Not an actual patient.

Busy financial advisor who **adjusts his daily life around symptoms of UC.**

UC=ulcerative colitis.

INDICATIONS

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

1. Moderately to severely active ulcerative colitis (UC) in adults

2. 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

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

ZEPOSIA® (ozanimod) 0.92 mg capsules

PATIENT ON 5-ASA WITH INCOMPLETE RESPONSE

Not an actual patient.

Busy financial advisor who adjusts his daily life around symptoms of UC.

Stephen's Background

- Male, age 36; married with 2 young children
- Wakes up early to use the bathroom before his commute and always packs a spare set of clothes for work travel

Stephen's Medical History

- Left-sided moderately active UC
- Mayo endoscopy subscore=2
- Abdominal pain and cramping, with about 6 loose stools per day and presence of blood
- Currently on 5-ASAs; 1 tapering course of steroids (in the past year)
- No history of cardiac or ophthalmic issues

Treatment Plan Considerations

- Prefers oral therapy
- Doesn't have the time to spend in an infusion clinic between work and family commitments

At TRUE NORTH Study Baseline (N=645)[1a]

- **86%** of patients had moderate disease (Mayo score 6–10)[1]
- **~66%** of patients were advanced therapy-naïve[2]
- **33%** of patients were taking concomitant oral steroids[1]

Get your patient started on ZEPOSIA today

You may be able to help patients like Stephen relieve symptoms[a] while achieving their treatment goals.

See below for considerations when starting ZEPOSIA.

Patients can initiate ZEPOSIA therapy if they have had CBC bloodwork, including lymphocyte count, within the past 6 months or after discontinuation of prior UC therapy and liver function tests (with transaminase and bilirubin levels) within the past 6 months; an ECG to determine if pre-existing conduction abnormalities are present; documented history of VZV or a full course of VZV vaccination; live attenuated vaccine immunization performed at least 1 month prior; and no history of uveitis, macular edema, or diabetes mellitus. Determine if patients are taking drugs that could slow heart rate or atrioventricular conduction. Consider possible unintended additive immunosuppressive effects before initiating treatment with ZEPOSIA if taking anti-neoplastic, non-corticosteroid immunosuppressive, or immune-modulating therapies, or if there is a history of prior use of these drugs.[1]

[a]**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 UC, defined as a Mayo score of 6 to 12 at baseline.[1]
Primary Endpoint of Clinical Remission Is Defined as: RBS=0, SFS=0 or 1 (and a decrease of ≥1 point from baseline SFS), and endoscopy subscore=0 or 1 without friability. At Week 10, 18% of patients taking ZEPOSIA achieved clinical remission vs 6% of patients taking placebo (p<0.0001). At Week 52, 37% of patients taking ZEPOSIA achieved clinical remission vs 19% of patients taking placebo (p<0.0001).[1]
Secondary Endpoint of Clinical Response Is Defined as: a reduction from baseline in the 3-component Mayo score of ≥2 and ≥35%, and a reduction from baseline in the RBS of ≥1 or an absolute RBS of 0 or 1.[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. Corticosteroid tapering was required upon entering this study for patients who were receiving corticosteroids during the induction period.[1]
5-ASA=5-aminosalicylic acid; CBC=complete blood count; ECG=electrocardiogram; RBS=rectal bleeding subscore; SFS=stool frequency subscore; VZV=varicella-zoster virus.

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 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.

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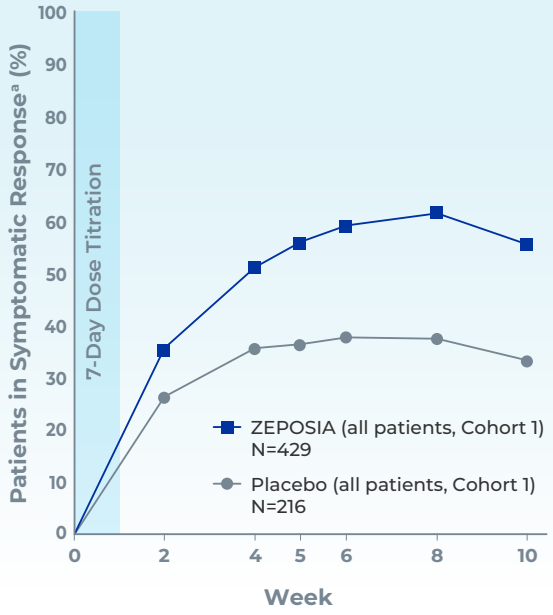
Post-Hoc Analysis:

