The first and only sphingosine 1-phosphate (S1P) receptor modulator approved for the treatment of moderately to severely active ulcerative colitis (UC) in adults[1]

ANOTHER DAY IS DAWNING IN THE CONTROL OF UC

Significantly higher clinical remission rates vs placebo in the pivotal trial: 18% (79/429) vs 6% (13/216) at Week 10 (p<0.0001) and 37% (85/230) vs 19% (42/227) at Week 52 (p<0.0001)[1]

Mechanism of Action (MOA)

ZEPOSIA is a small molecule that reversibly sequesters lymphocytes in lymphoid tissue, blocking their capacity to egress from the lymphoid tissue[1-3]

once-daily ZEPOSIA® (ozanimod) 0.92 mg capsules

Study Design: 2 multicenter, randomized, double-blind, placebo-controlled studies in adult patients with moderately to severely active UC, UC Study 1 (induction 10 weeks, N=645) and UC Study 2 (maintenance 42 weeks, N=457). To enter UC Study 2, patients had to have received ZEPOSIA in either UC Study 1 or in an open-label arm and be in clinical response at Week 10.[1]

Clinical Remission Is Defined as: RBS=0, SFS=0 or 1 (and a decrease of ≥1 point from the baseline of SFS), and endoscopy subscore 0 or 1 without friability.[1]

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of moderately to severely active ulcerative colitis (UC) in adults.

IMPORTANT SAFETY INFORMATION

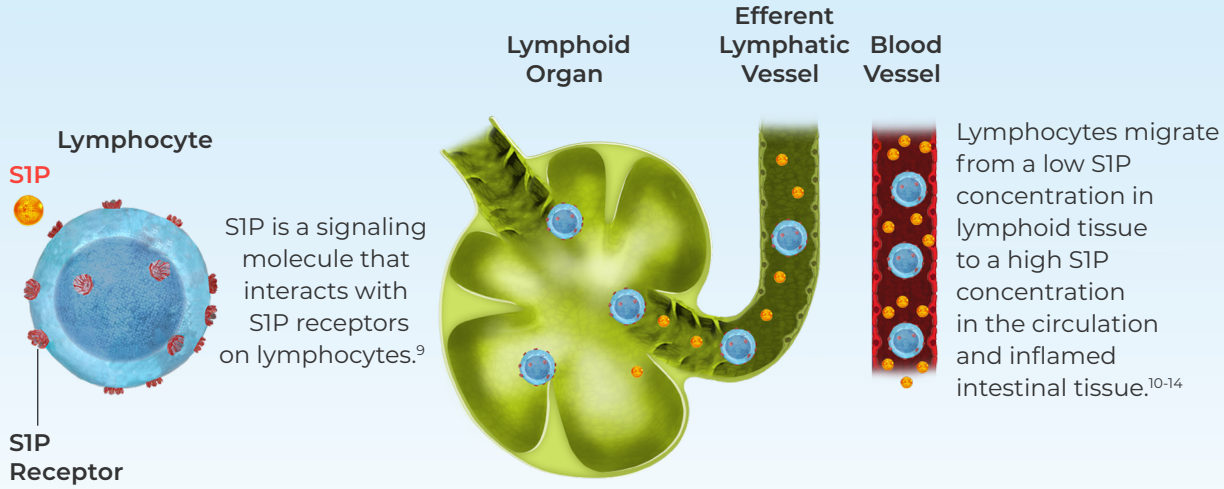
Contraindications:

- 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 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

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

ZEPOSIA—The First and Only S1P Receptor Modulator Approved for UC[1,6,7]

S1P signaling plays a role in the pathophysiology of inflammatory conditions like UC[8]



Lymphocyte migration is guided by an S1P concentration gradient to sites of inflammation.[8,10-13,15,16]

Artist rendering for illustrative purposes.

