Genetic Testing

NO
Ophthalmic Testing for Most Patients[1,2,a]

NO
First-Dose Observation Required

Minimal Pre-Initiation Requirements

Before Initiating Treatment With ZEPOSIA...

- 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**[1]
- 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[1]

[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; VZV=varicella zoster virus.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Contraindications (Continued)**:**

- 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 or UC 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.

ZEPOSIA 7-Day Titration Schedule

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

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 ~11 days[1]

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]

Learn more at **ZEPOSIAhcp.com/MS**

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.

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

ZEPOSIA 360 Support™ to Help Prescribed Patients Every Step of the Way

Nationwide, Over 90% of Patients With Commercial Coverage Have Access to ZEPOSIA*

ZEPOSIA Starter Kit

- **Free ZEPOSIA Starter Kit for Eligible Patients**[a]—which includes a 7-day starter pack along with an initial maintenance supply

Access Support

- **Electronic start form** and **prior authorization submissions** available through covermymeds®[†]
- **Access Assistance**—help with benefits investigation, prior authorization (PA), and appeals

Pre-Initiation Support

- **Assistance with baseline assessments**—including **in-home services** with scheduling and appointments available **7 days a week nationwide** for eligible, commercially insured patients[b,c]

24-Month Bridge Program

- A free supply of ZEPOSIA for up to 24 months for eligible, commercially insured patients if there is a delay or denial in coverage[d]

Co-Pay Assistance Program: May Pay as Little as $0

- Helps patients with co-pay costs, including prescription and medical benefits where eligible commercially insured patients may pay as little as $0 for their prescription and can be reimbursed for out-of-pocket costs associated with pre-initiation testing[c]

Local, Dedicated Support

- **Local, dedicated support** through an Access and Reimbursement Manager (ARM) team, along with dedicated **Nurse Navigators**[‡] available for patients every step of the way

See Terms and Conditions on the following page.

*Based on Weekly Field Intelligence Input and MMIT, as of August 2022.

†The accurate completion of reimbursement- or coverage-related documentation is the responsiblity of the healthscare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

‡Nurse Navigators can answer questions about ZEPOSIA, but they cannot provide medical advice.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Infections (Continued)**:**

- 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.
- In the MS and UC 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 and UC. 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.

Progressive Multifocal Leukoencephalopathy (PML): 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.

PML has been reported in patients treated with S1P receptor modulators, including ZEPOSIA, and other MS and UC 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.

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

Eligibility Requirements and Terms & Conditions

[a] ZEPOSIA Free Trial Offer

Patient must have a valid prescription for ZEPOSIA for an FDA-approved indication. Patient must be new to therapy and have not previously received a sample or filled a prescription for ZEPOSIA. Patient is responsible for applicable taxes, if any. This offer is limited to one use per patient per lifetime and is non-transferable. Cannot be combined with any other rebate/coupon, free trial, or similar offer. No substitutions permitted. Patients, pharmacists, and prescribers cannot seek reimbursement for the ZEPOSIA Free Trial from health insurance or any third party, including state or federally funded programs. Patients may not count the ZEPOSIA Free Trial as an expense incurred for purposes of determining out-of-pocket costs for any plan, including Medicare Part D true out-of-pocket costs (TrOOP). Offer is not conditioned on any past, present, or future purchase, including refills. Only valid in the United States and US Territories. Void where prohibited by law or restricted. The program is not insurance. Bristol Myers Squibb reserves the right to rescind, revoke, or amend this offer at any time without notice.

[b] ZEPOSIA In-Home Medical Services Program

Patient must have a valid prescription for ZEPOSIA for an FDA-approved indication. Patient must be commercially insured. Patients are not eligible if they have prescription insurance coverage through a state or federal healthcare program, including but not limited to Medicare, Medicaid, Medigap, CHAMPUS, TRICARE, Veterans Affairs (VA), or Department of Defense (DoD) programs, or reside in Rhode Island. To receive the In-Home Medical Services Program, the prescriber must request in-home assessment assistance through the ZEPOSIA 360 Support program. The patient's insurance will not be billed, and the patient will not be responsible for any out-of-pocket costs. Patients who move from commercial plans to state or federal healthcare programs will no longer be eligible. The program cannot be combined with any other offer, rebate, coupon, or free trial. The program is not conditioned on any past, present, or future purchase, including refills. Only valid in the United States and US Territories. Void where prohibited by law, taxed, or restricted. The program is not insurance. Bristol-Myers Squibb Company reserves the right to rescind, revoke, or amend this program at any time without notice. Other limitations may apply.