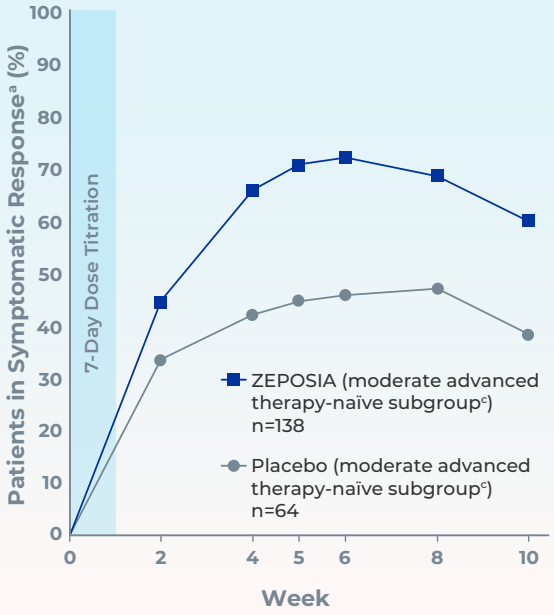
Patients Experienced Relief[a] From UC Symptoms as Early as 1 Week After Completing the 7-Day Dose Titration[2-4]

A decrease in both rectal bleeding subscore (RBS) and stool frequency subscore (SFS) was observed in patients taking ZEPOSIA as early as Week 2[1,4]

Post-Hoc Analysis of Symptomatic Response[a] in the All-Patients Group[3b]



Post-Hoc Analysis of Symptomatic Response[a] in the Moderate Advanced Therapy-Naïve Subgroup[2c]



These post-hoc analyses were not prespecified.[2]

[a]Symptomatic clinical response was defined as a decrease from baseline in the combined 6-point SFS + RBS by ≥1 point and ≥30%, and a decrease of ≥1 point in RBS or an absolute RBS of ≤1 point.[2,3]

[b]Data are based on the nonresponder imputation.[3]

[c]The moderate advanced therapy-naïve subgroup included patients with a Mayo endoscopy subscore of 2.[2]

IMPORTANT SAFETY INFORMATION (cont'd)

Infections (cont'd):

- 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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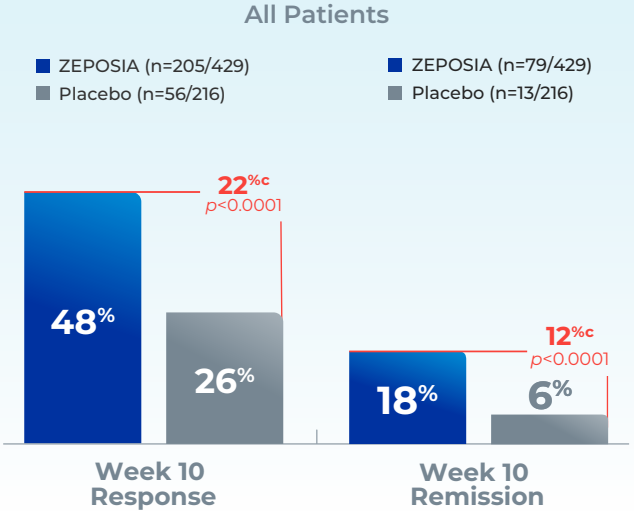
Primary and Key Secondary Endpoints:

ZEPOSIA Delivers Rapid Clinical Response and Remission[1]