IMPORTANT SAFETY INFORMATION (cont'd)

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 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 (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

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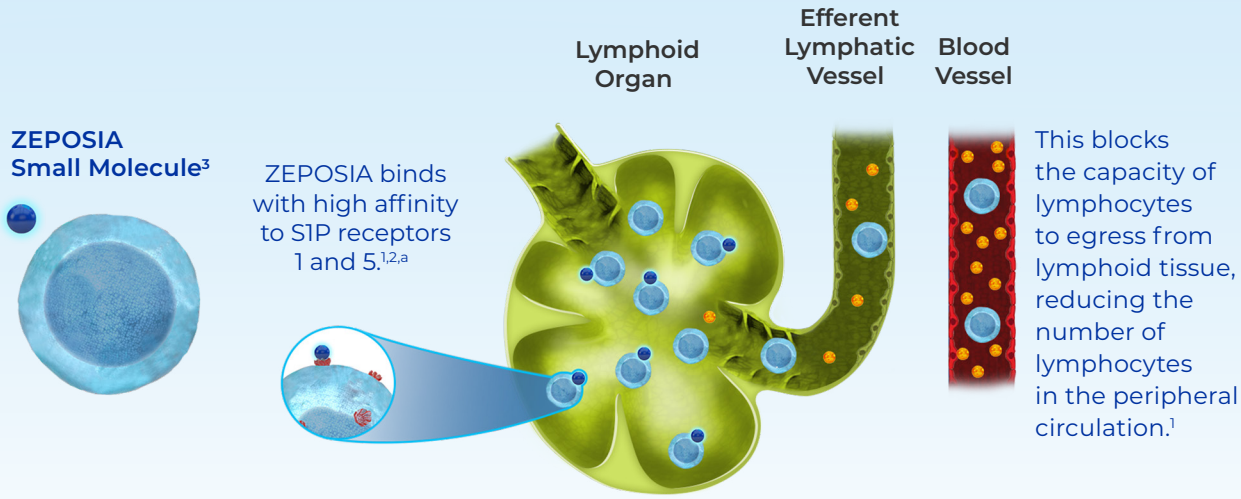
ZEPOSIA Is a Small Molecule That Reversibly Sequesters Lymphocytes in Lymphoid Tissue[1-3]

The mechanism by which ZEPOSIA exerts therapeutic effects in UC is unknown but may involve the reduction of lymphocyte migration into the intestine[1]



Artist rendering for illustrative purposes.
[a]ZEPOSIA has minimal or no activity on S1P receptors 2-4.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Infections: (cont'd)

- 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. PML has been reported in patients treated with S1P receptor modulators and other 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

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Getting Patients Started on ZEPOSIA

Screening for All Patients Prior to First Dose—Within the Last 6 Months[1]

- Obtain blood work
  - –Complete blood count (CBC), including lymphocyte count (within the last 6 months or after discontinuation of prior UC therapy)
  - –Transaminase and total bilirubin levels
- Obtain an electrocardiogram (ECG) to determine whether **preexisting** conduction abnormalities are present[a]

Screening Only for Select Patients Prior to First Dose[1]

- With a history of uveitis, macular edema, or diabetes mellitus—ophthalmic evaluation of the fundus, including the macula[b]
- Without documentation of history of varicella-zoster virus (VZV)/chicken pox, or documentation of a full course of vaccination, test for antibodies[c]
  - –If live *attenuated* immunizations are required, administer at least 1 month prior to initiation

Evaluate current and prior medications before initiation of treatment[1]

BMS Support Provided at the Homes of Eligible Patients[d]

- Blood work
- ECG with cardiologist overread
- Macular edema screening with licensed eye clinician overread
- VZV antibody testing

The full Prescribing Information for ZEPOSIA does not require routine lab monitoring unless clinically indicated

[a]In patients with certain preexisting conditions, advice from a cardiologist should be sought—see Warnings and Precautions in Prescribing Information.[1]
[b]Patients with a history of uveitis and patients with a history of diabetes mellitus are at increased risk of macular edema during ZEPOSIA therapy. The incidence of macular edema is also increased in patients with a history of uveitis. In addition to the examination of the fundus, including the macula, prior to treatment, patients with diabetes mellitus or a history of uveitis should have regular follow-up examinations.[1]
[c]VZV vaccination of antibody-negative patients is recommended prior to commencing treatment.[1]
[d]Home visits for initial routine medical tests are not available to people enrolled in Medicare, Medicaid, or other federal or state healthcare programs, or to people living in Rhode Island.
UC=ulcerative colitis.