[c] Combined Co-Pay Programs (Drug and Medical Benefit)

ZEPOSIA Co-Pay Program is valid only for patients with commercial insurance. The Program includes a prescription benefit offer for out-of-pocket drug costs and a medical assessment benefit offer for out-of-pocket costs for the initial blood tests, ECG screening, and eye exam where the full cost is not covered by patient's insurance. Patients are not eligible for the prescription benefit offer if they have prescription insurance coverage through a state or federal healthcare program, including but not limited to Medicare, Medicaid, Medigap, CHAMPUS, TRICARE, Veterans Affairs (VA), or Department of Defense (DoD) programs. Patients are not eligible for the medical assessment benefit offer if they have insurance coverage for their prescription or medical assessment through a state or federal healthcare program, or reside in Massachusetts, Minnesota, or Rhode Island. Patients who move from commercial plans to state or federal healthcare programs will no longer be eligible. Patient must be 18 years of age or older. Patients may pay as little as $0 in out-of-pocket costs per prescription, subject to a maximum benefit of $18,000 during a calendar year. Patients may pay as little as $0 in out-of-pocket costs for the medical assessment, subject to a maximum benefit of $2,000. The medical benefit offer only applies to clinical baseline assessment services covered by the Program. Patients are responsible for any costs that exceed the maximum amounts. To receive the medical assessment benefit, an Explanation of Benefits (EOB) form must be submitted, along with copies of receipts for any payments made. The Program expires on December 31, 2023. All Program payments are for the benefit of the patient only. Patients, pharmacists, and prescribers may not seek reimbursement from health insurance, health savings or flexible spending accounts, or any third party, for any part of the prescription or medical assessment benefit received by the patient through this Program. Patient's acceptance of any Program benefit confirms that it is consistent with patient's insurance and that patient will report the value received as may be required by his/her insurance provider. Program valid only in the United States and Puerto Rico. Void where prohibited by law, taxed, or restricted. The Program cannot be combined with any other offer, rebate, coupon, or free trial. The Program is not conditioned on any past, present or future purchase, including refills. The Program is not insurance. Other limitations may apply. Bristol Myers Squibb reserves the right to rescind, revoke, or amend this Program at any time without notice.

[d] Bridge Program

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, for up to 24 months (dispensed in 30-day increments). The Bridge Program is not available to patients who have prescription insurance coverage through a state or federal healthcare program, including but not limited to Medicare, Medicaid, Medigap, CHAMPUS, TRICARE, Veterans Affairs (VA), or Department of Defense (DoD) programs and is available for no more than 12 months to patients in MA, 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. Offer is not health insurance. Once coverage is approved by the patient's commercial insurance plan, the patient will no longer be eligible. Void where prohibited by law, taxed, or restricted. Bristol-Myers Squibb Company reserves the right to rescind, revoke, or amend this program at any time without notice. Other limitations may apply.

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 sino-atrial 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. Women who become pregnant while taking ZEPOSIA for MS may enroll in the ZEPOSIA pregnancy registry by calling 1-877-301-9314 or visiting www.zeposiapregnancyregistry.com.

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 Multiple Sclerosis (MS) Disability After Stopping ZEPOSIA: In MS, 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 that occurred in the MS clinical trials of ZEPOSIA-treated patients (≥ 4%): upper respiratory infection, hepatic transaminase elevation, orthostatic hypotension, urinary tract infection, back pain, and hypertension.

In the UC clinical trials, the most common adverse reactions that occurred in ≥4% of ZEPOSIA-treated patients and greater than in patients who received placebo were upper respiratory infection, liver test increased, and headache.

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

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

FOR YOUR PATIENTS WITH RMS[1]

PROTECT IT BEFORE IT'S GONE

WITH ZEPOSIA, YOU HAVE THE POWER TO HELP PRESERVE THEIR MOST VALUABLE RESOURCE[1]

- **Powerful efficacy** in reducing ARR, GdE lesions, and new/enlarging T2 lesions vs Avonex®[1a]

- **Data on brain volume and cognitive processing speed (SDMT)** in secondary, exploratory endpoints and post hoc analysis[3,4]

- **Safety comparable to Avonex in overall incidence of adverse events,**[3,4b] and generally similar safety in the ongoing long-term extension study; up to 8 years* of exposure[5,6c]

*From first patient randomized (October 18, 2012) through the DAYBREAK data cutoff (February 2, 2021), mean (range) continuous ozanimod 0.92 mg exposure was 67.4 (6.01-98.8) months.[6]

[a]**Study designs: SUNBEAM** (1 year; N=1346) and **RADIANCE** (2 years; N=1313) were multicenter, randomized, double-blind, double-dummy, active treatment-controlled studies of daily oral ozanimod 0.46 mg (not approved for maintenance dose) or 0.92 mg vs weekly Avonex (interferon beta-1a), 30-µg intramuscular injection. **Primary endpoint:** ZEPOSIA reduced ARR vs Avonex by 48% at 1 year (0.181 vs 0.350, respectively) and by 38% at 2 years (0.172 vs 0.276, respectively). **Secondary endpoints:** ZEPOSIA reduced the number of new or enlarging T2 lesions by 48% at 1 year and by 42% at 2 years and reduced the number of GdE lesions vs Avonex by 63% at 1 year and 53% at 2 years. 9 of 10 patients showed no confirmed 3-month disability progression. There was no significant difference in 3-month confirmed disability between ZEPOSIA and Avonex.[1,3,4]

