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.

DMT=disease-modifying therapy.

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
- Patients with severe untreated sleep apnea
- Patients taking a monoamine oxidase (MAO) inhibitor

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

ZEPOSIA® (ozanimod) 0.92 mg capsules

Female, late 20s | Married, no children | Evidence of disease activity

DMT-Naïve

Emily is a young, married woman with an active lifestyle, looking for her first DMT.

Emily's Medical History

- **Newly diagnosed** with Relapsing Multiple Sclerosis (RMS)
- Has **no prior experience** with treatments
- Presented with optic neuritis at time of diagnosis, which has now resolved
- **Evidence of disease activity** on MRI

Treatment Plan Considerations

- Wants a DMT that will **lower the chances of relapse**
- Prefers **once-daily* oral option**

In ZEPOSIA Pivotal Trials[1,2†]

- **~70%** were **DMT-naïve**
- **~67%** were **female**
- **~70%** were **≤40 years of age**

†In ZEPOSIA pivotal trials SUNBEAM (1 year; N=1346) and RADIANCE (2 years; N=1313): ~30% of participants had previous experience with disease-modifying therapy, ~33% of participants were male, and ~30% of participants were above the age of 40.[1,2]

*Patients with mild or moderate hepatic impairment (Child-Pugh class A or B), should initiate ZEPOSIA with a 7-day titration. After initial titration, the recommended dosage of ZEPOSIA in these patients is 0.92 mg taken orally once every other day, starting on Day 8. Use of ZEPOSIA in patients with severe hepatic impairment (Child-Pugh class C) is not recommended.
MRI=magnetic resonance imaging.

Why ZEPOSIA for DMT-naïve patients?

Visit ZeposiaHCP.com/MS to learn more

IMPORTANT SAFETY INFORMATION (CONTINUED)

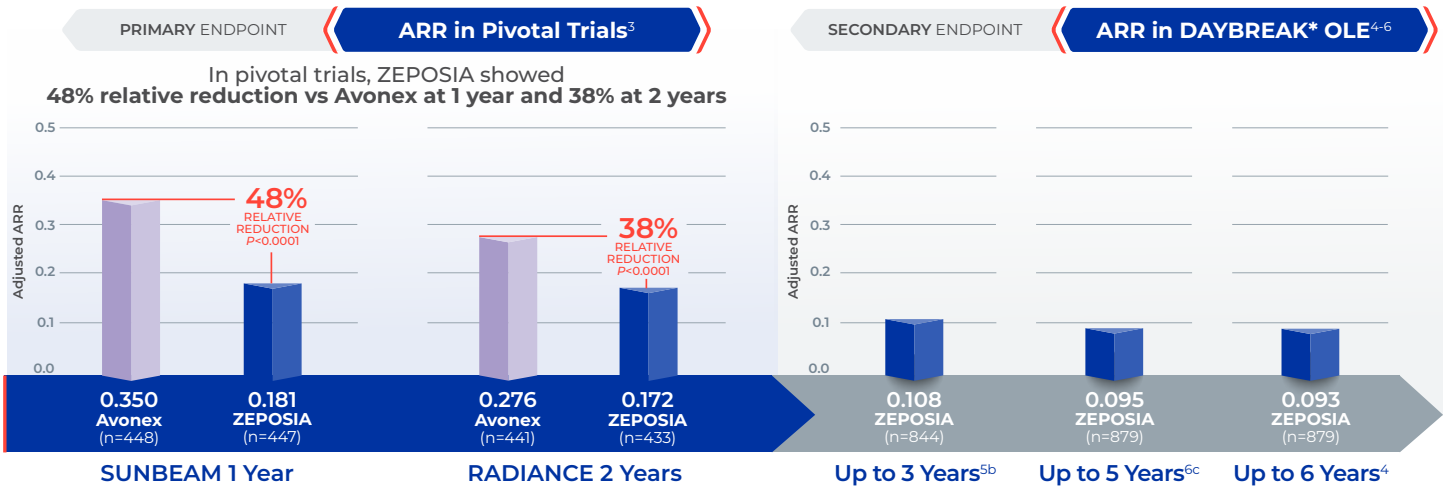
Infections: ZEPOSIA may increase the susceptibility to infections. Life-threatening and rare fatal infections have occurred in patients receiving ZEPOSIA. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS or UC therapy) complete blood count (CBC) including lymphocyte count before 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 (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 Delivered Powerful Efficacy in Reducing ARR vs Avonex® in Pivotal Trials[3]

In the ongoing open-label extension study, patients continuously treated with ZEPOSIA up to 6 years[a] had an ARR of 0.093[4]



A relapse was defined as the occurrence of new or worsening neurological symptoms persisting for more than 24 hours attributable to MS and immediately preceded by a relatively stable or improving neurological state of at least 30 days.[1,2]

*DAYBREAK is an ongoing OLE trial that enrolled participants from multiple randomized phase 1, 2, or 3 studies, including SUNBEAM and RADIANCE, and is presented as an interim analysis with a data cutoff of February 1, 2022. Endpoints were analyzed descriptively.[4-6]