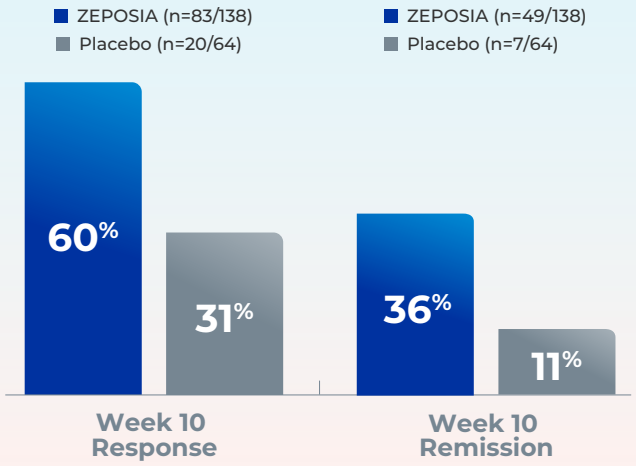
In the all-patients group, 48% of patients achieved clinical response and 18% achieved clinical remission at Week 10[1]

In the moderate advanced therapy-naïve subgroup, 60% of patients had clinical response and 36% had clinical remission at Week 10[2]

Clinical Response[a] (Key Secondary Endpoint) and Clinical Remission[b] (Primary Endpoint)[1]



Clinical Response[a] and Clinical Remission[b] (Post-Hoc Analyses)[2]



Efficacy analyses in the moderate advanced therapy-naïve subgroup were not prespecified.[2]

- At Week 52, clinical response[a] in the all-patients group was 60% (n=138/230) for patients taking ZEPOSIA vs 41% (n=93/227) (p<0.0001) for patients taking placebo[1e]
- Clinical response[a] at Week 52 in the moderate advanced therapy-naïve subgroup[d] was 67% (n=48/72) for patients taking ZEPOSIA vs 51% (n=43/85) for patients taking placebo[5f]
- At Week 52, clinical remission[b] in the all-patients group was 37% (n=85/230) for patients taking ZEPOSIA vs 19% (n=42/227) (p<0.0001) for patients taking placebo[1e]
- Clinical remission[b] in the moderate advanced therapy-naïve subgroup[d] was 47% (n=34/72) for patients taking ZEPOSIA vs 26% (n=22/85) for patients taking placebo[5f]

[a]Clinical response is defined as a reduction from baseline in the 3-component Mayo score of ≥2 points and ≥35%, and a reduction from baseline in the RBS of ≥1 point or an absolute RBS of 0 or 1.[1,2]
[b]Clinical remission is defined as: RBS=0, SFS=0 or 1 (and a decrease of ≥1 point from baseline SFS), and endoscopy subscore=0 or 1 without friability.[1,2]
[c]Treatment difference (adjusted for stratification factors of prior TNFi exposure and corticosteroid use at baseline).[1]
[d]The moderate advanced therapy-naïve subgroup included patients with a Mayo endoscopy subscore of 2.[2]
[e]Treatment difference (adjusted for stratification factors of clinical remission and concomitant corticosteroid use at Week 10).[1]
[f]Efficacy analyses in the moderate advanced therapy-naïve subgroup were not prespecified.[5]
TNFi=tumor necrosis factor inhibitor.

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.