IMPORTANT SAFETY INFORMATION (cont'd)

Infections: (cont'd)

- In the 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 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

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Another Day Starts With a Once-Daily Oral Administration[1]

The ZEPOSIA Starter Pack is designed to make the titration instructions easier to follow[1]

- Initiate ZEPOSIA with a 7-day titration schedule. After initial titration, the recommended once-daily dosage of ZEPOSIA is 0.92 mg taken orally, starting on Day 8.[1]
  - An up-titration schedule should be used to reach the maintenance dose, as a transient decrease in heart rate and atrioventricular (AV) conduction delays may occur[1]
  - ZEPOSIA can be taken with or without food[1]

Recommended Dosage[1]

ZEPOSIA 7-Day Titration Schedule[1] | **DAYS 1-4** 0.23 mg › **DAYS 5-7** 0.46 mg › **DAY 8** 0.92 mg

Additional Dosing Considerations

- If a dose of ZEPOSIA is missed during the first 2 weeks of treatment, reinitiate treatment using the titration regimen[1]
- If a dose of ZEPOSIA is missed after the first 2 weeks of treatment, continue with the treatment as planned[1]

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

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:

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IMPORTANT SAFETY INFORMATION (cont'd)

Bradyarrhythmia and Atrioventricular Conduction Delays: (cont'd)

- 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

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

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IMPORTANT SAFETY INFORMATION (cont'd)

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

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: Most common adverse reactions (incidence ≥4%) are: liver test increased, upper respiratory infection, and headache

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ANOTHER DAY IS DAWNING IN THE CONTROL OF UC

Now many of your patients can choose another path forward before biologics.[1a] ZEPOSIA delivers:

Lasting Remission[1]

Significantly higher clinical remission rates vs placebo in the pivotal trial: 18% (79/429) vs 6% (13/216) at Week 10 (p<0.0001) and 37% (85/230) vs 19% (42/227) at Week 52 (p<0.0001)

Demonstrated Safety Profile[1b]

Studied in 4 clinical trials with over 1370 ZEPOSIA-treated patients across multiple indications

One Capsule, Once Daily[1]

Once-daily oral administration, with or without food

[a]**ZEPOSIA demonstrated higher rates of clinical remission vs placebo in tumor necrosis factor inhibitor (TNFi)-naïve patients at Week 10 (22% [66/299] vs 7% [10/151]) and at Week 52 (41% [63/154] vs 22% [35/158], respectively).[1]**
In UC Study 1 and UC Study 2, of the ZEPOSIA-treated patients who were TNFi-naïve, 288 and 145 were also biologic-naïve, respectively.[4]
Efficacy analysis by prior TNFi therapy was prespecified, but not powered to detect a difference in the treatment effect in these subgroups.[5]

[b]ZEPOSIA has been studied across multiple indications in 4 clinical trials, including TRUE NORTH (NCT02435992), a multicenter, randomized, double-blind, placebo-controlled phase 3 clinical trial; TOUCHSTONE (NCT01647516), a randomized, double-blind, placebo-controlled phase 2 clinical trial; and SUNBEAM (NCT02294058) and RADIANCE (NCT02047734), 2 multicenter, randomized, double-blind, double-dummy, active treatment-controlled phase 3 clinical trials. 496 patients receiving the 0.92-mg dose of ZEPOSIA during induction in TRUE NORTH or TOUCHSTONE and 882 patients receiving the 0.92-mg dose of ZEPOSIA in SUNBEAM or RADIANCE were assessed in the safety analysis.[1]

Clinical Trial: The efficacy and safety of ZEPOSIA were evaluated in 2 multicenter, randomized, double-blind, placebo-controlled clinical studies [UC Study 1 (induction) and UC Study 2 (maintenance)] in adult patients with moderately to severely active ulcerative colitis, defined as a Mayo score of 6 to 12 at baseline.[1]

Primary Endpoint of Clinical Remission Is Defined as: rectal bleeding subscore (RBS)=0, stool frequency subscore (SFS) 0 or 1 (and a decrease of ≥1 point from baseline SFS), and endoscopy subscore 0 or 1 without friability.[1]

UC Study 1 (10-week induction): 645 patients were randomized 2:1 to either ZEPOSIA 0.92 mg given orally once daily or placebo for 10 weeks, beginning with a dosage titration. The trial included patients who had an inadequate response or were intolerant to any of the following: oral aminosalicylates, corticosteroids, immunomodulators, or a biologic. Patients were required to be on stable doses of oral aminosalicylates and/or corticosteroids.[1]

UC Study 2 (42-week maintenance): 457 patients who received ZEPOSIA in either UC Study 1 or in an open-label arm and achieved clinical response at Week 10 were re-randomized 1:1 and were treated with either ZEPOSIA 0.92 mg (n=230) or placebo (n=227) for 42 weeks (UC Study 2), for a total of 52 weeks of treatment.[1]

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IMPORTANT SAFETY INFORMATION (cont'd)

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

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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.

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