Introducing a new oral option for your patients with relapsing forms of multiple sclerosis[1]...

Think beyond t

EXPLO

ZEPOS

Are You a Healthcare Professional?

This information is intended for U.S. Healthcare Professionals.

NO | YES

IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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

Introducing a new oral option for your patients with relapsing forms of multiple sclerosis[1]...

Think beyond t

EXPLO

ZEPOS

You Are About to Leave the ZEPOSIA® (ozanimod) Website

Do you wish to continue?

NO | YES

IMPORTANT SAFETY INFORMATION

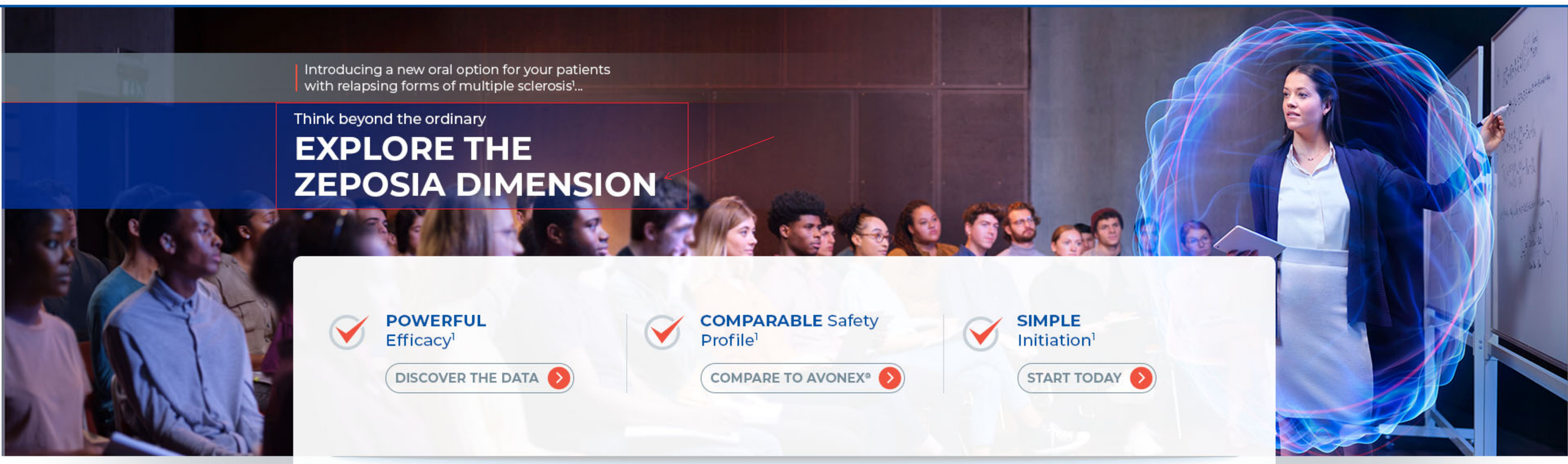
INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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



Introducing a new oral option for your patients with relapsing forms of multiple sclerosis[1]...

Think beyond the ordinary

EXPLORE THE ZEPOSIA DIMENSION

POWERFUL Efficacy[1]

DISCOVER THE DATA

COMPARABLE Safety Profile[1]

COMPARE TO AVONEX®

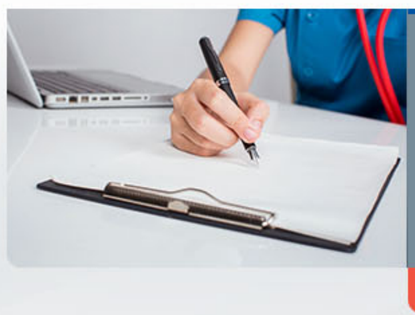
SIMPLE Initiation[1]

START TODAY

Superior Efficacy and Proven Safety Was Evaluated[1]:

- In 2 clinical trials
- Against an active comparator

ROBUST STUDY DESIGN >>



Support Made Simple:

- Start Form
- ZEPOSIA 360 Support™ Tool Kit
- Letter of Medical Necessity

FIND OUT MORE >>

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 0.92 mg vs weekly Avonex (interferon beta-1a), 30 µg intramuscular injection. **Primary endpoint:** ZEPOSIA reduced ARR vs Avonex by 48% at 1 year and by 38% at 2 years. **Secondary endpoints:** ZEPOSIA reduced the number of new or enarging 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.

Adverse events: Across 2 head-to-head trials, the most common AEs with an incidence of >2% for ZEPOSIA were nasopharyngitis, 11.1% (vs 9.5% for Avonex); alanine aminotransferase increased, 5.3% (vs 3.2% for Avonex), gamma-glutamyl transferase increased, 4.5% (vs 1.2% for Avonex); urinary tract infection, 4.1% (vs 3.1% for Avonex); hypertension, 3.4 (vs 2.0 for Avonex); pharyngitis, 3.2 (vs 2.3 for Avonex); respiratory tract infection viral, 2.4% (vs 1.2% for Avonex). **Serious infections:** The rates of serious infections at 1 year for ZEPOSIA was 1.0% vs 0.6% for Avonex and the rate at 2 years was 0.9% for ZEPOSIA vs 0.9% for Avonex. **Malignancy rates:** The rates 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.

REGISTER FOR MORE INFORMATION

For updates about ZEPOSIA, please provide your contact information below.

*Required

Email Address*

Ex: John@email.com

First Name*

Ex: John

Last Name*

Ex: Smith

NPI Number

Ex: 123456789

Specialty*

Select a speciality

☐ I am a healthcare professional. By checking this box, I authorize Bristol-Myers Squibb, its affiliates, and its agents to analyze and use my information to improve or develop services and programs and contact me about marketing programs or research about ZEPOSIA and other related health topics that may be of interest to me. I would like to receive more information about ZEPOSIA, updates on clinical data on ZEPOSIA, the support program for patients, and more.

Bristol-Myers Squibb values your privacy

Bristol-Myers Squibb, its affiliates, and its agents will not sell or rent your personal information. By providing your information, you acknowledge that you have read and agree to the terms of Bristol-Myers Squibb's privacy policy.

SIGN ME UP

References: 1. ZEPOSIA® (ozanimod) [package insert]. Summit, NJ: Bristol-Myers Squibb Company; 2019. **2.** Data on file, Bristol-Myers Squibb Company.

IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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 history or presence of second-degree atrioventricular (AV) block Type II or third-degree AV block or sick sinus syndrome unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients who have had a hypersensitivity reaction to ozanimod or are allergic to any of the excipients in ZEPOSIA

WARNINGS AND PRECAUTIONS:

Bradycardia: In all patients, dose escalation is recommended for initiation of ZEPOSIA treatment to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater reductions in heart rate

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, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine, should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Patients with preexisting liver disease may be at increased risk of developing elevated hepatic enzymes when taking ZEPOSIA

Infections: ZEPOSIA may increase the susceptibility to infections. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS 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

- Prior and Concomitant Treatment with Antineoplastic, Immunosuppressive, or Immune-modulating Therapies: In 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. 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
- No cases of Progressive Multifocal Leukoencephalopathy (PML) were identified in active-controlled MS clinical trials with ZEPOSIA. However, PML has been observed in patients treated with other MS therapies. Should symptoms present that are suggestive of PML, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued
- 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

Macular edema: Patients with risk factors for macular edema, such as a history of uveitis or diabetes mellitus, should have an ophthalmologic evaluation prior to treatment with ZEPOSIA. Patients who present with visual symptoms of macular edema should be evaluated and, if confirmed, treatment with ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): PRES is a syndrome characterized by sudden onset of severe headache, confusion, seizures, and visual loss. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. In animals, findings at similar exposure levels included embryo-fetal death, abnormal/delayed ossification, and abnormalities of the viscera and large blood vessels. Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping ZEPOSIA

Most common Adverse Reactions (≥2%): Nasopharyngitis, abnormal liver tests, urinary tract infections, hypertension, pharyngitis, and respiratory tract infections

Most common Adverse Reactions (>5%): Nasopharyngitis and abnormal liver tests (ALT/GGT)

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

DRAFT

Bristol-Myers Squibb

© 2020 Bristol-Myers Squibb Company.
ZEPOSIA is a registered trademark of Bristol-Myers Squibb Company.
All rights reserved. 01/20 US-ZEP-19-0095

REGISTER FOR MORE INFORMATION

For updates about ZEPOSIA, please provide your contact information below.

*Required

There was a problem with your submission. Errors have been highlighted below.

Email Address*

Ex: John@email.com

Please enter a valid email address.