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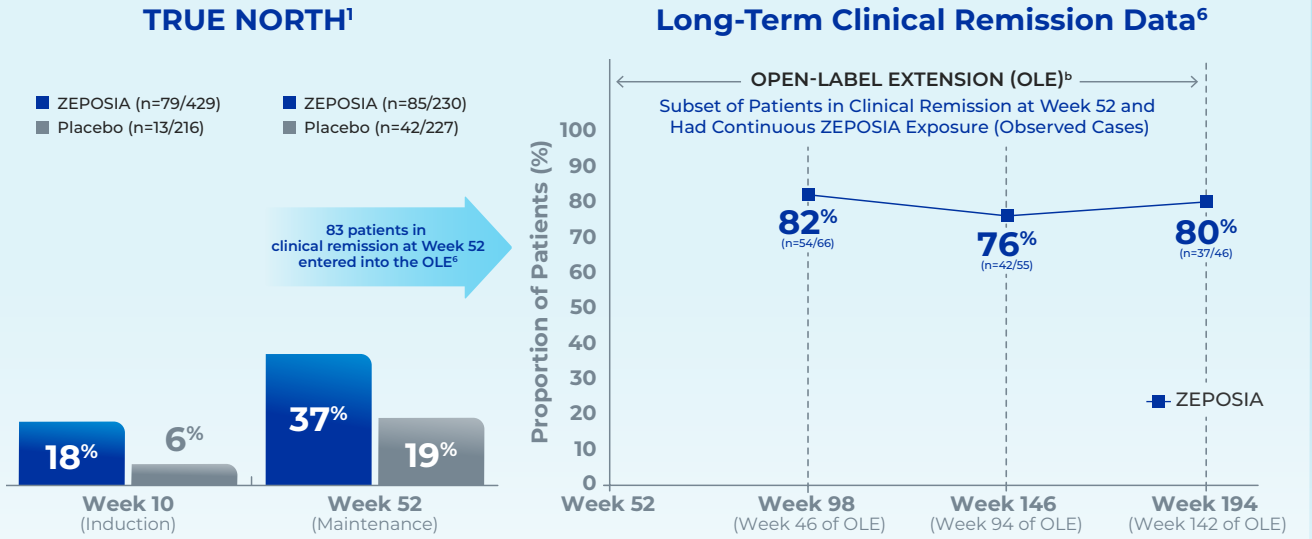
Long-Term Clinical Remission Data Observed up to ~4 Years[6]

Clinical remission[a] data up to 194 weeks in the open-label extension trial[6]



Data were analyzed in the ITT population using OC and NRI. OC used the number of patients remaining in the study at the corresponding time point. NRI used the number of patients remaining in the study at the corresponding time point and those who withdrew before the time point but would have reached the time point if they had stayed.[7]

In the NRI analysis of a subset of patients in clinical remission at Week 52 and had continuous ZEPOSIA exposure, 65% (n=54/83) were in clinical remission at Week 98 (Week 46 of OLE), 51% (n=42/83) were in clinical remission at Week 146 (Week 94 of OLE), and 45% (n=37/83) were in clinical remission at Week 194 (Week 142 of OLE).[6]

Study Design for OLE

The TRUE NORTH OLE is an ongoing trial that enrolled participants who were nonresponders at the end of induction, experienced disease relapse during maintenance, or completed maintenance treatment in the phase 3 TRUE NORTH study or remained at study closure and received once-daily oral ZEPOSIA 0.92 mg in the phase 2 TOUCHSTONE open-label extension. A total of 823 patients from TRUE NORTH entered the TRUE NORTH OLE.[7-9]

Endpoints were evaluated at Weeks 46, 94, and 142 of the OLE for all patients who entered the OLE from the TRUE NORTH parent study and for a subset of patients in clinical remission or clinical response at Week 52 and had continuous ZEPOSIA exposure. Endpoints include clinical remission, clinical response, endoscopic improvement, and CS-free remission. Safety was evaluated for all 823 patients who entered the OLE from the TRUE NORTH parent study.[7,8,10-12]

These analyses were not prespecified and represent a subgroup of all patients from TRUE NORTH who entered the OLE.[12]
[a]Clinical remission (3-component Mayo score) is defined as RBS=0, SFS ≤1 (and a decrease of ≥1 point from the baseline SFS), and endoscopy subscore ≤1.[6]
[b]The OLE did not include a placebo comparator arm.[6,13]
CS=corticosteroid; ITT=intent-to-treat; NRI=nonresponder imputation; OC=observed case; OLE=open-label extension.

IMPORTANT SAFETY INFORMATION (cont'd)

Infections (cont'd):

- 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.

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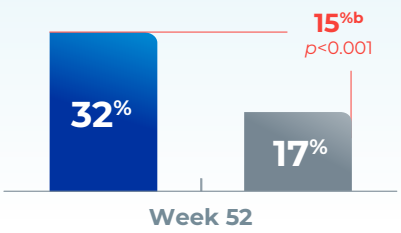
Key Secondary Endpoint:

ZEPOSIA Can Help Patients Achieve Remission Without the Use of Corticosteroids[1]

32% of all patients on ZEPOSIA achieved corticosteroid (CS)-free remission at Week 52[1]
43% of patients in the moderate advanced therapy-naïve subgroup had CS-free remission at Week 52[5]

