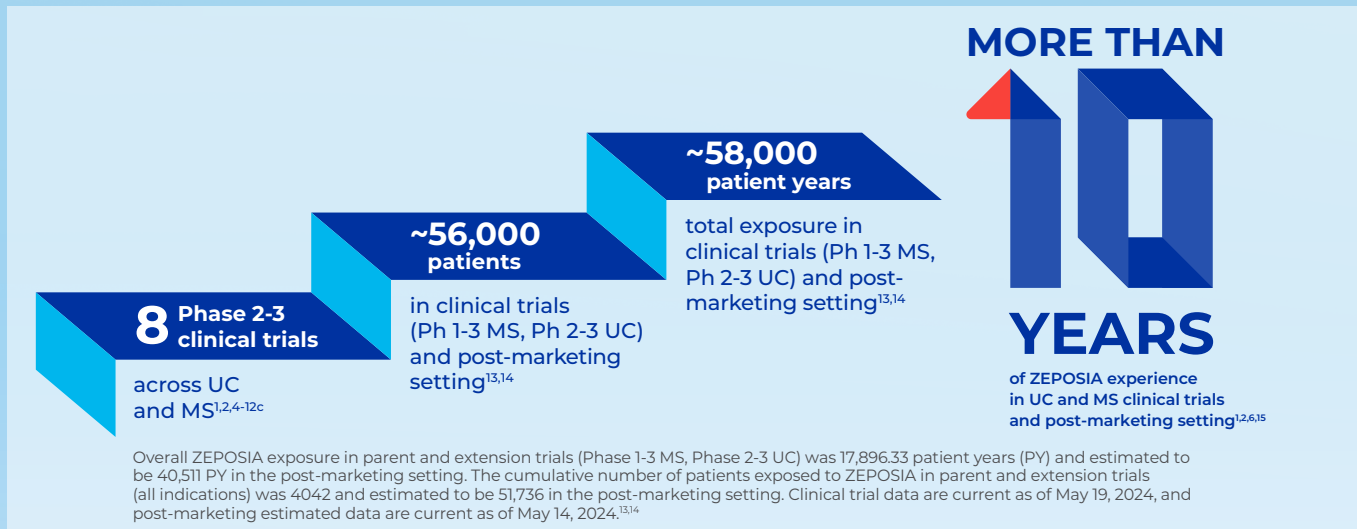


ZEPOSIA—a highly selective SIP with more than a decade of clinical trial experience across multiple indications^{1-3ab}



Real-world experience with ZEPOSIA across UC and MS

4+ Years available in market^{16,17}

UC approval: May 2021; MS approval: March 2020^{16,17}



Prescribed by **5,800+** HCPs¹⁸

Across UC & MS through May 2024 data cutoff

Visit ZEPOSIAhcp.com for more information

^aZEPOSIA is an SIP receptor modulator that binds with high affinity to SIP receptors 1 and 5. The mechanism by which ZEPOSIA exerts therapeutic effects in UC is unknown.¹

^bIn UC, from the start of the TOUCHSTONE Phase 2 clinical trial (December 26, 2012) through TRUE NORTH OLE study data cutoff (June 30, 2023). In MS, from the start of the RADIANCE Phase 2 clinical trial (September 18, 2012) through the DAYBREAK OLE database lock (April 7, 2023). Only includes patients receiving the 0.92-mg dose of ZEPOSIA.^{2,3,5,6,19}

^cZEPOSIA has been studied across multiple indications in 8 Phase 2-3 clinical trials.^{1,2,4-12}

Moderate-to-severe UC: TRUE NORTH (NCT02435992), a Phase 3, multicenter, randomized, double-blind, placebo-controlled clinical trial; TRUE NORTH OLE (NCT02531126), an ongoing Phase 3, multicenter, OLE trial; TOUCHSTONE (NCT01647516), a Phase 2, multicenter, randomized, double-blind, placebo-controlled trial; and JAPAN TRUE NORTH (NCT03915769), a Phase 2/3, multicenter, randomized, double-blind, placebo-controlled, treat-through study.^{2,7-9,11}

Relapsing MS: SUNBEAM (NCT02294058) and RADIANCE (NCT02047734), 2 Phase 3, multicenter, randomized, double-blind, double-dummy, active treatment-controlled studies; DAYBREAK (NCT02576717), a Phase 3, multicenter, OLE trial; and ENLIGHTEN (NCT04140305), an ongoing Phase 3b, multicenter, longitudinal, open-label, single-arm study.^{14,5,10,12,15}

MS=multiple sclerosis; OLE=open-label extension; Ph=phase; SIP=sphingosine 1-phosphate; UC=ulcerative colitis.