First Name*

Ex: John

This field is required.

Last Name*

Ex: Smith

This field is required.

NPI Number

Ex: 123456789

Specialty*

Select a speciality

This field is required.

I am a healthcare professional. By checking this box, I authorize Bristol-Myers Squibb, its affiliates, and its agents to analyze and use my information to improve or develop services and programs and contact me about marketing programs or research about ZEPOSIA and other related health topics that may be of interest to me. I would like to receive more information about ZEPOSIA, updates on clinical data on ZEPOSIA, the support program for patients, and more.

Bristol-Myers Squibb values your privacy

Bristol-Myers Squibb, its affiliates, and its agents will not sell or rent your personal information. By providing your information, you acknowledge that you have read and agree to the terms of Bristol-Myers Squibb's privacy policy.

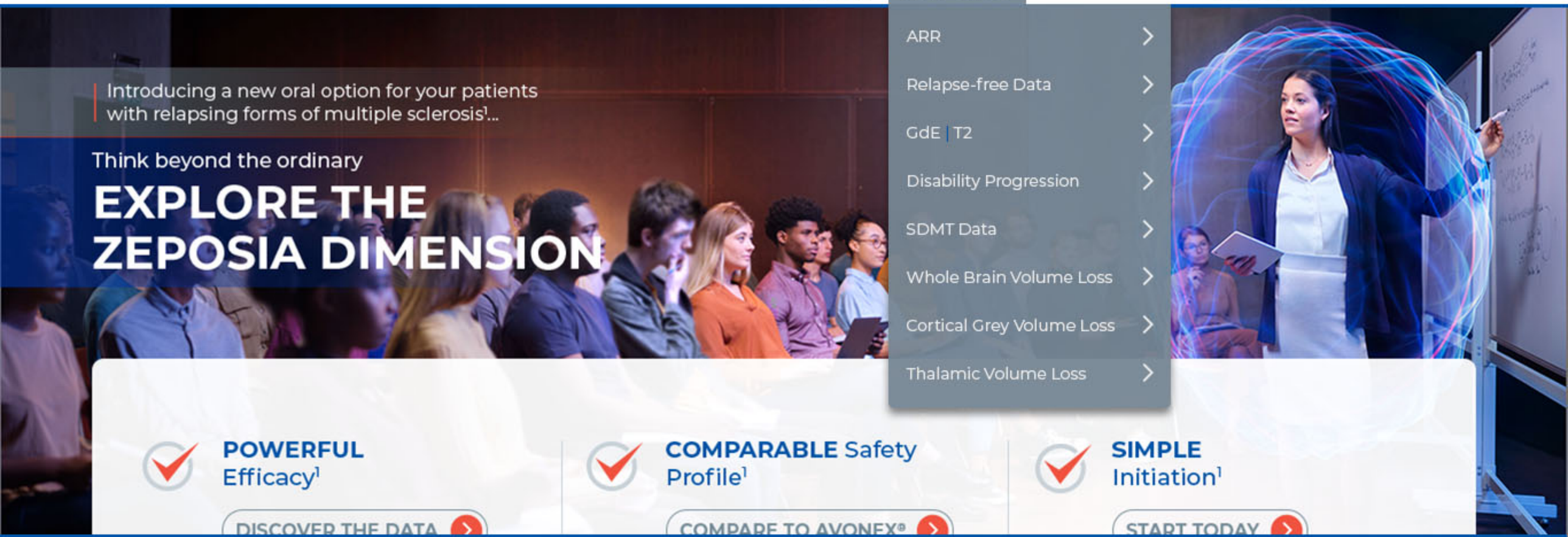
SIGN ME UP

IMPORTANT SAFETY INFORMATION

Thank you

You have been successfully registered to receive future updates about ZEPOSIA.

IMPORTANT SAFETY INFORMATION



POWERFUL Efficacy[1]

DISCOVER THE DATA

COMPARABLE Safety Profile[1]

COMPARE TO AVONEX®

SIMPLE Initiation[1]

START TODAY

IMPORTANT SAFETY INFORMATION

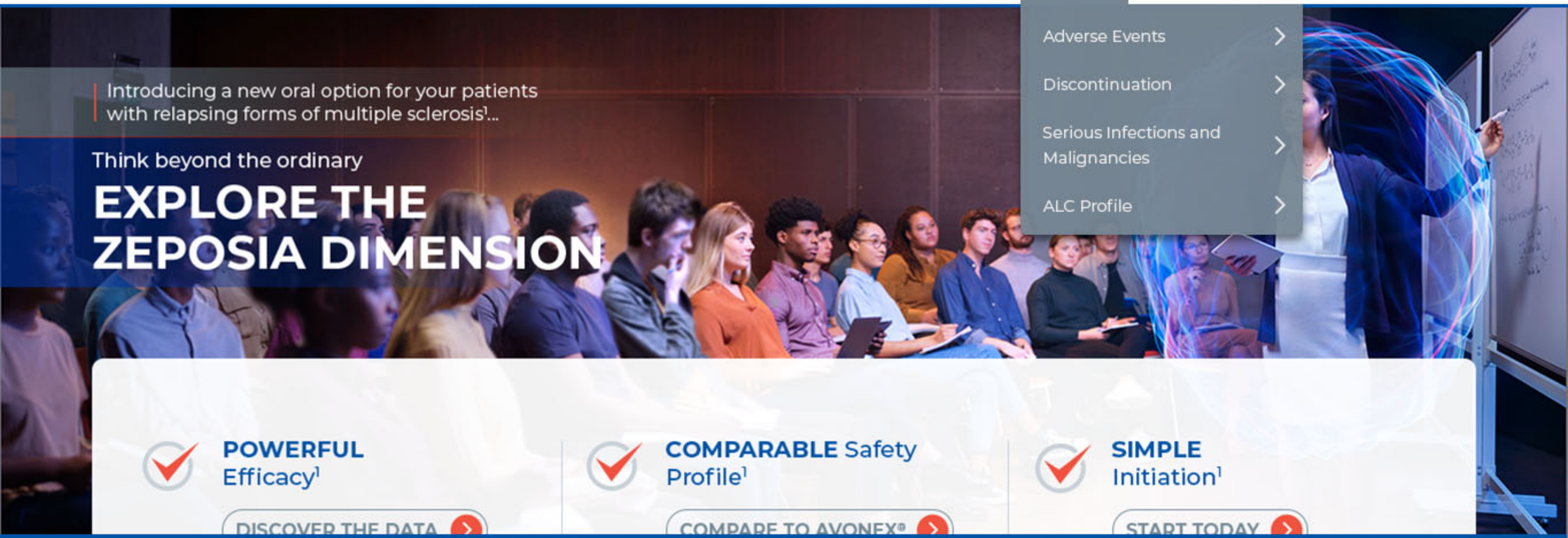
INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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



IMPORTANT SAFETY INFORMATION

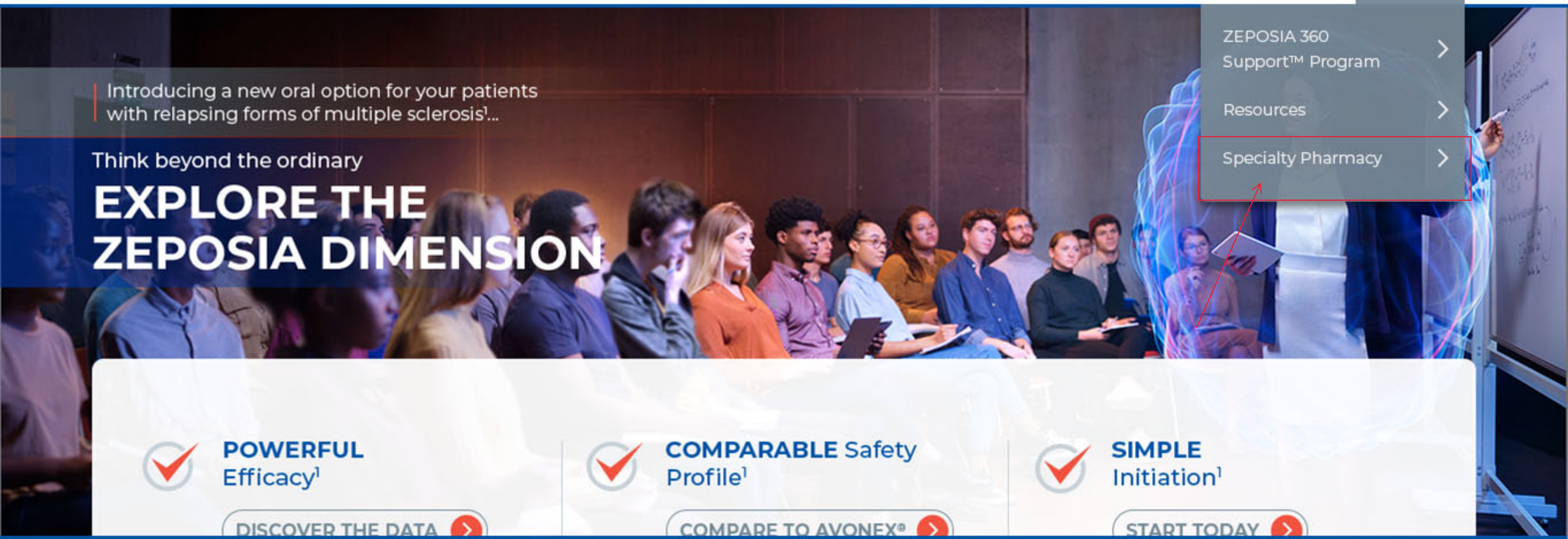
INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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



IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting disease, and active secondary progressive disease, in adults.