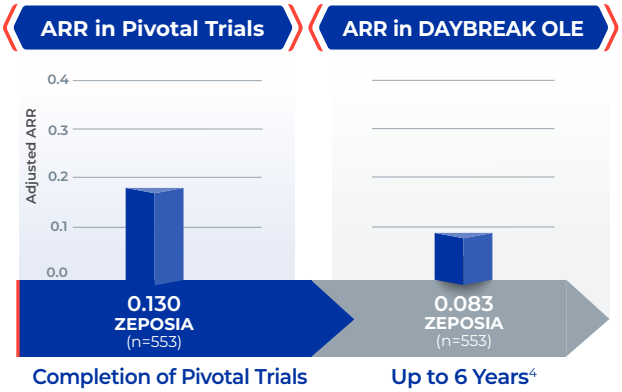
[a]At data cutoff (February 1, 2022), mean (range) continuous ozanimod 0.92 mg oral daily dose exposure in DAYBREAK was 56.4 (0.03-74.7) months.[4]

[b]Study period includes DAYBREAK Day 1 through last treatment date or the data cutoff date of December 20, 2019.[5]

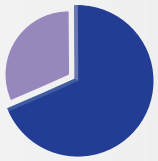
[c]At data cutoff date of February 2, 2021.[6]

Post Hoc Analysis: Adjusted ARR for DMT-Naïve Patients[7a]

DMT-naïve at baseline



~70%
of patients in ZEPOSIA pivotal trials were **DMT-naïve**[1,2]



In ZEPOSIA pivotal trials SUNBEAM (1 year; N=1346) and RADIANCE (2 years; N=1313): ~30% of participants had previous experience with disease-modifying therapy.[1,2]

In SUNBEAM and RADIANCE, prior treatment status (treatment naïve vs previously treated) was pre-specified, but not powered to detect a difference in the treatment effect in these subgroups.

[a]This analysis includes DMT-naïve patients who received ozanimod 0.92 mg oral daily dose in SUNBEAM (≥12 months) and RADIANCE (24 months). Phase 3 trial completers were eligible for enrollment in the OLE trial (DAYBREAK-NCT02576717) of ozanimod 0.92 mg/d (1 Feb 2022 cutoff).[4]

Analyses were based on the negative binomial regression model with parent treatment group, adjusted for region (Eastern Europe vs rest of world), age at parent baseline, and the parent baseline number of gadolinium-enhancing lesions. The natural log transformation of time on treatment is used as an offset term to adjust for patients having different exposure times.

DMT-experienced patients who received ozanimod 0.92 mg oral daily dose (n=207), had ARR of 0.194 at the completion of the pivotal trials and ARR of 0.118 at February 1, 2022 cutoff in DAYBREAK.

ARR=annualized relapse rate; OLE=open-label extension.

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.

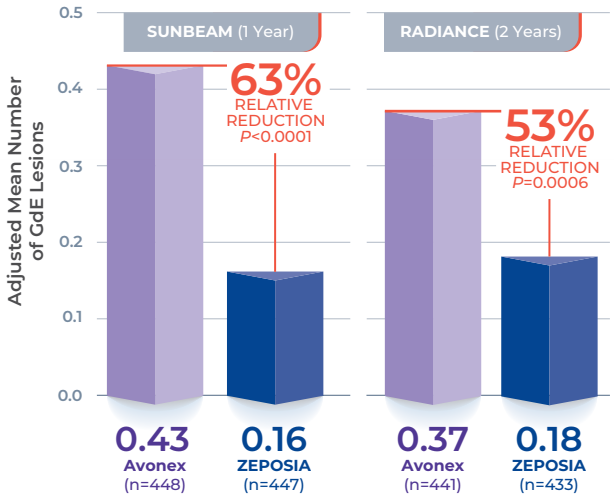
Please see Important Safety Information throughout and full Prescribing Information and Medication Guide.

ZEPOSIA® (ozanimod) | 0.92 mg capsules

ZEPOSIA Reduced Lesions Across All Secondary Measures of MRI Activity[3]

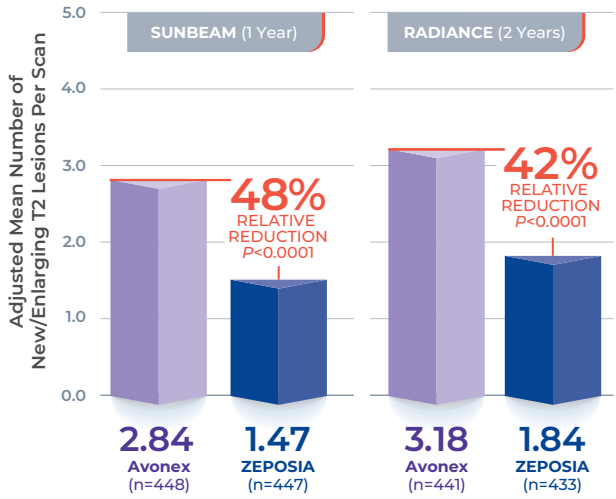
Number of GdE Lesions

SECONDARY ENDPOINT



Number of New/Enlarging T2 Lesions

SECONDARY ENDPOINT



In the 1-year SUNBEAM study, brain MRIs were performed at baseline, Month 6, and Month 12. In the 2-year RADIANCE study, brain MRIs were performed at baseline, Month 12, and Month 24.[1,2]

9 of 10 Patients Showed No 3-Month CDP in SUNBEAM and RADIANCE

SECONDARY ENDPOINT — **3-month CDP at 2 Years (Pooled Analysis)[2,3*†]**

At 2 years,

92.4%

vs **92.2% for Avonex** Showed **No Confirmed** 3-Month **Disability Progression**

Statistical significance was not reached for the pooled CDP.