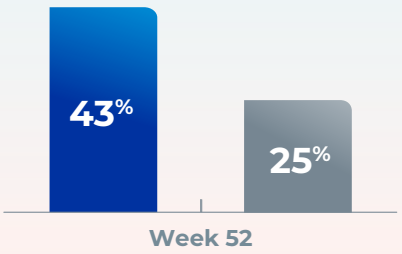
CS-Free Remission[a] (Key Secondary Endpoint)[1]

All Patients



CS-Free Remission[a] (Post-Hoc Analysis)[5]

Moderate Advanced Therapy-Naïve Subgroup[c]



Efficacy analyses in the moderate advanced therapy-naïve subgroup were not prespecified.[5]

[a]CS-free remission is defined as clinical remission[d] at Week 52 while off corticosteroids for ≥12 weeks.[1,5]
[b]Treatment difference (adjusted for stratification factors of clinical remission and concomitant corticosteroid use at Week 10).[1]
[c]The moderate advanced therapy-naïve subgroup included patients with a Mayo endoscopy subscore of 2.[5]
[d]Clinical remission is defined as: RBS=0, SFS=0 or 1 (and a decrease of ≥1 point from baseline SFS), and endoscopy subscore=0 or 1 without friability.[1,5]

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 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.

Immune reconstitution inflammatory syndrome (IRIS) has been reported in MS patients treated with S1P 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 S1P receptor modulator discontinuation. Monitoring for development of IRIS and appropriate treatment of the associated inflammation should be undertaken.

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ZEPOSIA Offers Patients a Demonstrated Safety Profile

No boxed warning
Select Contraindications in patients with specific cardiovascular conditions. Select Warnings and Precautions: Infections, PML, Bradyarrhythmia and AV Conduction Delays, and Liver Injury. See US Prescribing Information.[1]

Incidences of Common Adverse Reactions in the Induction and Maintenance Phases[1]

Adverse Reactions With an Incidence of at Least 2% in ZEPOSIA-Treated Patients and at Least 1% Greater Than Placebo in Patients With UC (Pooled UC Study 1 and Study 3)[1]

	Induction (UC Study 1 and Study 3)[a]	
Adverse Reaction	**ZEPOSIA 0.92 mg (n=496)[de]**	**Placebo (n=281)[d]**
Upper Respiratory Infection[b]	5%	4%
Liver Test Increased[c]	5%	0%
Headache	4%	3%
Pyrexia	3%	2%
Nausea	3%	2%
Arthralgia	3%	1%

Adverse Reactions With an Incidence of at Least 4% in ZEPOSIA-Treated Patients and at Least 1% Greater Than Placebo in Patients With UC (UC Study 2)[1]

	Maintenance (UC Study 2)	
Adverse Reaction	**ZEPOSIA 0.92 mg (n=230)**	**Placebo (n=227)**
Liver Test Increased[f]	11%	2%
Headache	5%	<1%

- In the induction phase of TRUE NORTH (UC Study 1), 40.1% (n=172/429) of patients taking ZEPOSIA had an adverse event compared to 38% (n=82/216) of patients taking placebo. Serious adverse events were experienced by 4% (n=17/429) of patients taking ZEPOSIA compared to 3.2% (n=7/216) of patients taking placebo[14a]
- In the maintenance phase, 49.1% (n=113/230) of patients taking ZEPOSIA had an adverse event compared to 36.6% (n=83/227) of patients taking placebo. Serious adverse events were experienced by 5.2% (n=12/230) of patients taking ZEPOSIA compared to 7.9% (n=18/227) of patients taking placebo[14]