IMPORTANT SAFETY INFORMATION

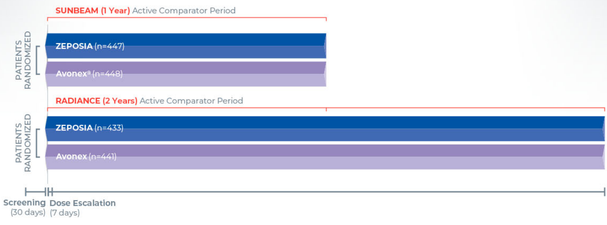
Contraindications

- Patients who in the last 6 months experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring

Robust Study Design

ROBUST DATA FROM 2 CLINICAL TRIALS WITH MORE THAN 2600 PATIENTS[1,2a]

The Largest Number of Patients With RMS Studied in Pivotal Head-to-Head Trials With an Active Comparator



[a]2600 patients includes all 3 arms of the study; the 0.92-mg dose of ZEPOSIA, the 0.46-mg maintenance dose of ZEPOSIA (not approved for maintenance dose), and the 30-µg dose of Avonex.[2,3]

Avonex (interferon beta-1a) is a registered trademark of Biogen.

+ VIEW BASELINE CHARACTERISTICS[3,4b]

— VIEW BASELINE CHARACTERISTICS[3,4b]

Baseline characteristics remained consistent across both studies.[3,4]

	Mean Age	Mean EDSS Score (Range 0.0 to 5.0)	Mean Time Since Initial MS Diagnosis	Mean Number of Relapses in Previous 12 Months	Mean GdE Lesion Count	Mean T2 Lesion Count	Mean % of Patients Previously Treated With DMTs[c]
SUNBEAM	35 Years	2.6	3.7 Years	1.3	1.8	54	31%
RADIANCE	36 Years	2.6	3.8 Years	1.3	1.7	48	29%

[b]Baseline characteristics include the 0.92-mg dose of ZEPOSIA and the 30-µg dose of Avonex. The 0.46-mg maintenance dose of ZEPOSIA (not approved for maintenance dose) is not included.

[c]DMT includes interferon beta-1a, pegylated interferon beta-1a, interferon beta-1b, glatiramer acetate, daclizumab, dimethyl fumarate, teriflunomide, and mitoxantrone (SUNBEAM only).

DMT=disease-modifying therapy; EDSS=Expanded Disability Status Scale; GdE=gadolinium enhancing; RMS=relapsing multiple sclerosis.

+ KEY INCLUSION CRITERIA[3,4]

— KEY INCLUSION CRITERIA[3,4]

- Ages 18 to 55
- EDSS score of 0.0 to 5.0
- Diagnosis of relapsing-remitting MS with at least 1 documented relapse during the previous year or 1 relapse during the previous 2 years before screening plus at least 1 GdE lesion in the year before randomization
- Clinically stable, with no relapse or corticosteroid treatment 1 month prior to screening until randomization

+ KEY EXCLUSION CRITERIA[2-4]

— KEY EXCLUSION CRITERIA[2-4]

- Disease duration >15 years
- Specific cardiac conditions (eg, recent MI/stroke, prolonged QTcF interval)
- Resting heart rate <55 bpm at screening
- Diabetes mellitus type 1, or uncontrolled diabetes mellitus type 2 with hemoglobin A1C >9% (SUNBEAM) or A1C >7% (RADIANCE), or diabetes with significant comorbidities

bpm=beats per minute; MI=myocardial infarction; QTcF=corrected QT interval using Fridericia's formula.

At Least 90% of Patients Taking ZEPOSIA Stayed on Therapy Through 1 and 2 Years[1]

SUNBEAM

92% Avonex VS 94% ZEPOSIA

RADIANCE

85% Avonex VS 90% ZEPOSIA

NEXT: Clinical Endpoints

REGISTER FOR MORE INFORMATION

For updates about ZEPOSIA, please provide your contact information below.

*Required

Email Address*

Ex: John@email.com

First Name*

Ex: John

Last Name*

Ex: Smith

NPI Number

Ex: 1234567789

Specialty*

Select a speciality

I am a healthcare professional. By checking this box, I authorize Bristol-Myers Squibb, its affiliates, and its agents to analyze and use my information to improve or develop services and programs and contact me about marketing programs or research about ZEPOSIA and other related health topics that may be of interest to me. I would like to receive more information about ZEPOSIA, updates on clinical data on ZEPOSIA, the support program for patients, and more.

Bristol-Myers Squibb values your privacy

Bristol-Myers Squibb, its affiliates, and its agents will not sell or rent your personal information. By providing your information, you acknowledge that you have read and agree to the terms of Bristol-Myers Squibb's privacy policy.

SIGN ME UP

References: 1. ZEPOSIA® (ozanimod) [package insert]. Summit, NJ: Bristol-Myers Squibb Company; 2019. **2.** Data on file, Bristol-Myers Squibb Company. **3.** Corri G, Kappos L, Selmaj KW, et al; for the SUNBEAM Study Investigators. Safety and efficacy of ozanimod versus interferon beta-1a in relapsing multiple sclerosis (SUNBEAM): a multicentre, randomised, minimum 12-month, phase 3 trial. *Lancet Neurol.* 2019;18(11):1009-1020. **4.** Cohen JA, Corri G, Selmaj KW, et al; for the 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.

IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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 history or presence of second-degree atrioventricular (AV) block Type II or third-degree AV block or sick sinus syndrome unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients who have had a hypersensitivity reaction to ozanimod or are allergic to any of the excipients in ZEPOSIA

WARNINGS AND PRECAUTIONS:

Bradycardia: In all patients, dose escalation is recommended for initiation of ZEPOSIA treatment to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater reductions in heart rate

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, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine, should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Patients with preexisting liver disease may be at increased risk of developing elevated hepatic enzymes when taking ZEPOSIA

Infections: ZEPOSIA may increase the susceptibility to infections. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS 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

- Prior and Concomitant Treatment with Antineoplastic, Immunosuppressive, or Immune-modulating Therapies: In 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. 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
- No cases of Progressive Multifocal Leukoencephalopathy (PML) were identified in active-controlled MS clinical trials with ZEPOSIA. However, PML has been observed in patients treated with other MS therapies. Should symptoms present that are suggestive of PML, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued
- 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

Macular edema: Patients with risk factors for macular edema, such as a history of uveitis or diabetes mellitus, should have an ophthalmologic evaluation prior to treatment with ZEPOSIA. Patients who present with visual symptoms of macular edema should be evaluated and, if confirmed, treatment with ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): PRES is a syndrome characterized by sudden onset of severe headache, confusion, seizures, and visual loss. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. In animals, findings at similar exposure levels included embryo-fetal death, abnormal/delayed ossification, and abnormalities of the viscera and large blood vessels. Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping ZEPOSIA

Most common Adverse Reactions (≥2%): Nasopharyngitis, abnormal liver tests, urinary tract infections, hypertension, pharyngitis, and respiratory tract infections

Most common Adverse Reactions (>5%): Nasopharyngitis and abnormal liver tests (ALT/GGT)

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

Bristol-Myers Squibb

© 2020 Bristol-Myers Squibb Company.
ZEPOSIA is a registered trademark of Bristol-Myers Squibb Company.
All rights reserved. 01/20 US-ZEP-19-0095

DRAFT

Powerful Efficacy of ZEPOSIA

ZEPOSIA DELIVERS POWERFUL EFFICACY VS AVONEX®

Proven Superior vs Avonex in Reducing ARR[1]

Absolute ARR for ZEPOSIA: SUNBEAM 0.18 RADIANCE 0.17

In analyses pre-defined for the occurrence of new or worsening neurological symptoms persisting for more than 24 hours (pre-defined subset of MS and immediately preceded by a relapse) stable or improving neurological status at least 30 days.[1]
ARR not calculated relapse rate.