- **7.6% of patients** treated with ZEPOSIA (n=67/880) experienced
- **3-month CDP, as measured by EDSS, similar to Avonex** (7.8%; n=69/889) (*P*=NS)

POST HOC ANALYSIS — **3-month CDP at 6 Years[4*‡]**

Rate of CDP measured at 6 years

78.9%

Showed **No Confirmed** 3-Month **Disability Progression (n=600/760)**

- **21.1% of patients** treated with ZEPOSIA (n=160/760) experienced
- **3-month CDP, as measured by EDSS**

Endpoints were analyzed descriptively.

*CDP was defined as at least a 1-point increase from baseline EDSS confirmed after 3 months and after 6 months.[3,4]
†CDP was prospectively evaluated in a pooled analysis from the SUNBEAM (≥1 year) and RADIANCE (2 years) studies.[3]
‡This post hoc analysis includes patients who received ozanimod 0.92 mg oral daily dose in SUNBEAM (≥1 year) and RADIANCE (2 years). Phase 3 trial completers were eligible for enrollment in OLE DAYBREAK. Data cutoff for this interim analysis is February 2022.[4]
CDP=confirmed disability progression; EDSS=Expanded Disability Status Scale; GdE=gadolinium-enhancing; NS=not significant.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Infections (continued)**:**

- 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.

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

Compelling Efficacy in Brain Volume Loss Data in Pivotal Trials[1,2]

Whole Brain Volume Loss

SECONDARY ENDPOINT

Mean Percent Change From Baseline

SUNBEAM (1 Year)

31% RELATIVE REDUCTION

ZEPOSIA: –0.41 (n=397)
vs Avonex: –0.61 (n=406)

RADIANCE (2 Years)

26% RELATIVE REDUCTION

ZEPOSIA: –0.71 (n=390)
vs Avonex: –0.94 (n=397)

Thalamic Volume Loss

EXPLORATORY ENDPOINT

Mean Percent Change From Baseline

SUNBEAM (1 Year)

32% RELATIVE REDUCTION

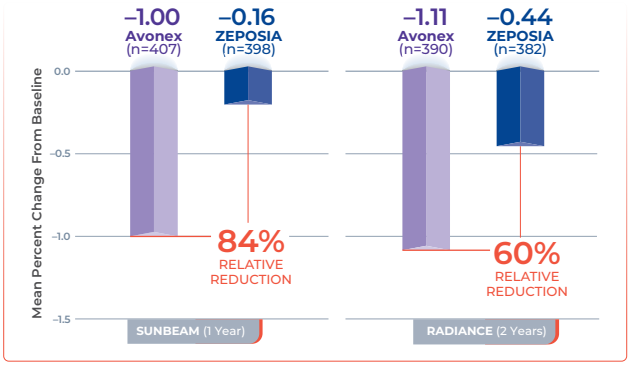
ZEPOSIA: –1.12 (n=393)
vs Avonex: –1.72 (n=406)

RADIANCE (2 Years)

27% RELATIVE REDUCTION

ZEPOSIA: –1.40 (n=385)
vs Avonex: –1.85 (n=391)

EXPLORATORY ENDPOINT | **Cortical Grey Matter Volume Loss**

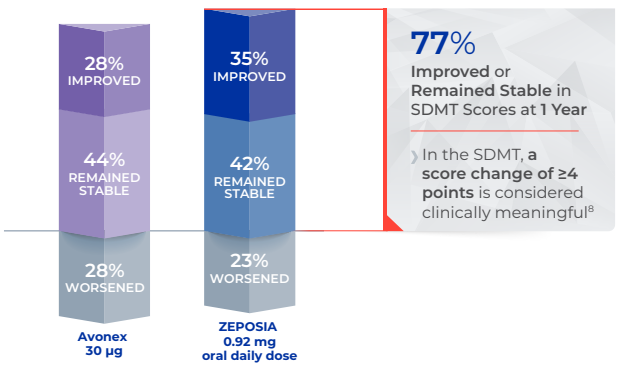


Volume loss endpoints were not part of the statistical analysis hierarchy.[1,2]

In the 1-year SUNBEAM study, brain MRIs were performed at baseline, Month 6, and Month 12.[1]
In the 2-year RADIANCE study, brain MRIs were performed at baseline, Month 12, and Month 24.[2]

Post Hoc Analysis: Cognitive Processing Speed Data From SUNBEAM and DAYBREAK[8]

POST HOC ANALYSIS | **SDMT Scores From SUNBEAM** (1 Year)[8]