INDICATIONS

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

- Moderately to severely active ulcerative colitis (UC) in adults.
- 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-degree or third-degree atrioventricular (AV) block, sick sinus syndrome, or sino-atrial block, 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 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.

- 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 (SIP) 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 SIP 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.

Please see additional Important Safety Information throughout and the full [Prescribing Information](#) and [Medication Guide](#).

IMPORTANT SAFETY INFORMATION (cont'd) Infections (cont'd)

- 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 SIP receptor modulators, including ZEPOSIA, and other MS and UC therapies and has been associated with some risk factors (e.g., immunocompromised patients, polytherapy with immunosuppressants, duration of use). Based on data from patients with MS, longer treatment duration increases the risk of PML in patients treated with SIP receptor modulators, and the majority of PML cases have occurred in patients treated with SIP receptor modulators for at least 18 months. If PML is suspected, withhold ZEPOSIA and perform an appropriate diagnostic evaluation.

If confirmed, treatment with ZEPOSIA should be discontinued.

Immune reconstitution inflammatory syndrome (IRIS) has been reported in MS patients treated with SIP receptor modulators who developed PML and subsequently discontinued treatment. IRIS presents as a clinical decline in the patient's condition that may be rapid, can lead to serious neurological complications or death, and is often associated with characteristic changes on MRI. The time to onset of IRIS in patients with PML was generally within a few months after SIP receptor modulator discontinuation. Monitoring for development of IRIS and appropriate treatment of the associated inflammation should be undertaken.

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 Ia 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: SIP modulators have been associated with an increased risk of macular edema. Perform an examination of the fundus, including the macula, periodically while on therapy and any time there is a change in vision.

Continuation of ZEPOSIA therapy in patients with macular edema has not been evaluated. Macular edema over an extended period of time (i.e. 6 months) can lead to permanent visual loss. Consider discontinuing ZEPOSIA if macular edema develops; this decision should include an assessment of the potential benefits and risks for the individual patient. The risk of recurrence after rechallenge has not been evaluated.

Macular Edema in Patients with a History of Uveitis or Diabetes Mellitus Patients with a history of uveitis and patients with a history of diabetes mellitus are at increased risk of macular edema during ZEPOSIA therapy.

Cutaneous Malignancies: The risk of cutaneous malignancies (including basal cell carcinoma and squamous cell carcinoma) is increased in patients treated with SIP receptor modulators, including ZEPOSIA. Skin examinations are recommended prior to or shortly after the start of treatment with ZEPOSIA and periodically thereafter for all patients,

particularly those with risk factors for skin cancer. Providers and patients are advised to monitor for suspicious skin lesions. If a suspicious skin lesion is observed, it should be promptly evaluated. As usual for patients with increased risk for skin cancer, exposure to sunlight and ultraviolet light should be limited by wearing protective clothing and using sunscreen with a high protection factor. Concomitant phototherapy with UV-B radiation or PUV-A photochemotherapy is not recommended in patients taking ZEPOSIA.

Posterior Reversible Encephalopathy Syndrome (PRES): Rare cases of PRES have been reported in patients receiving a SIP 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 SIP receptor modulator. The possibility of severe exacerbation of disease should be considered after stopping ZEPOSIA treatment so patients should be monitored upon discontinuation. After stopping ZEPOSIA in the setting of PML, monitor for development of immune reconstitution inflammatory syndrome (PML-IRIS).

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 ($\geq 4\%$): 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 $\geq 4\%$ of ZEPOSIA-treated patients and greater than in patients who received placebo were upper respiratory infection, liver test increased, and headache.

Use in Specific Populations: Hepatic Impairment: Dosage adjustment in patients with mild or moderate hepatic impairment (Child-Pugh class A or B) is required, and use of ZEPOSIA in patients with severe hepatic impairment (Child-Pugh class C) is not recommended.

For additional safety information, please see the full Prescribing Information and Medication Guide.