ZEPOSIA—THE POWER TO ACHIEVE ZERO RELAPSES FOR MOST PATIENTS[1]

The Majority of Patients Had No Relapses in Clinical Trials

SUNBEAM (1 Year)
78% of patients treated with ZEPOSIA were relapse free
n=144 of patients treated with Avonex (P<0.0001)

RADIANCE (2 Years)
76% of patients treated with ZEPOSIA were relapse free
n=162 of patients treated with Avonex (P<0.0001)

In analyses pre-defined for the occurrence of new or worsening neurological symptoms persisting for more than 24 hours (pre-defined subset of MS and immediately preceded by a relapse) stable or improving neurological status at least 30 days.[1]

The Mean Number of Relapses Experienced During the 12 Months Prior to Initiating Therapy Was 1.3 for Both SUNBEAM and RADIANCE[1]

ZEPOSIA—PROVEN SUPERIOR TO AVONEX IN REDUCING LESIONS ACROSS ALL MEASURES OF MRI ACTIVITY[1]

GdE Lesions | T2 Lesions

Up to 63% Fewer GdE Lesions vs Avonex[1]

GdE Lesions at Baseline: The mean number of GdE lesions observed in patients at baseline for both ZEPOSIA and Avonex was 0.6 in SUNBEAM and 0.7 in RADIANCE.[1]

In the Lesion SUNBEAM study, least-squares (LS) means were performed at baseline, month 6, and month 12. In the Lesion RADIANCE study, least-squares (LS) means were performed at baseline, month 12, and month 24.[1]

GdE Lesions | T2 Lesions

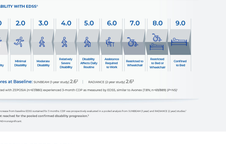
Up to 48% Fewer New or Enlarging T2 Lesions vs Avonex[1]

T2 Lesions at Baseline: The mean number of T2 lesions observed in patients at baseline for both ZEPOSIA and Avonex was 9.6 in SUNBEAM and 10.9 in RADIANCE.[1]

In the Lesion SUNBEAM study, least-squares (LS) means were performed at baseline, month 6, and month 12. In the Lesion RADIANCE study, least-squares (LS) means were performed at baseline, month 12, and month 24.[1]

9 OF 10 PATIENTS SHOWED NO SIGNS OF 3-MONTH DISABILITY PROGRESSION[1]

CDP Results From Clinical Trials



92.4% vs **92.2%** for **Avonex** Showed No Signs of 3-Month **Disability Progression**

Patients Classified as Having No Disability Progression Did Not Show Sustained Worsening for 3 Consecutive Months[1]

QUANTIFYING DISABILITY WITH EDSS[1]

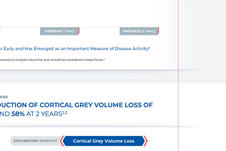
Mean EDSS Scores at Baseline: SUNBEAM 3 (per study) 2.6[1] RADIANCE 3 (per study) 2.6[1]

Tale of patients treated with ZEPOSIA (n=1196) experienced 3-month CDP as measured by EDSS, similar to Avonex (1,184; n=1195196) (P=0.92)[1]

TCDP was defined as at least 1 point increase from baseline EDSS sustained for 3 months. CDP was calculated and analyzed in a post-hoc analysis from SUNBEAM (1 year) and RADIANCE (2 year) studies.[1]
Bonferroni significance was not reached for the pooled confirmed disability progression.[1]
CDP=confirmed disability progression; EDS=expanded.

COGNITIVE PROCESSING SPEED DATA[2]

Cognitive Impairment Has Been Shown to Occur in the Earliest Stages of Disease[1]

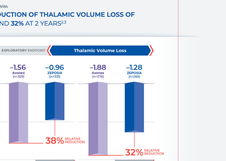


Defining SDMT: The SDMT is a measure of executive function (cognition that assesses processing speed, flexibility, and calculation ability. In clinical trials it was a commonly used measure. the Multiple Sclerosis Functional Composite[2]

NOTE: Online change of a or whatever clinically meaningful.
Endpoint was not part of the statistical analysis hierarchy and should be considered insignificant.[1]
SDMT=Symbol Digit Modalities Test

ZEPOSIA Was Associated With

A RELATIVE REDUCTION OF WHOLE BRAIN VOLUME LOSS OF 32% AT 1 YEAR AND 27% AT 2 YEARS[1,3]

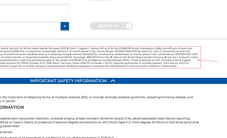


Brain Atrophy Starts Early and Has Emerged as an Important Measure of Disease Activity[4]

Endpoint was not part of the statistical analysis hierarchy and should be considered insignificant.[1]

ZEPOSIA Was Associated With

A RELATIVE REDUCTION OF CORTICAL GREY VOLUME LOSS OF 84% AT 1 YEAR AND 58% AT 2 YEARS[1,3]



Grey Matter Pathology Affects Both the Cortex and the Thalamus, a Deep Grey Matter Structure

Endpoint was not part of the statistical analysis hierarchy and should be considered insignificant.[1]

ZEPOSIA Was Associated With

A RELATIVE REDUCTION OF THALAMIC VOLUME LOSS OF 38% AT 1 YEAR AND 32% AT 2 YEARS[1,3]

Grey Matter Pathology Affects Both the Cortex and the Thalamus, a Deep Grey Matter Structure

Endpoint was not part of the statistical analysis hierarchy and should be considered insignificant.[1]

PRIV Study Design | NMT Safety

REGISTER FOR MORE INFORMATION

For updates about ZEPOSIA, please provide your contact information below.

*Required

Email Address*
e.g. name@email.com

First Name*
e.g. Joseph

Last Name*
e.g. Smith

NPI Number
e.g. 1234567890

Specialty*
Select a specialty

SIGN UP

I am a healthcare professional. By checking this box I authorize Bristol-Myers Squibb to use my personal information to provide me with information I requested or information about products, services, and programs which may be of interest to me. I understand that Bristol-Myers Squibb may share my health topics that may be of interest to me. I would like to receive more information about Bristol-Myers Squibb products, services, and programs, and about ZEPOSIA, the support program for patients, and more.

Bristol-Myers Squibb values your privacy

We collect information about you so we can provide you with the services you request, for example, to provide you information you asked for or to process your application. We also use information about you to know what you have read and agree to the terms of Bristol-Myers Squibb's privacy policy.