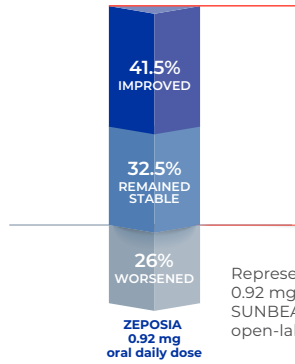
77%
Improved or **Remained Stable** in SDMT Scores at **1 Year**

In the SDMT, **a score change of ≥4 points** is considered clinically meaningful[8]

ZEPOSIA: n=397 at Month 12 for SDMT; Avonex: n=395 at Month 12 for SDMT

POST HOC ANALYSIS | **SDMT Scores From DAYBREAK** (OLE)[8]

Categorical Analysis of Clinically Meaningful Change in SDMT Relative to SUNBEAM Baseline[a]



74%
Improved or **Remained Stable** in SDMT Scores at 5 years

In the SDMT, **a score change of ≥4 points** is considered clinically meaningful[8]

Represents participants receiving ZEPOSIA 0.92 mg oral daily dose who completed the SUNBEAM phase 3 trial and enrolled in the open-label extension study.[3,8]

ZEPOSIA: n=323 at 5 years for SDMT

Endpoint was not part of the statistical analysis hierarchy and was analyzed descriptively.[1,5]

The MSFC was a secondary endpoint made up of 3 components: 9-hole peg test (arm/hand function), timed 25-foot walk (ambulation), and SDMT (cognitive function).[1,9]

SDMT is a tool that measures cognitive processing speed.[1]

[a]The data cutoff for this interim analysis was February 1, 2022.[8]

MSFC=Multiple Sclerosis Functional composite; SDMT=Symbol Digit Modalities Test.

IMPORTANT SAFETY INFORMATION (CONTINUED)

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.

ZEPOSIA Has a Well-Established Safety Profile[3,10a]

Nearly 10 YEARS

of experience across multiple indications[3,10b]

6 phase 2-3 clinical trials[3,10-17c]

across UC and MS

~38,000 patients

in clinical trials and post-marketing setting[18,19]

~40,000 patient years

total exposure in clinical trials and post-marketing setting[18,19]

≥90% of Patients Stayed on Therapy Through Completion of Pivotal Trials*

*In the 1-year SUNBEAM trial, 94% of patients who received ZEPOSIA and 92% who received Avonex completed the study.[3] In the 2-year RADIANCE trial, 90% of patients who received ZEPOSIA and 85% who received Avonex completed the study.[3]

Overall ozanimod exposure in parent and extension trials (Phase 1-3 MS, Phase 2-3 UC) was 17,321.31 patient years (PY) and estimated to be 22,652 PY in the post-marketing setting. The cumulative number of patients exposed to ozanimod in parent and extension trials (all indications) was 3789 and estimated to be 34,910 in the post-marketing setting. All trials have a data cutoff of May 19, 2023 and all post-marketing data have a cutoff date of April 30, 2023.[18,19]

[a]ZEPOSIA has been studied across multiple indications in 4 clinical trials, including TRUE NORTH (Ph 3); TOUCHSTONE (Ph 2); and SUNBEAM (Ph 3) and RADIANCE (Ph 3). 496 patients receiving the 0.92 mg oral daily dose of ZEPOSIA during induction in TRUE NORTH or TOUCHSTONE and 882 patients receiving the 0.92 mg oral daily dose of ZEPOSIA in SUNBEAM or RADIANCE were assessed in the safety analysis.[10-12,14]

[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 oral daily dose of ZEPOSIA.[3,4,10,12,20]

[c]ZEPOSIA has been studied across multiple indications in 6 phase 2-3 clinical trials[3,10-17]:

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.[10,14-16]

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.[3,4,11,12,17]

PY=patient years; UC=ulcerative colitis.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Progressive Multifocal Leukoencephalopathy (PML) (Continued)**:**
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.

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

Safety Comparable to Avonex in Overall Incidence of AEs, and Generally Similar Safety in Ongoing Long-Term Extension Study; Nearly 10 Years of Experience[1-4]*

IN PIVOTAL TRIALS: Incidence of Adverse Reactions[1-3]

	SUNBEAM (1 YEAR)		RADIANCE (2 YEARS)	
Summary of Adverse Reactions	**Avonex (n=445)**	**ZEPOSIA (n=448)**	**Avonex (n=440)**	**ZEPOSIA (n=434)**
Overall incidence of adverse reactions	75.5%	59.8%	83.0%	74.7%
Severe adverse reactions	2.2%	1.6%	4.3%	3.5%
Serious adverse reactions	2.5%	2.9%	6.4%	6.5%

Adverse Reactions With an Incidence of at Least 2% in Patients Treated With ZEPOSIA and at Least 1% Greater Than Avonex[3a]

SUNBEAM AND RADIANCE: POOLED DATA

Adverse Reactions	Avonex (n=885)	ZEPOSIA (n=882)
Upper respiratory infection[b]	23%	26%
Hepatic transaminase elevation[c]	5%	10%
Orthostatic hypotension	3%	4%
Urinary tract infection	3%	4%
Back pain	3%	4%
Hypertension[d]	2%	4%
Abdominal pain upper	1%	2%