[a]Additional data from the induction period of a randomized, double-blind, placebo-controlled study (UC Study 3/TOUCHSTONE) included 67 patients who received ZEPOSIA 0.92 mg once daily.[1]
[b]Includes the following terms: streptococcal pharyngitis, pharyngotonsillitis, bacterial pharyngitis, nasopharyngitis, upper respiratory tract infection, pharyngitis, sinusitis, tonsillitis, viral upper respiratory tract infection, laryngitis, acute sinusitis, catarrh, chronic sinusitis, upper respiratory tract inflammation, chronic tonsillitis, viral pharyngitis, viral sinusitis, bacterial sinusitis, bacterial upper respiratory tract infection, viral labyrinthitis, laryngeal inflammation, and pharyngeal inflammation.[1]
[c]Includes the following terms: gamma-glutamyl transferase increased, alanine aminotransferase increased, aspartate aminotransferase increased, hepatic enzyme increased, hyperbilirubinemia, liver function test increased, blood alkaline phosphatase increased, and transaminases increased.[1]
[d]Percentages were calculated as the sum of each individual study percentage multiplied by its Cochran-Mantel-Haenszel weight.[1]
[e]ZEPOSIA was initiated with a 7-day titration.[1]
[f]Includes the following terms: gamma-glutamyl transferase increased, alanine aminotransferase increased, aspartate aminotransferase increased, hepatic enzyme increased, hyperbilirubinemia, liver function test increased, and blood alkaline phosphatase increased.[1]

Low discontinuation rates due to treatment-emergent adverse events that are comparable to placebo[14g]

[g]Overall rates of discontinuation were 6.5% with ZEPOSIA (N=429) vs 11.1% with placebo (N=216) in the induction phase, and 20% with ZEPOSIA (N=230) vs 45.4% with placebo (N=227) in the maintenance phase. Discontinuation rates due to TEAEs in induction were 3.3% for patients taking ZEPOSIA vs 3.2% for patients taking placebo. In maintenance, TEAE discontinuation rates were 1.3% for patients taking ZEPOSIA vs 2.6% for patients taking placebo.[1,14]

Rates of serious infection were low and comparable to placebo in clinical trials[1hi]

[h]Overall rates of infection were 9.9% with ZEPOSIA (N=496)[i] vs 10.7% with placebo (N=281) in the induction phase, and 23% with ZEPOSIA (N=230) vs 12% with placebo (N=227) in the maintenance phase. Serious infection rates in the induction phase (UC Study 1 and UC Study 3/TOUCHSTONE) were 0.8% with ZEPOSIA vs 0.4% with placebo. Serious infection rates in the maintenance phase were 0.9% with ZEPOSIA vs 1.8% with placebo.[1]
[i]Additional data from the induction period of a randomized, double-blind, placebo-controlled study (UC Study 3/TOUCHSTONE) included 67 patients who received ZEPOSIA 0.92 mg once daily.[1]

AV=atrioventricular; PML=progressive multifocal leukoencephalopathy; TEAE=treatment-emergent adverse event.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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

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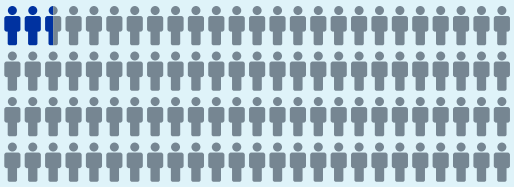
Long-Term Safety Data Observed Over ~4 Years With ZEPOSIA[10]

This safety analysis includes patients with UC from the TRUE NORTH parent study who entered the TRUE NORTH OLE for up to 194 weeks of ZEPOSIA exposure[6]

Estimated Annual Risk = 2.5 per 100 treated patients[6]



TEAEs Leading to Treatment Discontinuation[6] **2.5** EAIR per 100 PY[a]

Serious TEAEs[6] **7.0** EAIR per 100 PY[a]

Serious Infection[6] **1.8** EAIR per 100 PY[a]

Infection (Occurring in ≥3% of Patients)[6]

COVID-19: 4.3 EAIR per 100 PY[a]

Nasopharyngitis: 3.8 EAIR per 100 PY[a]

Upper Respiratory Tract Infection: 2.4 EAIR per 100 PY[a]

- Three deaths were reported during the OLE: 1 sudden death, 1 due to COVID-19, and 1 due to adenocarcinoma. These deaths were deemed to be unrelated to ZEPOSIA treatment by investigators[10,15]

[a]EAIRs were calculated as numbers of patients/PY × 100.[6]
[b]Laboratory values were flagged by the central laboratory if they fell outside the standard reference range; investigators decided whether laboratory values qualified as adverse events.[12]
EAIR=exposure-adjusted incidence rate; PY=patient-years.