[b]**Adverse reactions:** Overall incidence of adverse reactions for ZEPOSIA vs Avonex at 1 year was 59.8% and 75.5%, respectively, and at 2 years was 74.7% and 83.0%, respectively. Across 2 head-to-head trials, the most common adverse reactions with an incidence of at least 2% in patients treated with ZEPOSIA and at least 1% greater than Avonex, respectively, were as follows: upper respiratory infection, 26% (vs 23%); hepatic transaminase elevation, 10% (vs 5%); orthostatic hypotension, 4% (vs 3%); urinary tract infection, 4% (vs 3%); back pain, 4% (vs 3%); hypertension, 4% (vs 2%); and abdominal pain upper, 2% (vs 1%). Data are not an adequate basis for comparison of rates between ZEPOSIA and the active control. Upper respiratory infection includes nasopharyngitis, upper respiratory tract infection, pharyngitis, respiratory tract infection, bronchitis, rhinitis, respiratory tract infection viral, viral upper respiratory tract infection, rhinorrhea, tracheitis, and laryngitis. Hepatic transaminase elevation includes alanine aminotransferase increased, gamma-glutamyl transferase increased, aspartate aminotransferase increased, hepatic enzyme increased, liver function test abnormal, and transaminase increased. Hypertension includes hypertension, essential hypertension, and orthostatic hypertension. **Severe adverse reactions:** The rate of severe adverse reactions at 1 year for ZEPOSIA was 1.6% vs 2.2% for Avonex and the rate at 2 years for ZEPOSIA was 3.5% vs 4.3% for Avonex. **Serious adverse reactions:** The rate of serious adverse reactions at 1 year for ZEPOSIA was 2.9% vs 2.5% for Avonex and the rate at 2 years for ZEPOSIA was 6.5% vs 6.4% for Avonex.[2-3] Please visit ZeposiaHCP.com/MS for additional SUNBEAM and RADIANCE data.

[c]**Study design: DAYBREAK** is an ongoing open-label extension (OLE) trial that enrolled participants from multiple randomized phase 1 to 3 studies including SUNBEAM and RADIANCE. These data are presented as an interim analysis with a data cutoff of February 2, 2021. Patients evaluated in this analysis included those receiving ZEPOSIA 0.92 mg (n=881) who completed the randomized phase 1 to 3 trials. Primary objective evaluated the long-term safety of ZEPOSIA. Secondary objectives included ARR, new/enlarging T2 lesions, and GdE lesions. Endpoints were analyzed descriptively.[5]

Treatment-emergent adverse events (TEAEs): At the data cutoff (up to 5 years), the overall incidence of TEAEs for ZEPOSIA in the DAYBREAK OLE trial was 84.7%. The most common TEAEs with an incidence of at least 4% in patients treated with ZEPOSIA, sorted by decreasing incidence, were as follows: nasopharyngitis, 19.3%; headache, 15.6%; upper respiratory tract infection, 10.9%; ALC decreased, 8.9%; lymphopenia, 8.7%; back pain, 8.1%; gamma-glutamyl transferase increased, 5.9%; bronchitis, 5.8%; urinary tract infection, 5.8%; hypertension, 5.4%; respiratory tract infection, 5.4%; viral respiratory tract infection, 5.0%; and depression-related TEAEs, 4.9%. The rate of TEAEs leading to permanent treatment discontinuation was 2.7%. **Severe TEAEs:** The rate of severe TEAEs was 6.0%. **Serious TEAEs:** The rate of serious TEAEs was 11.7%.[5]

RMS=relapsing forms of multiple sclerosis; ARR=annualized relapse rate; GdE=gadolinium enhancing; SDMT=Symbol Digit Modalities Test.

References: 1. ZEPOSIA. Prescribing information. Bristol Myers Squibb; 2021. **2.** Marrie RA. Comorbidity in multiple sclerosis: implications for patient care. *Nat Rev Neurol.* 2017;13(6):375-382. doi:10.1038/nrneurol.2017.33. **3.** Comi G, Kappos L, Selmaj KW, et al; SUNBEAM Study Investigators. Safety and efficacy of ozanimod versus interferon beta-1a in relapsing multiple sclerosis (SUNBEAM): a multicentre, randomised, minimum 12-month, phase 3 trial. *Lancet Neurol.* 2019;18(11):1009-1020. **4.** Cohen JA, Comi G, Selmaj KW, et al; RADIANCE Trial Investigators. Safety and efficacy of ozanimod versus interferon beta-1a in relapsing multiple sclerosis (RADIANCE): a multicentre, randomised, 24-month, phase 3 trial. *Lancet Neurol.* 2019;18(11):1021-1033. **5.** Selmaj KW et al. Poster at 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 13-15, 2021; The Digital Experience. P737. **6.** Data on file. BMS-REF-OZA-0004. Princeton, NJ: Bristol-Myers Squibb Company; 2021.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Use in Specific Populations: Hepatic Impairment: Use is not recommended.

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

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™