Adverse reactions are sorted by decreasing incidence in patients treated with ZEPOSIA. For adverse reactions pertaining to liver function tests, increases were transient and generally resolved without discontinuation.[1,2] Elevations of 3-fold the ULN or greater occurred in 5.5% of patients taking ZEPOSIA and in 3.1% of patients taking Avonex. The majority (79%) continued treatment with ZEPOSIA with values returning to less than 3 times the ULN within approximately 2 to 4 weeks.[3]

*From the first patient randomized (October 18, 2012) through the DAYBREAK data cutoff (February 1, 2022), the maximum continuous exposure was 110.8 months. The mean exposure to ZEPOSIA 0.92 mg oral daily dose in the parent trials and DAYBREAK was 70.4 months.[4]

[a]Data are not an adequate basis for comparison of rates between ZEPOSIA and the active control.[3]

[b]Includes the following terms: nasopharyngitis, upper respiratory tract infection, pharyngitis, respiratory tract infection, bronchitis, rhinitis, respiratory tract infection viral, viral upper respiratory tract infection, rhinorrhea, tracheitis, and laryngitis.[3]

[c]Includes the following terms: alanine aminotransferase increased, gamma-glutamyl transferase (GGT) increased, aspartate aminotransferase increased, hepatic enzyme increased, liver function test abnormal, and transaminases increased.[3]

[d]Includes hypertension, essential hypertension, and orthostatic hypertension.[3]

[e]ALC reductions are an expected pharmacodynamic effect related to the mechanism of ozanimod; although investigators were not required to report ALC reductions as TEAEs, lymphopenia and ALC decreases were reported as TEAEs according to investigator determination.[4]

[f]Includes preferred terms of hypertension, essential hypertension, labile hypertension, and systolic hypertension.[4]

[g]Includes preferred terms of depression, depressed mood, and depressive symptoms.[4]

IR=Incidence rate; TEAEs=treatment-emergent adverse events; ULN=upper limit of normal.

DAYBREAK OLE: Incidence of Adverse Events[4]

Summary of TEAEs (PRIMARY ENDPOINT)	ZEPOSIA (N=2494)	IR/1000 PY
Any TEAE	88.2%	657.0
Severe TEAEs	8.9%	19.6
Serious TEAEs	14.1%	32.0
TEAEs leading to permanent treatment discontinuation	3.6%	7.6

TEAEs in ≥5% of Patients Treated With ZEPOSIA[4]

TEAEs	ZEPOSIA (N=2494)	IR/1000 PY
Nasopharyngitis	20.6%	51.0
Headache	16.9%	40.3
Upper respiratory tract infection	11.9%	27.3
Lymphopenia[e]	10.5%	24.2
ALC decreased[e]	9.2%	20.9
Back pain	9.1%	20.5
Hypertension[f]	8.7%	19.5
GGT increased	7.3%	16.3
Arthralgia	6.3%	13.8
Respiratory tract infection	6.3%	13.8
Urinary tract infection	6.3%	13.8
Bronchitis	6.2%	13.6
Viral respiratory tract infection	5.5%	12.0
Depression-related TEAEs[g]	5.5%	12.0

Similar safety patterns were seen in the continuous ZEPOSIA 0.92 mg oral daily dose (n=881) population[4]

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

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

ZEPOSIA® (ozanimod) 0.92 mg capsules

Demonstrated Tolerability Profile With Low Discontinuation Rates Due to Adverse Events[1-4]

Low Discontinuation Rates Due to AEs[1,2,4]

SUNBEAM (1 Year)

2.9% for ZEPOSIA and **3.6%** for Avonex[1]

RADIANCE (2 Years)

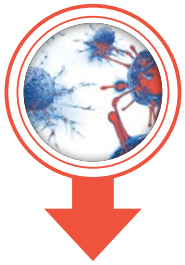
3.0% for ZEPOSIA and **4.1%** for Avonex[2]

DAYBREAK (Up to 6 Years) n=2494

3.6% for ZEPOSIA in Long-Term Extension Study[4]

≥90% of Patients Stayed on Therapy Through Completion of Pivotal Trials*

*In the 1-year SUNBEAM trial, 94% of patients who received ZEPOSIA and 92% who received Avonex completed the study.[3] In the 2-year RADIANCE trial, 90% of patients who received ZEPOSIA and 85% who received Avonex completed the study.[3]



Rates of Serious Infections and Malignancies Consistent vs Avonex

The rate of serious infections at 1 year for ZEPOSIA was 1.1% vs 0.7% for Avonex and the rate at 2 years for ZEPOSIA was 0.9% vs 0.9% for Avonex. The rate of malignancies at 1 year for ZEPOSIA was 0.2% vs 0% for Avonex and the rate at 2 years for ZEPOSIA was 0.9% vs 0.5% for Avonex.[1,2]

Overall Infections

In SUNBEAM and RADIANCE, the overall rate of infections with ZEPOSIA (35%) was similar to Avonex (34%). ZEPOSIA causes a reduction in peripheral blood lymphocyte count and may increase the risk of infection.[3]

Herpetic Infection: In active-controlled MS trials, herpes zoster was reported as an adverse reaction in 0.6% of patients treated with ZEPOSIA 0.92 mg oral daily dose and in 0.2% of patients taking Avonex.[3]

IMPORTANT SAFETY INFORMATION (CONTINUED)

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.