Safety From All TRUE NORTH Patients in OLE (N=823)[6]

Adverse Events	All Patients in OLE (N=823)
	EAIR per 100 PY[a]
TEAEs	**85.5**
Serious TEAEs	**7.0**
TEAEs Leading to Treatment Discontinuation	**2.5**
Most Frequent TEAEs (Occurring in ≥7% of Patients)	
Lymphopenia[b]	6.1
COVID-19	4.3
Nasopharyngitis	3.8
Anemia[b]	3.7
Lymphocyte Count Decreased[b]	3.7
Alanine Aminotransferase Increased[b]	3.2
Arthralgia	3.2
Headache	2.8
Infection (Occurring in ≥3% of Patients)	
Serious Infection	1.8
COVID-19	4.3
Nasopharyngitis	3.8
Upper Respiratory Tract Infection	2.4
Herpes Zoster	1.2
Sinusitis	1.2
Bronchitis	1.1
Influenza	1.0
Malignancy (Serious TEAE)	
Colon Adenocarcinoma	0.04
Pancreatic Adenocarcinoma	0.04
Basal Cell Carcinoma	0.04
B-Cell Lymphoma	0.04
Follicular Lymphoma, Stage IV	0.04
Malignant Lung Neoplasm	0.04
Prostate Cancer	0.04
Rectal Adenocarcinoma	0.04
Rectal Cancer, Stage II	0.04
Cardiovascular Disorders	
Hypertension	2.3
Hypertensive Crisis	0.16
Bradycardia	0.12
Third-Degree AV Block	0.04
Myocardial Ischemia	0.12
Ischemic Stroke	0.12
Pulmonary Embolism	0.12
Deep Vein Thrombosis	0.12
Macular Edema	**0.12**

IMPORTANT SAFETY INFORMATION (cont'd)

Bradyarrhythmia and Atrioventricular Conduction Delays (cont'd): 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

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ZEPOSIA—a Highly Selective S1P With Nearly a Decade of Clinical Trial Experience Across Multiple Indications[1,16ab]

6 phase 2–3 clinical trials
across UC and MS[1,14,16-22c]

~38,000 patients
in clinical trials (Ph 1–3 MS, Ph 2–3 UC) and post-marketing setting[23,24]

~40,000 patient-years
total exposure in clinical trials (Ph 1–3 MS, Ph 2–3 UC) and post-marketing setting[23,24]

UP TO 10 YEARS
of ZEPOSIA experience in UC and MS clinical trials and post-marketing setting[1,16,19,25]

Overall ZEPOSIA exposure in parent and extension trials (all indications) was 17,321.31 PY and estimated to be 22,652 PY in the post-marketing setting. The cumulative number of patients exposed to ZEPOSIA in parent and extension trials (all indications) was 3789 and estimated to be 34,910 in the post-marketing setting. All trials had a data cutoff of May 19, 2023, and all post-marketing data had a cutoff date of April 30, 2023.[23,24]

Real-world experience with ZEPOSIA across UC and MS

3+ Years available in market[26,27]
MS approval: March 2020; UC approval: May 2021[26,27]

Prescribed by 4,300+ HCPs[28]
Through July 2023 data cutoff

[a]ZEPOSIA is an S1P receptor modulator that binds with high affinity to S1P receptors 1 and 5. The mechanism by which ZEPOSIA exerts therapeutic effects in UC is unknown.[1]
[b]In UC, from the start of the TOUCHSTONE phase 2 clinical trial (December 26, 2012) through TRUE NORTH OLE study data cutoff (January 10, 2022). In MS, from the start of the RADIANCE phase 2 clinical trial (September 18, 2012) through the DAYBREAK OLE data cutoff (February 1, 2022). Only includes patients receiving the 0.92-mg dose of ZEPOSIA.[8,16,18,19,25]
[c]ZEPOSIA has been studied across multiple indications in 6 phase 2–3 clinical trials[1,14,16-22]:
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, open-label extension trial; TOUCHSTONE (NCT01647516), a phase 2, multicenter, randomized, double-blind, placebo-controlled trial.[14,16,20,21]
Relapsing MS: SUNBEAM (NCT02294058) and RADIANCE (NCT02047734), phase 3, multicenter, randomized, double-blind, double-dummy, active treatment-controlled studies; DAYBREAK (NCT02576717): an ongoing phase 3, multicenter, open-label extension trial.[1,17,18,22,25]
MS=multiple sclerosis; Ph=phase; S1P=sphingosine 1-phosphate.