References: 1. Prescribing information for ZEPOSIA. Bristol-Myers Squibb Company. 2. Rao SM, Leo GJ, Ellington L, Nauertz T, Bernardin F, Unverzagt FW. Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns, and prediction. Neurology. 1991;41(5):685-691. 3. Cohen JA, Cree BAC, Spiegel DR, et al. Long-term inflammatory disease activity and disability in patients with relapsing multiple sclerosis treated with ravamsomab (anti-CD52 monoclonal antibody) or interferon beta-1a: a post-hoc analysis of the CAMMS223 trial. Lancet Neurol. 2020;19(8):673-681. 4. Fisher-Wellman DM, Bloomer RJ. Acute exercise and oxidative stress: 30 years of discovery and present perspectives. Sports Med. 2009;39(1):1-25. 5. Ontaneda D, Fox RJ, Cohen JA. Progressive multiple sclerosis: prospects for disease therapy, repair, and restoration of function. Lancet. 2017;389(10076):1357-1366. 6. Ontaneda D, Thompson AJ, Fox RJ, Cohen JA. Progressive multiple sclerosis: prospects for disease therapy, repair, and restoration of function. Lancet. 2017;389(10076):1357-1366. 7. Ontaneda D, Hyland M, Cohen JA. Multiple sclerosis: prognostic factors and prognostication. Lancet Neurol. 2012;11(10):1083-1092. 8. Ontaneda D, Tallantyre E, Kalra S, Jenkins TM, Raza I, Miller DH, Muraro PA. Early highly effective disease-modifying therapy after the first relapse in oligoclonal band positive multiple sclerosis: a randomized and 2-year follow-up. Ann Neurol. 2019;86(6):890-899. 9. Cohen JA, Coles AJ, Arnason BG, et al. Alemtuzumab versus interferon beta 1a in early relapsing multiple sclerosis. N Engl J Med. 2010;362(1):1544-1552. 10. Coles AJ, Cohen JA, Fox DA, et al. Alemtuzumab CARE-MS II 5-year follow-up: efficacy results in patients who received alemtuzumab treatment in CARE-MS II extension studies. Neurology. 2017;89(1):1076-1084. 11. Hauser SL, Bar-Or A, Cohen JA, et al. Ocrelizumab versus interferon beta-1a in relapsing multiple sclerosis. N Engl J Med. 2017;376(22):221-234. 12. Fox RJ, Cree BAC, Bar-Or A, et al. Ocrelizumab versus interferon beta-1a in patients with relapsing multiple sclerosis (P1 subgroup analysis of the randomized, double-blind, active-controlled, phase III ocrelizumab clinical trial). Mult Scler. 2020;26(1):1-12. 13. Wolinsky JS, Narayana PA, Nauert DW, et al. Brain atrophy in relapsing multiple sclerosis: experience from the glatiramer acetate trials. Ann Neurol. 2007;61(1):35-45. 14. Fisher-Wellman DM, Bloomer RJ. Acute exercise and oxidative stress: 30 years of discovery and present perspectives. Sports Med. 2009;39(1):1-25. 15. Ontaneda D, Fox RJ, Cohen JA. Progressive multiple sclerosis: prospects for disease therapy, repair, and restoration of function. Lancet. 2017;389(10076):1357-1366. 16. Ontaneda D, Tallantyre E, Kalra S, Jenkins TM, Raza I, Miller DH, Muraro PA. Early highly effective disease-modifying therapy after the first relapse in oligoclonal band positive multiple sclerosis: a randomized and 2-year follow-up. Ann Neurol. 2019;86(6):890-899. 17. Cohen JA, Coles AJ, Arnason BG, et al. Alemtuzumab versus interferon beta 1a in early relapsing multiple sclerosis. N Engl J Med. 2010;362(1):1544-1552. 18. Coles AJ, Cohen JA, Fox DA, et al. Alemtuzumab CARE-MS II 5-year follow-up: efficacy results in patients who received alemtuzumab treatment in CARE-MS II extension studies. Neurology. 2017;89(1):1076-1084. 19. Hauser SL, Bar-Or A, Cohen JA, et al. Ocrelizumab versus interferon beta-1a in relapsing multiple sclerosis. N Engl J Med. 2017;376(22):221-234. 20. Fox RJ, Cree BAC, Bar-Or A, et al. Ocrelizumab versus interferon beta-1a in patients with relapsing multiple sclerosis (P1 subgroup analysis of the randomized, double-blind, active-controlled, phase III ocrelizumab clinical trial). Mult Scler. 2020;26(1):1-12. 21. Wolinsky JS, Narayana PA, Nauert DW, et al. Brain atrophy in relapsing multiple sclerosis: experience from the glatiramer acetate trials. Ann Neurol. 2007;61(1):35-45.

IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ravamsomab) is indicated for the treatment of 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

Hypersensitivity to any of its ingredients (ravamsomab, polysorbate 80, sodium chloride, sodium citrate, sodium phosphate, sodium hydroxide, and hydrochloric acid)

Severe active infection, including active tuberculosis (TB), uncontrolled fungal, viral, or bacterial infections

Severe active hepatic or renal disease

Severe active cardiac disease (including but not limited to uncontrolled hypertension, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization or Class III/IV heart failure or have a history or presence of second degree atrioventricular (AV) block type II or third degree AV block or sick sinus syndrome unless they have a functioning pacemaker)

Patients with severe untreated sleep apnea

Patients who have had a hypersensitivity reaction to ravamsomab or are allergic to any of the excipients in ZEPOSIA

WARNINGS AND PRECAUTIONS

Bradycardia: In all patients, dose escalation is required for initiation of ZEPOSIA treatment to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may cause severe bradycardia and heart block.

Liver Injury: Elevations of aminotransferases may occur in patients receiving ZEPOSIA. Obtain hepatic function tests, if not recently available (e.g., within 6 months), before initiation of ZEPOSIA. Patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine should be promptly evaluated for liver function abnormalities. Discontinue ZEPOSIA if liver injury is confirmed. Patients with preexisting liver disease may be at increased risk of developing elevated hepatic enzymes when taking ZEPOSIA.

Infections: ZEPOSIA may increase the susceptibility to infections. Obtain a recent (i.e., within 6 months) or other documentation of pre-HIV therapy complete blood count, including lymphocyte count, before initiation of ZEPOSIA treatment. Do not initiate treatment in patients with an active infection until the infection is resolved. Consider interruption of treatment with ZEPOSIA if a patient develops a serious infection.

Pre- and Concomitant Treatment with Ivabradine, Immunosuppressants, or Vaccines: Ivabradine: In clinical studies, patients who received ZEPOSIA were more susceptible to bradycardia when ivabradine was administered concomitantly. Immunosuppressants: Immune system function may be altered for an extended period of time after ZEPOSIA and any of these therapies could be additive in suppressing immune function, increasing the susceptibility to infections and malignancies. Vaccines: Immunization with live vaccines may not be sufficiently effective and should be avoided during treatment with ZEPOSIA and for 3 months after discontinuation of treatment.

No cases of Progressive Multifocal Leukoencephalopathy (PML) have occurred in clinical studies with ZEPOSIA. However, PML has been observed in patients treated with other MS therapies. Should opportunistic infection or a suspicion of PML, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, discontinue ZEPOSIA treatment.

Use of the alemtuzumab vaccine should be avoided during and for 4 months after treatment with ZEPOSIA. If the alemtuzumab vaccine immunizations are required, administer at least 1 month prior to initiation of ZEPOSIA.

Herpes Infections: Patients with the herpes family virus such as a history of varicella or diabetes mellitus, should have an ophthalmologic evaluation prior to treatment. Herpes infections, including herpes simplex and herpes zoster, have been observed in patients treated with immunosuppressants, including ZEPOSIA.

Posterior Reversible Encephalopathy Syndrome (PRES): PRES is a syndrome characterized by sudden onset of severe headache, confusion, seizures, and visual loss, confirmed by MRI or CT scan. Discontinue ZEPOSIA if PRES is suspected. Patients with PRES should be promptly treated. Symptoms of PRES usually resolve or improve when appropriate treatment is initiated. Safety of ZEPOSIA rechallenge in patients who experienced PRES is unknown.

Fetal Risk: There are no adequate and well-controlled studies in pregnant women or women of childbearing potential taking ZEPOSIA. Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping ZEPOSIA.

Most common adverse reactions (≥10%): headache, fatigue, nasopharyngitis, urinary tract infections, hypertension, pharyngitis, and respiratory tract infections

Most common laboratory abnormalities (≥10%): lymphocyte and eosinophil count decreases

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

© 2020 Bristol-Myers Squibb Company
Bristol-Myers Squibb
P.O. Box 4500
Princeton, NJ 08543-4500
Medical Information: 1-800-321-1335
Medical Information Website: www.bmsmedinfo.com

Favorable Safety Profile of ZEPOSIA

ZEPOSIA—A SAFETY PROFILE COMPARABLE TO AVONEX

Rates of Adverse Events Were Similar Across 2 Pivotal Head-to-Head Trials (N=2659)[1]

AEs With an Incidence of ≥2% for ZEPOSIA[1]

SUNBEAM and RADIANCE: POOLED DATA		
AEs	**Avonex[a] (n=885) (%)**	**ZEPOSIA (n=1892) (%)**
Nasopharyngitis	84 (9.5)	116 (11.1)
ALT increased	28 (3.2)	47 (5.3)
GGT increased	11 (1.2)	40 (4.5)
UTI	27 (3.1)	36 (4.1)
Hypertension	18 (2.0)	30 (3.4)
Pharyngitis	20 (2.3)	28 (3.2)
Respiratory tract infection viral	11 (1.2)	21 (2.4)

AEs are sorted by decreasing incidence in patients treated with ZEPOSIA.
For AEs pertaining to liver function tests, increases were transient and generally resolved without discontinuation. No cases of severe drug-induced liver injury were reported with ZEPOSIA in the active-controlled MS clinical trials.[1]
Elevations of 5-fold the ULN or greater occurred in 5.3% 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.[1]

AE=adverse event; ALT=alanine aminotransferase; GGT=gamma-glutamyl transferase; ULN=upper limit of normal; UTI=urinary tract infection.
Avonex (interferon beta-1a) is a registered trademark of Biogen.