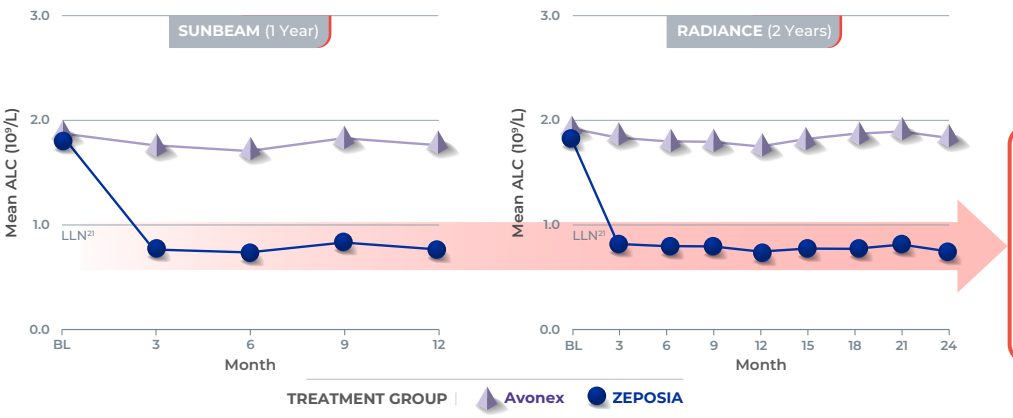
Increased Blood Pressure: Increase in systolic pressure was observed after about 3 months of treatment and persisted throughout treatment. Blood pressure should be monitored during treatment and managed appropriately. Certain foods that may contain very high amounts of tyramine could cause severe hypertension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

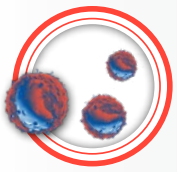
Respiratory Effects: ZEPOSIA may cause a decline in pulmonary function. Spirometric evaluation of respiratory function should be performed during therapy, if clinically indicated.

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

ZEPOSIA Consistently Maintained ALC Near the Lower Limit of Normal[1,2,21]

ALC Consistently Maintained Near LLN at ≈0.8 x 10^9/L





Maintained Near the LLN at a Mean Lymphocyte Count of

≈800 lymphocytes/ µL of blood

Lymphocyte Numbers Can be Restored to Normal Values by Discontinuing Therapy[1-3,6,22]

- **After discontinuing** ZEPOSIA 0.92 mg oral daily dose, the median time for peripheral blood lymphocytes to return to the normal range was 30 days, with approximately 90% of patients in the normal range within 3 months[3]
- **Mean ALC was approximately 0.8 × 10^9 cells/L** for both SUNBEAM and RADIANCE (at 1 year and 2 years, respectively)[1,2]
- **Patients who received** ZEPOSIA 0.92 mg oral daily dose during the parent trials exhibited stable ALCs (mean of 0.7-0.8 × 10^9/L at each time point) throughout the first 48 months of DAYBREAK[3,4]
- **ZEPOSIA causes a mean reduction** in peripheral blood lymphocyte count to approximately 45% of baseline values because of reversible sequestration of lymphocytes in lymphoid tissues; ZEPOSIA may therefore increase the susceptibility to infections, some serious in nature[1,22]

BL=baseline; LLN=lower limit of normal.

IMPORTANT SAFETY INFORMATION (CONTINUED)

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.

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

ZEPOSIA® (ozanimod) 0.92 mg capsules

One Capsule, Once a Day[a], From the Start With Minimal Pre-Initiation Requirements[3]

ZEPOSIA 7-Day Titration Schedule

Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8 & thereafter
0.23 mg once daily				0.46 mg once daily			0.92 mg once daily[a]

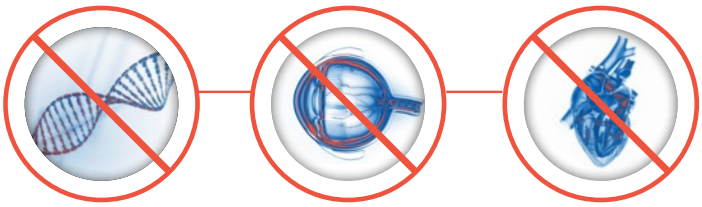
[a]Recommended dosage in patients with hepatic impairment

- In patients with mild or moderate hepatic impairment (Child-Pugh class A or B), initiate ZEPOSIA with a 7-day titration. After initial titration, the recommended dosage of ZEPOSIA in these patients is 0.92 mg taken orally once every other day, starting on Day 8. Use of ZEPOSIA in patients with severe hepatic impairment (Child-Pugh class C) is not recommended

Additional dosing consideration

- 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
- If a dose is missed within the first 2 weeks of treatment, reinitiate treatment using the titration regimen
- If a dose is missed after the first 2 weeks of treatment, continue with the treatment as planned
- ZEPOSIA may be taken with or without food

Full Prescribing Information for ZEPOSIA Has



NO Genetic Testing

NO Ophthalmic Testing for Most Patients[3,23b]

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**
- 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

[b]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.[3]

AV=atrioventricular; CBC=complete blood count; ECG=electrocardiogram; VZV=varicella zoster virus.