IMPORTANT SAFETY INFORMATION (cont'd)

Bradyarrhythmia and Atrioventricular Conduction Delays (cont'd):

- 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

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IMPORTANT SAFETY INFORMATION (cont'd)

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.

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. After stopping ZEPOSIA in the setting of PML, monitor for development of immune reconstitution inflammatory syndrome (PML-IRIS).

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IMPORTANT SAFETY INFORMATION (cont'd)

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.

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Not an actual patient.

Start Patients Like Stephen on ZEPOSIA Today[a]

Patients experienced relief[b] from symptoms as early as Week 2[2-4]
A decrease in both RBS and SFS was observed in patients taking ZEPOSIA as early as Week 2[1,4]

Rapid clinical response and remission at Week 10[1c]

Long-term clinical remission data observed up to ~4 years[6]

ZEPOSIA can help patients achieve remission without the use of corticosteroids[1d]

A demonstrated safety profile and long-term safety data observed over ~4 years with ZEPOSIA[1,10,14]

[a]Patients can initiate ZEPOSIA therapy if they have had CBC bloodwork, including lymphocyte count, within the past 6 months or after discontinuation of prior UC therapy and liver function tests (with transaminase and bilirubin levels) within the past 6 months; an ECG to determine if pre-existing conduction abnormalities are present; documented history of VZV or a full course of VZV vaccination; live attenuated vaccine immunization performed at least 1 month prior; and no history of uveitis, macular edema, or diabetes mellitus. Determine if patients are taking drugs that could slow heart rate or atrioventricular conduction. Consider possible unintended additive immunosuppressive effects before initiating treatment with ZEPOSIA if taking anti-neoplastic, non-corticosteroid immunosuppressive, or immune-modulating therapies, or if there is a history of prior use of these drugs.[1]

[b]Symptomatic clinical response was defined as a decrease from baseline in the combined 6-point SFS + RBS by ≥1 point and ≥30%, and a decrease of ≥1 point in RBS or an absolute RBS of ≤1 point.[3]

[c]Significantly higher clinical response rates vs placebo in the pivotal trial: 48% (205/429) vs 26% (56/216) at Week 10 (p<0.0001). Significantly higher clinical remission rates vs placebo in the pivotal trial: 18% (79/429) vs 6% (13/216) at Week 10 (p<0.0001).[1]

[d]At Week 52, 32% of patients taking ZEPOSIA achieved CS-free remission vs 17% of patients taking placebo (p<0.001).[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 UC, defined as a Mayo score of 6 to 12 at baseline.[1]

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

Secondary Endpoint of Clinical Response Is Defined as: a reduction from baseline in the 3-component Mayo score of ≥2 and ≥35%, and a reduction from baseline in the RBS of ≥1 or an absolute RBS of 0 or 1.[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. Corticosteroid tapering was required upon entering this study for patients who were receiving corticosteroids during the induction period.[1]

Study Design for OLE: the TRUE NORTH OLE is an ongoing trial that enrolled participants who were nonresponders at the end of induction, experienced disease relapse during maintenance, or completed maintenance treatment in the phase 3 TRUE NORTH study or remained at study closure and received once-daily oral ZEPOSIA 0.92 mg in the phase 2 TOUCHSTONE open-label extension. A total of 823 patients from TRUE NORTH entered the TRUE NORTH OLE.[7-9]

Endpoints were evaluated at Weeks 46, 94, and 142 of the OLE for all patients who entered the OLE from the TRUE NORTH parent study and for a subset of patients in clinical remission or clinical response at Week 52 and had continuous ZEPOSIA exposure. Endpoints include clinical remission, clinical response, endoscopic improvement, and CS-free remission. Safety was evaluated for all 823 patients who entered the OLE from the TRUE NORTH parent study.[7,8,10-12]

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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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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