ZEPOSIA—CONSISTENTLY LOW DISCONTINUATION RATES VS AVONEX

Discontinuation Rates Were ≤3% in a Large-scale, Double-blind Clinical Studies[1]

Discontinuation Rates Due to AEs

SUNBEAM (1 Year): **3.6%** AVONEX vs **2.9%** ZEPOSIA

RADIANCE (2 Years): **4.1%** AVONEX vs **3.0%** ZEPOSIA

Overall Discontinuation Rates[1]: Avonex **8%** | ZEPOSIA **6%** (SUNBEAM) ; Avonex **15%** | ZEPOSIA **10%** (RADIANCE)

SEE ADVERSE EVENTS THAT LED TO DISCONTINUATION[1a]

SEE ADVERSE EVENTS THAT LED TO DISCONTINUATION[1a]

SUNBEAM

Adverse Events	Avonex n=445 (%)	ZEPOSIA n=448 (%)
ALT increased	0 (0)	2 (0.4)
Back pain	1 (0.2)	2 (0.4)
Headache	0 (0)	2 (0.4)

RADIANCE

Adverse Events	Avonex n=440 (%)	ZEPOSIA n=434 (%)
ALT increased	3 (0.7)	2 (0.5)
Urticaria	0 (0.0)	2 (0.5)

*Includes all AEs ≥0.4% that led to discontinuation of ZEPOSIA.[1]

ZEPOSIA—COMPARABLE RATES OF SERIOUS INFECTIONS AND MALIGNANCIES VS AVONEX

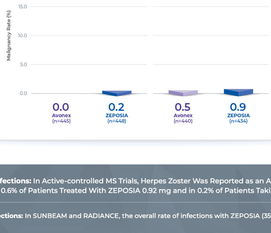
Results Were Consistent Across 2 Separate, Pivotal Head-to-Head Trials With More Than 2600 Patients[1]

Serious Infection Rates | Malignancy Rates

Serious Infection Rates at 1 and 2 Years[1]

Serious Infection Rates | Malignancy Rates

Malignancy Rates at 1 and 2 Years[1]



Herpetic Infections: In Active-controlled MS Trials, Herpes Zoster Was Reported as an Adverse Reaction in 0.6% of Patients Treated With ZEPOSIA 0.92 mg and in 0.2% of Patients Taking Avonex[1]

- **Overall Infections:** In SUNBEAM and RADIANCE, the overall rate of infections with ZEPOSIA (35%) was similar to Avonex[1]
- **Progressive Multifocal Leukoencephalopathy (PML):** There were no cases of PML identified in clinical trials[1]
  - JCV infection resulting in PML has been observed in patients treated with other MS therapies and has been associated with some risk factors (eg, polytherapy with immunosuppressants, patients who are severely immunocompromised)[1]

ZEPOSIA causes a mean reduction in peripheral blood lymphocyte count to 45% of baseline values because of reversible retention of lymphocytes in lymphoid tissues. Therefore, ZEPOSIA may increase the susceptibility to infections.[1]

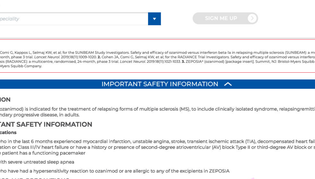
JCV=John Cunningham virus.

ZEPOSIA CONSISTENTLY MAINTAINED ALC NEAR THE LLN

ALCs Were Consistent Across Large-Scale 1-Year and 2-Year Pivotal Trials[1]

Mean ALC

Values Were at or Above the LLN



ALC=absolute lymphocyte count; LLN=lower limit of normal.

Lymphocyte Numbers Can Be Restored to Normal Values by Discontinuing Therapy[1,3]

- **Mean ALC** was 0.75 × 10^9 cells/L for both SUNBEAM and RADIANCE (at 1 year and 2 years, respectively)
- **During clinical trials,** a combined total of 29 patients treated with ZEPOSIA 0.92 mg from SUNBEAM and RADIANCE had an ALC of <200 cells/μL. If ALC was <200 cells/μL after a repeated test, patients were temporarily discontinued, then monitored weekly until ALC recovered to >500 cells/μL, and restarted on therapy
- **Upon discontinuation** of ZEPOSIA, median time to recovery of ALC to within a normal range was 30 days, with 90% of patients recovering within 3 months

PREV: Clinical Endpoints
NEXT: MOA

REGISTER FOR MORE INFORMATION

For updates about ZEPOSIA, please provide your contact information below.

*Required

Email Address*
Ex: Jane@email.com

First Name*
Ex: Jane

Last Name*
Ex: Smith

NPI Number
Ex: 1234567891

Specialty*
Select a specialty

I am a healthcare professional. By checking this box, I authorize Bristol-Myers Squibb, its affiliates, and its agents to analyze and use my personal information to provide me with information about ZEPOSIA and my use of marketing programs or research about ZEPOSIA and other related health topics that may be of interest to me. I would like to receive more information about ZEPOSIA, updates on clinical data on ZEPOSIA, the support program for patients, and more.

SIGN ME UP!

Bristol-Myers Squibb values your privacy

Bristol-Myers Squibb, its affiliates, and its agents will not sell or rent your personal information. By providing your information, you acknowledge that you have read and agree to the terms of Bristol-Myers Squibb's **privacy policy**.

References: 1. Cohn G, Kappos L, Selmaj KW, et al. For the SUNBEAM Study Investigators. Safety and efficacy of ozanimod versus interferon beta-1a in relapsing multiple sclerosis (SUNBEAM): a multicentre, randomised, minimum 24-month, phase 3 trial. Lancet Neurol. 2019;18(1):1021-1033. 2. ZEPOSIA (ozanimod) capsules, for oral use. Prescribing Information. Bristol-Myers Squibb Company. 2020. 3. Cohen JA, et al. For the RADIANCE Study Investigators. Ozanimod in relapsing multiple sclerosis (RADIANCE): a multicentre, randomised, 24 month, phase 3 trial. Lancet Neurol. 2019;18(1):1021-1033. 4. ZEPOSIA (ozanimod) (package insert). Summit, NJ: Bristol-Myers Squibb Company; 2019. 5. Data on file, Bristol-Myers Squibb Company.

IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of 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 history or presence of second-degree atrioventricular (AV) block Type II or third-degree AV block or sick sinus syndrome unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients who have had a hypersensitivity reaction to ozanimod or are allergic to any of the excipients in ZEPOSIA

WARNINGS AND PRECAUTIONS:

Bradycardia: In all patients, dose escalation is recommended for initiation of ZEPOSIA treatment to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater reductions in heart rate

Liver Injury: Elevations of aminotransferases may occur in patients receiving ZEPOSIA. Obtain liver function tests if not recently available (ie, within 6 months) before initiation of ZEPOSIA. In patients without concomitant multiple sclerosis (MS) disease activity or medication effects that may explain liver enzyme elevations, jaundice and/or dark urine, should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Patients with preexisting liver disease may be at increased risk of developing elevated hepatic enzymes when taking ZEPOSIA

Infections: ZEPOSIA may increase the susceptibility to infections. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS 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

- Prior and Concomitant Treatment with Antineoplastic, Immunosuppressive, or Immune-modulating Therapies: In 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. 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
- No cases of Progressive Multifocal Leukoencephalopathy (PML) were identified in active-controlled MS clinical trials with ZEPOSIA. However, PML has been observed in patients treated with other MS therapies. Should symptoms present that are suggestive of PML, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued
- 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

Macular edema: Patients with risk factors for macular edema, such as a history of uveitis or diabetes mellitus, should have an ophthalmologic evaluation prior to treatment with ZEPOSIA. Patients who present with visual symptoms of macular edema should be evaluated and, if confirmed, treatment with ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): PRES is a syndrome characterized by sudden onset of severe headache, confusion, seizures, and visual loss. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. In animals, findings at similar exposure levels included embryo-fetal death, abnormal/delayed ossification, and abnormalities of the viscera and large blood vessels. Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping ZEPOSIA

Most common Adverse Reactions (≥2%): Nasopharyngitis, abnormal liver tests, urinary tract infections, hypertension, pharyngitis, and respiratory tract infections

Most common Adverse Reactions (>1%): Nasopharyngitis and abnormal liver tests (ALT/GGT)