IMPORTANT SAFETY INFORMATION (CONTINUED)

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).

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.

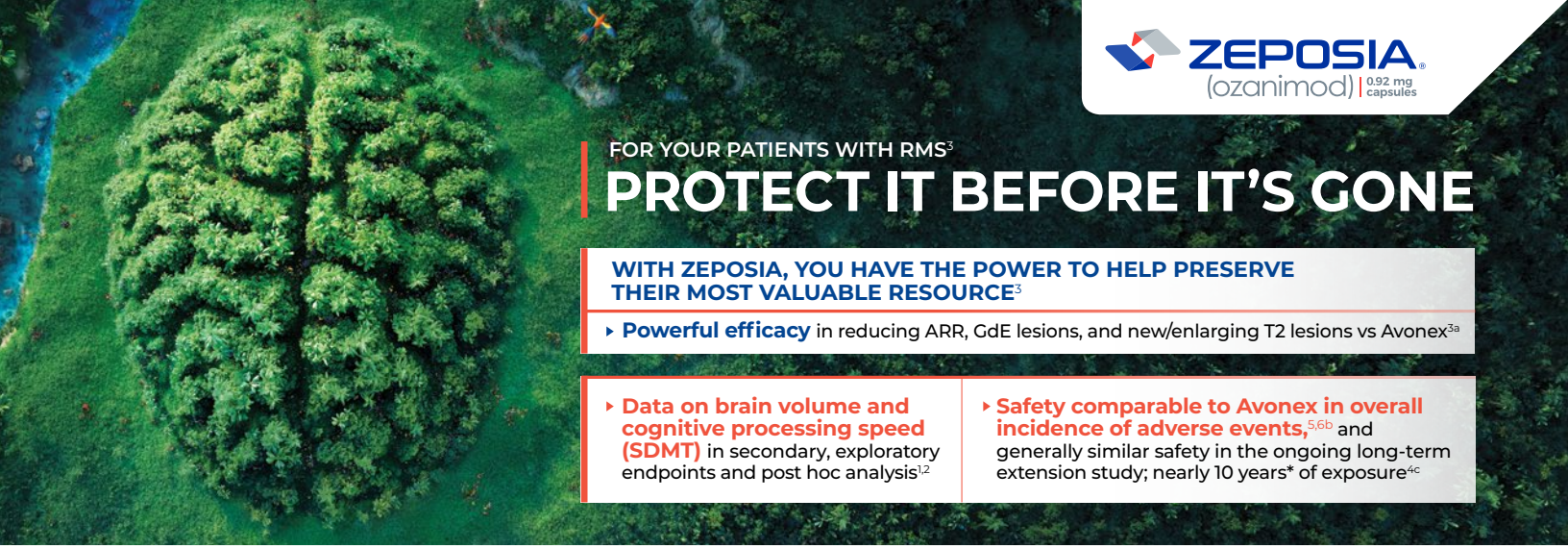
In the UC clinical trials, the most common adverse reactions that occurred in ≥4% of ZEPOSIA-treated patients and greater than in patients who received placebo were upper respiratory infection, liver test increased, and headache.

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

Learn How to Get Your Patients Started on ZEPOSIA With the Start Form

ZEPOSIA®
(ozanimod) | 0.92 mg capsules

Learn More About ZEPOSIA 360 Support™ Services



ZEPOSIA® (ozanimod) | 0.92 mg capsules

FOR YOUR PATIENTS WITH RMS[3]

PROTECT IT BEFORE IT'S GONE

WITH ZEPOSIA, YOU HAVE THE POWER TO HELP PRESERVE THEIR MOST VALUABLE RESOURCE[3]

- **Powerful efficacy** in reducing ARR, GdE lesions, and new/enlarging T2 lesions vs Avonex[3a]
- **Data on brain volume and cognitive processing speed (SDMT)** in secondary, exploratory endpoints and post hoc analysis[1,2]
- **Safety comparable to Avonex in overall incidence of adverse events,**[5,6b] and generally similar safety in the ongoing long-term extension study; nearly 10 years* of exposure[4c]

*From the first patient randomized (October 18, 2012) through the DAYBREAK data cutoff (February 1, 2022), the maximum continuous exposure was 110.8 months. The mean exposure to ZEPOSIA 0.92 mg oral daily dose in the parent trials and DAYBREAK was 70.4 months.[4]

[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 oral daily dose 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]

[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. **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.[1-3] Please see the full Prescribing Information for additional SUNBEAM and RADIANCE data. See the IN PIVOTAL TRIALS table within this piece for definitions of these terms.