References: 1. Zeposia. Prescribing Information. Bristol-Myers Squibb Company; 2024. 2. Efficacy and safety study of ozanimod in ulcerative colitis (Touchstone). ClinicalTrials.gov. <https://clinicaltrials.gov/study/NCT01647516>. Updated May 19, 2021. Accessed July 26, 2023. 3. Long-term safety and efficacy of ozanimod in relapsing multiple sclerosis: final analysis of the DAYBREAK open-label extension study. Selmaj KW, Steinman L, Comi G, et al. Poster presented at: Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum 2024; West Palm Beach, FL; February 29–March 2, 2024. Poster P090. 4. Study of ozanimod (RPC1063) in relapsing multiple sclerosis (MS) (SUNBEAM). ClinicalTrials.gov. <https://clinicaltrials.gov/study/NCT02294058>. Updated November 25, 2020. Accessed July 26, 2023. 5. Efficacy and safety study of ozanimod in relapsing multiple sclerosis (RADIANCE). ClinicalTrials.gov. <https://clinicaltrials.gov/study/NCT02047734>. Updated February 11, 2021. Accessed July 26, 2023. 6. Efficacy and safety study of ozanimod (RPC1063) in relapsing multiple sclerosis patients (RADIANCE). ClinicalTrials.gov. <https://clinicaltrials.gov/study/NCT01628393>. Updated February 11, 2021. Accessed July 26, 2023. 7. Sandborn WJ, Feagan BC, D'Haens G, et al; True North Study Group. Ozanimod as induction and maintenance therapy for ulcerative colitis. *N Engl J Med*. 2021;385(14):1280–1291. 8. Safety and efficacy trial of RPC1063 for moderate to severe ulcerative colitis. ClinicalTrials.gov. <https://clinicaltrials.gov/study/NCT02435992>. Updated September 1, 2021. Accessed July 26, 2023. 9. An extension study of RPC1063 as therapy for moderate to severe ulcerative colitis. ClinicalTrials.gov. <https://clinicaltrials.gov/study/NCT02531126>. Updated September 18, 2023. Accessed September 25, 2023. 10. A multi-site, open-label extension trial of oral RPC1063 in relapsing multiple sclerosis. ClinicalTrials.gov. <https://clinicaltrials.gov/study/NCT02576717>. Updated January 30, 2024. Accessed February 6, 2024. 11. Nakase H, Fujii T, Hisamatsu T, et al. Ozanimod as induction and maintenance therapy for ulcerative colitis: a randomized, double-blind, placebo-controlled study in Japan (J-True North). Poster presented at Digestive Disease Week (DDW); Washington, DC; May 18–21. Poster SU795. 12. Study describing cognitive processing speed changes in relapsing multiple sclerosis subjects treated with ozanimod (RPC-1063) [ENLIGHTEN]. ClinicalTrials.gov. <https://clinicaltrials.gov/study/NCT0414035>. Updated November 15, 2023. Accessed June 18, 2024. 13. Data on File. BMS-REF-OZA-0076. Princeton, NJ: Bristol-Myers Squibb Company; 2024. 14. Data on File. BMS-REF-OZA-0077. Princeton, NJ: Bristol-Myers Squibb Company; 2024. 15. Selmaj KW, Steinman L, Comi G, et al. Long-term safety and efficacy of ozanimod in relapsing multiple sclerosis: interim analysis of the DAYBREAK open-label extension study. Poster presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); Amsterdam, Netherlands; October 26–28, 2022. Poster P334. 16. Press Release. U.S. Food and Drug Administration approves Bristol Myers Squibb's ZEPOSIA® (ozanimod), a new oral treatment for relapsing forms of multiple sclerosis. Princeton, NJ: Bristol-Myers Squibb Company; 2020. 17. Press Release. U.S. Food and Drug Administration approves Bristol Myers Squibb's ZEPOSIA® (ozanimod), an oral treatment for adults with moderately to severely active ulcerative colitis. Princeton, NJ: Bristol-Myers Squibb Company; 2021. 18. Data on File. BMS-REF-OZA-0079. Princeton, NJ: Bristol-Myers Squibb Company; 2024. 19. Siegel CA, Danese S, Rubin DT, et al. Safety of long-term ozanimod treatment for up to 4 years in patients with moderately to severely active ulcerative colitis: an interim analysis of the True North open-label extension. Oral presentation at: European Crohn's and Colitis Organisation (ECCO) 2024; Stockholm, Sweden; February 21–24.



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/ulcerative-colitis/cost.