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

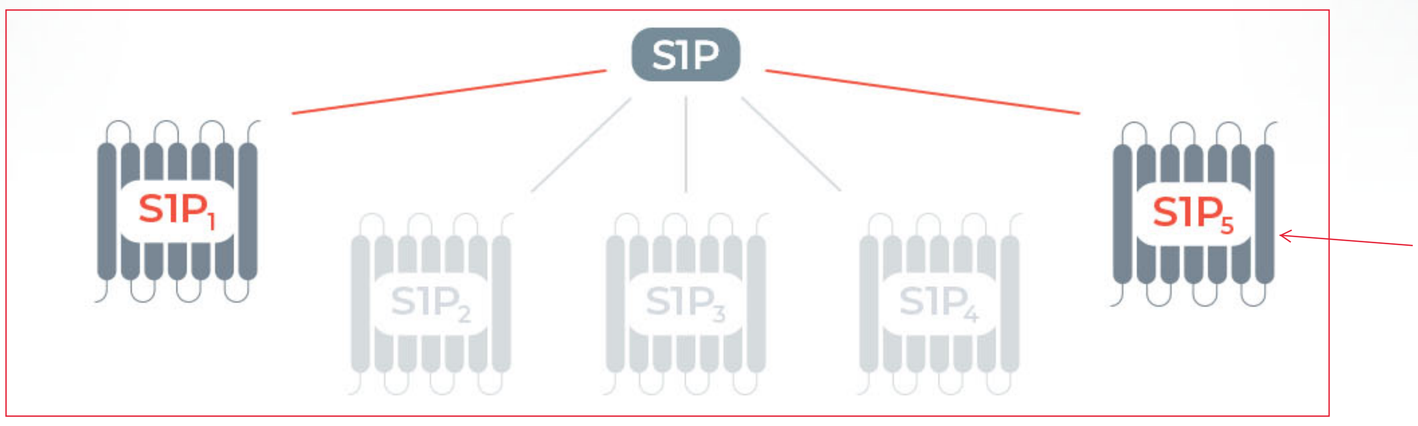
Bristol-Myers Squibb
© 2021 Bristol-Myers Squibb Company
Bristol-Myers Squibb Company of
Princeton, New Jersey, USA
All rights reserved. 1030 US-ZEP-19-0086

ZEPOSIA—A Selective S1P

REDISCOVER WHAT S1P THERAPY CAN MEAN FOR YOUR PATIENTS

An S1P Optimized to Target With Selectivity

ZEPOSIA Works to Reduce Lymphocyte Movement Into the CNS, Targeting Disease Activity at Its Source by Selectively Binding to $S1P_1$ and $S1P_5$ Receptors[1]



ZEPOSIA is **10-fold more selective** for $S1P_1$ relative to $S1P_5$ and has little activity on other S1P receptors ($S1P_2$, $S1P_3$, and $S1P_4$)[1]

The mechanism by which ZEPOSIA exerts therapeutic effects in MS is unknown, but may involve the reduction of lymphocytes in areas of inflammation.[1]

+ EXPRESSION OF S1P RECEPTORS

— EXPRESSION OF S1P RECEPTORS

$S1P_1$	$S1P_2$	$S1P_3$	$S1P_4$	$S1P_5$
· T and B lymphocytes, other immune cells[2] · Astrocytes, neurons[3] · Vascular endothelial cells, cardiac myocytes[4,5]	· Vascular endothelial, smooth muscle cells[4,6]	· Cardiac myocytes[5]	· T lymphocytes · Megakaryocytes[6,7]	· Natural killer cells · Oligodendrocytes · Vascular endothelial cells[6]

S1P=sphingosine-1-phosphate.

PREV: Safety

NEXT: Initiation and Dosing

REGISTER FOR MORE INFORMATION

For updates about ZEPOSIA, please provide your contact information below.

*Required

Email Address*

Ex: John@email.com

First Name*

Ex: John

Last Name*

Ex: Smith

NPI Number

Ex: 123456789

Specialty*

Select a speciality

☐ I am a healthcare professional. By checking this box, I authorize Bristol-Myers Squibb, its affiliates, and its agents to analyze and use my information to improve or develop services and programs and contact me about marketing programs or research about ZEPOSIA and other related health topics that may be of interest to me. I would like to receive more information about ZEPOSIA, updates on clinical data on ZEPOSIA, the support program for patients, and more.

Bristol-Myers Squibb values your privacy

Bristol-Myers Squibb, its affiliates, and its agents will not sell or rent your personal information. By providing your information, you acknowledge that you have read and agree to the terms of Bristol-Myers Squibb's privacy policy.

SIGN ME UP

References: 1. ZEPOSIA® (ozanimod) [package insert]. Summit, NJ: Bristol-Myers Squibb Company; 2019. **2.** Spiegel S, Milstien S. The outs and the ins of sphingosine-1 phosphate in immunity. *Nat Rev Immunol.* 2011;11(6):403-415. **3.** Choi JW, Gardell SE, Herr DR, et al. FTY720 (fingolimod) efficacy in an animal model of multiple sclerosis requires astrocyte sphingosine 1-phosphate receptor 1 ($S1P_1$) modulation. *Proc Natl Acad Sci U S A.* 2011;108(2):751-756. **4.** Prager B, Spampinato SF, Ransohoff RM. Sphingosine 1-phosphate signaling at the blood–brain barrier. *Trends Mol Med.* 2015;21(6):354-363. **5.** Li N, Zhang F. Implication of sphingosin-1-phosphate in cardiovascular regulation. *Front Biosci (Landmark Ed).* 2016;21:1296-1313. **6.** Peyrin-Biroulet L, Christopher R, Behan D, Lassen C. Modulation of sphingosine-1-phosphate in inflammatory bowel disease. *Autoimmun Rev.* 2017;16(5):495-503. **7.** Olesch C, Ringel C, Brüne B, Weigert A. Beyond immune cell migration: the emerging role of the sphingosine-1-phosphate receptor S1PR4 as a modulator of innate immune cell activation. *Mediators Inflamm.* 2017;2017:6059203. doi:10.115/2017/6059203

IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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 history or presence of second-degree atrioventricular (AV) block Type II or third-degree AV block or sick sinus syndrome unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients who have had a hypersensitivity reaction to ozanimod or are allergic to any of the excipients in ZEPOSIA

WARNINGS AND PRECAUTIONS:

Bradycardia: In all patients, dose escalation is recommended for initiation of ZEPOSIA treatment to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater reductions in heart rate

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, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine, should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Patients with preexisting liver disease may be at increased risk of developing elevated hepatic enzymes when taking ZEPOSIA

Infections: ZEPOSIA may increase the susceptibility to infections. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS 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

- Prior and Concomitant Treatment with Antineoplastic, Immunosuppressive, or Immune-modulating Therapies: In 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. 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
- No cases of Progressive Multifocal Leukoencephalopathy (PML) were identified in active-controlled MS clinical trials with ZEPOSIA. However, PML has been observed in patients treated with other MS therapies. Should symptoms present that are suggestive of PML, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued
- 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

Macular edema: Patients with risk factors for macular edema, such as a history of uveitis or diabetes mellitus, should have an ophthalmologic evaluation prior to treatment with ZEPOSIA. Patients who present with visual symptoms of macular edema should be evaluated and, if confirmed, treatment with ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): PRES is a syndrome characterized by sudden onset of severe headache, confusion, seizures, and visual loss. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. In animals, findings at similar exposure levels included embryo-fetal death, abnormal/delayed ossification, and abnormalities of the viscera and large blood vessels. Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping ZEPOSIA

Most common Adverse Reactions (≥2%): Nasopharyngitis, abnormal liver tests, urinary tract infections, hypertension, pharyngitis, and respiratory tract infections

Most common Adverse Reactions (>5%): Nasopharyngitis and abnormal liver tests (ALT/GGT)

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

DRAFT

Bristol-Myers Squibb

© 2020 Bristol-Myers Squibb Company.
ZEPOSIA is a registered trademark of Bristol-Myers Squibb Company.
All rights reserved. 01/20 US-ZEP-19-0095

Start Simple With ZEPOSIA

THE ONLY S1P THAT LETS PATIENTS START TODAY[1-3]

Initiation Made Simple: No Genetic Testing, No Ophthalmic Testing Required for Most Patients, and No FDO for Most Patients[1,4b]

Routine Pre-initiation Requirements[1]:

- Obtain a recent **CBC** (within 6 months)
- Obtain an **ECG** to determine whether an FDO is recommended
- Obtain **aminotransferase and total bilirubin levels** (within 6 months)
- Evaluate **current and prior medications**
- For patients who need **immunizations**, including VZV, administer at least 1 month prior to initiation

One Capsule, Once a Day, From the Start[1]