[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 1, 2022. Patients evaluated in this analysis included those receiving an FDA-approved maintenance dose of 0.92 mg orally once daily (n=881) who completed the randomized phase 1 to 3 trials (the "continuous" arm), and those who received ZEPOSIA 0.46 mg daily oral dose (n=877) or Avonex 30 µg (n=736) during phase 1 to 3 trials before receiving ZEPOSIA 0.92 mg oral daily dose at DAYBREAK baseline. The primary objective was to evaluate the long-term safety of ZEPOSIA. Secondary efficacy outcomes included ARR, new/enlarging T2 lesions, and GdE lesions. Endpoints were analyzed descriptively.[3-5]

Treatment-emergent adverse events (TEAEs): At the data cutoff (February 1, 2022), the overall incidence of TEAEs for ZEPOSIA in the DAYBREAK OLE trial was 88.2%. The most common TEAEs with an incidence of at least 5% in patients treated with ZEPOSIA, sorted by decreasing incidence, were as follows: nasopharyngitis, 20.6%; headache, 16.9%; upper respiratory tract infection, 11.9%; lymphopenia, 10.5%; ALC decreased, 9.2%; back pain, 9.1%; hypertension, 8.7%; gamma-glutamyl transferase increased, 7.3%; arthralgia, 6.3%; repiratory tract infection, 6.3%; urinary tract infection, 6.3%; bronchitis, 6.2%; viral respiratory tract infection, 5.5%; and depression-related TEAEs, 5.5%. The rate of TEAEs leading to permanent treatment discontinuation was 3.5%. **Severe TEAEs:** The rate of severe TEAEs was 8.9%. **Serious TEAEs:** The rate of serious TEAEs was 14.1%.[4]

FDA=US Food and Drug Administration.

References: 1. 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 and Suppl 1-26. doi:10.1016/S1474-4422(19)30239-X. **2.** 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 and Suppl 1-31. doi:10.1016/S1474-4422(19)30238-8. **3.** ZEPOSIA. Prescribing Information. Bristol-Myers Squibb Company; 2023. **4.** Selmaj KW et al. Poster presented at ECTRIMS; October 26-28, 2022; Amsterdam, Netherlands. Poster P334. **5.** Selmaj KW, Steinman L, Comi G, et al. Long-term safety and efficacy of ozanimod in relapsing multiple sclerosis in DAYBREAK: an open-label extension study of ozanimod phase 1-3 trials. Presented at: 8th Joint ACTRIMS-ECTRIMS Meeting; September 11-13, 2020; MSVirtual2020. Presentation P0217. **6.** Cree BAC, Selmaj KW, Steinman L, et al. Long-term safety and efficacy of ozanimod in relapsing multiple sclerosis: Up to 5 years of follow-up in the DAYBREAK open-label extension trial. *Mult Scler.* 2022;28(12):1944-1962. doi:10.1177/13524585221102584. **7.** Data on file. BMS-REF-02176-2084. Princeton, NJ: Bristol-Myers Squibb Company. **8.** DeLuca J et al. Presented at; ACTRIMS; February 23-25, 2023; San Diego, CA. Presentation 074. **9.** Polman CH, Rudick RA. The multiple sclerosis functional composite: a clinically meaningful measure of disability. *Neurology.* 2010;74(suppl 3):S8-S15. **10.** 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. **11.** 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. **12.** 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. **13.** Efficacy and safety study of ozanimod (RPC1063) in relapsing multiple sclerosis patients (RADIANCE). Clinicaltrials.gov. https://clinicaltrials.gov/study/NCT01628393. Updated November 2, 2021. Accessed September 6, 2023. **14.** Sandborn WJ, Feagan BG, D'Haens, et al; True North Study Group. Ozanimod as induction and maintenance therapy for ulcerative colitis. *N Engl J Med.* 2021;385(14):1280-1291. **15.** 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. **16.** 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. **17.** A multi-site, open-label extension trial of oral RPC1063 in relapsing multiple sclerosis. Clinicaltrials.gov. https://clinicaltrials.gov/study/NCT02576717. Updated March 13, 2023. Accessed July 26, 2023. **18.** Data on file. BMS-REF-OZA-0038. Princeton, NJ: Bristol-Myers Squibb Company; 2023. **19.** Data on file. BMS-REF-OZA-0039. Princeton, NJ: Bristol-Myers Squibb Company; 2023. **20.** Danese S, Abreu MT, Wolf DC, et al. Efficacy and safety of 3 years of continuous ozanimod treatment: an interim analysis of the True North open-label extension study. Oral presentation at: European Crohn's and Colitis Organisation (ECCO) 2023: Copenhagen, Denmark; March 1-4, 2023. Presentation DOP37 **21.** Lymphocytopenia. National Heart, Lung, and Blood Institute (NHLBI). Accessed November 11, 2022. www.nhlbi.nih.gov/health-topics/lymphocytopenia **22.** Steinman L, Comi G, Bar-Or A, et al. Poster presented at: 35th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); September 11-13, 2019; Stockholm, Sweden. Poster P1031. **23.** Marrie RA. Comorbidity in multiple sclerosis: implications for patient care. *Nat Rev Neurol.* 2017;13(6):375-382. doi:10.1038/ nrneurol.2017.33

IMPORTANT SAFETY INFORMATION (CONTINUED)

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.

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

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