DAYS 1-4	DAYS 5-7	DAY 8
ZEPOSIA 7-DAY INITIATION SCHEDULE		
0.23 mg	0.46 mg	0.92 mg

Starting at a Low Dose and Gradually Elevating Helps to Mitigate the Risk of Bradycardia[1]

Dosing Considerations[1]

ZEPOSIA—Single maintenance dose of 0.92 mg for all patients	If ZEPOSIA therapy is interrupted for **more than 14 consecutive days**, re-initiate therapy using the dose escalation regimen

The Mean (CV%) Plasma Half-Life ($t_{1/2}$) of ZEPOSIA Was Approximately 21 Hours (15%). The Mean Half Life of the Active Metabolite CC112273 Was 11 Days[1]

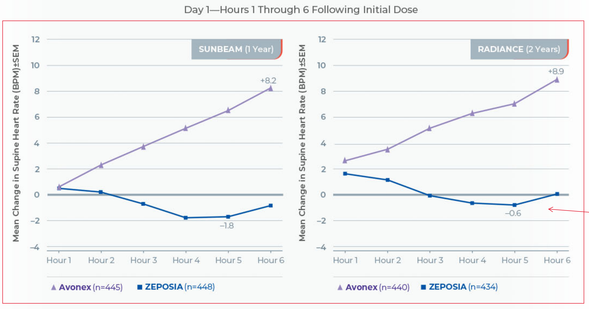
+ FIRST 6-HOUR HEART RATE DATA FOR ZEPOSIA

— FIRST 6-HOUR HEART RATE DATA FOR ZEPOSIA

Changes in Heart Rate Observed Over First 6 Hours From 2 Clinical Trials[4]

Mean Change from Baseline in Supine Heart Rate

Day 1—Hours 1 Through 6 Following Initial Dose



Heart Rate Data for Day 1 Initiation Dose (0.25 mg)[5,6]

In SUNBEAM (1 year), the largest mean change from baseline in supine heart rate on Day 1 was **-1.8 bpm for ZEPOSIA at Hour 5** and +8.2 bpm for Avonex at Hour 6

In RADIANCE (2 years), the largest mean change from baseline in supine heart rate on Day 1 was **-0.6 bpm for ZEPOSIA at Hour 5** and +8.9 bpm for Avonex at Hour 6

On Day 1, bradycardia was reported in 0.5% of patients taking ZEPOSIA and in 0% of those taking Avonex

After Day 1, the incidence was 0.8% in patients taking ZEPOSIA and 0.7% in those taking Avonex

[4]Patients with risk factors for macular edema, such as a history of uveitis or diabetes mellitus, should have an ophthalmologic evaluation prior to treatment with ZEPOSIA. Patients who present with visual symptoms of macular edema should be evaluated and, if confirmed, treatment with ZEPOSIA should be discontinued.

[4b]An FDO of 6 hours is only needed for patients with sinus bradycardia (HR <55 bpm), first- or second-degree Mobitz type I AV block, or a history of myocardial infarction or heart failure. Monitoring should continue for 6 hours after the first dose to evaluate for signs and symptoms of bradycardia. An ECG should be conducted at the end of the observation period.

AV=atrioventricular; CBC=complete blood count; ECG=electrocardiography; FDO=first-dose observation; VZV=varicella-zoster virus.

Avonex (interferon beta-1a) is a registered trademark of Biogen.

PREV: MOA

NEXT: Support

REGISTER FOR MORE INFORMATION

For updates about ZEPOSIA, please provide your contact information below.

*Required

Email Address*

Ex: John@email.com

First Name*

Ex: John

Last Name*

Ex: Smith

NPI Number

Ex: 1234567789

Specialty*

Select a speciality

I am a healthcare professional. By checking this box, I authorize Bristol-Myers Squibb, its affiliates, and its agents to analyze and use my information to improve or develop services and programs and contact me about marketing programs or research about ZEPOSIA and other related health topics that may be of interest to me. I would like to receive more information about ZEPOSIA, updates on clinical data on ZEPOSIA, the support program for patients, and more.

Bristol-Myers Squibb values your privacy

Bristol-Myers Squibb, its affiliates, and its agents will not sell or rent your personal information. By providing your information, you acknowledge that you have read and agree to the terms of Bristol-Myers Squibb's privacy policy.

SIGN ME UP

References: 1. ZEPOSIA® (ozanimod) [package insert]. Summit, NJ: Bristol-Myers Squibb Company; 2019. **2.** Gilenya® (fingolimod) [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2019. **3.** Mayzent® (siponimod) [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2019. **4.** Data on file, Bristol-Myers Squibb Company. **5.** Comi G, Kappos L, Selmaj KW, et al; for the 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. **6.** Cohen JA, Comi G, Selmaj KW, et al; for the 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.

IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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 history or presence of second-degree atrioventricular (AV) block Type II or third-degree AV block or sick sinus syndrome unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients who have had a hypersensitivity reaction to ozanimod or are allergic to any of the excipients in ZEPOSIA

WARNINGS AND PRECAUTIONS:

Bradycardia: In all patients, dose escalation is recommended for initiation of ZEPOSIA treatment to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater reductions in heart rate

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, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine, should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Patients with preexisting liver disease may be at increased risk of developing elevated hepatic enzymes when taking ZEPOSIA

Infections: ZEPOSIA may increase the susceptibility to infections. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS 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

- Prior and Concomitant Treatment with Antineoplastic, Immunosuppressive, or Immune-modulating Therapies: In 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. 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
- No cases of Progressive Multifocal Leukoencephalopathy (PML) were identified in active-controlled MS clinical trials with ZEPOSIA. However, PML has been observed in patients treated with other MS therapies. Should symptoms present that are suggestive of PML, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued
- 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

Macular edema: Patients with risk factors for macular edema, such as a history of uveitis or diabetes mellitus, should have an ophthalmologic evaluation prior to treatment with ZEPOSIA. Patients who present with visual symptoms of macular edema should be evaluated and, if confirmed, treatment with ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): PRES is a syndrome characterized by sudden onset of severe headache, confusion, seizures, and visual loss. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. In animals, findings at similar exposure levels included embryo-fetal death, abnormal/delayed ossification, and abnormalities of the viscera and large blood vessels. Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping ZEPOSIA

Most common Adverse Reactions (≥2%): Nasopharyngitis, abnormal liver tests, urinary tract infections, hypertension, pharyngitis, and respiratory tract infections

Most common Adverse Reactions (>5%): Nasopharyngitis and abnormal liver tests (ALT/GGT)

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

Bristol-Myers Squibb

© 2020 Bristol-Myers Squibb Company.
ZEPOSIA is a registered trademark of Bristol-Myers Squibb Company.
All rights reserved. 01/20 US-ZEP-19-0095

DRAFT

Support Available for You and Your Patients

ACCESS RESOURCES

Helpful Resources to Get Patients Started on ZEPOSIA

Start Form

Access the ZEPOSIA Start Form and refer to the guide provided to help you and your patients complete the form correctly

DOWNLOAD

ZEPOSIA 360 Support™ Tool Kit

Help patients start therapy with the ZEPOSIA 360 Support™ Tool Kit

DOWNLOAD

Letter of Medical Necessity

Help protect your patient's choice by accessing the Letter of Medical Necessity

DOWNLOAD

Financial Support Resources

Two core programs are available to provide financial assistance for patients who need it:

1. **Co-pay Program**—A service that enables eligible patients to pay $0 per month for ZEPOSIA.
2. **ZEPOSIA Bridge Program**—Offers eligible commercially insured patients up to 1 year of ZEPOSIA for $0.

PREV: Initiation and Dosing

REGISTER FOR MORE INFORMATION

For updates about ZEPOSIA, please provide your contact information below.

*Required

Email Address*

Ex: John@email.com

First Name*

Ex: John

Last Name*

Ex: Smith

NPI Number

Ex: 123456789

Specialty*

Select a speciality

☐ I am a healthcare professional. By checking this box, I authorize Bristol-Myers Squibb, its affiliates, and its agents to analyze and use my information to improve or develop services and programs and contact me about marketing programs or research about ZEPOSIA and other related health topics that may be of interest to me. I would like to receive more information about ZEPOSIA, updates on clinical data on ZEPOSIA, the support program for patients, and more.

Bristol-Myers Squibb values your privacy

Bristol-Myers Squibb, its affiliates, and its agents will not sell or rent your personal information. By providing your information, you acknowledge that you have read and agree to the terms of Bristol-Myers Squibb's privacy policy.

SIGN ME UP

IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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 history or presence of second-degree atrioventricular (AV) block Type II or third-degree AV block or sick sinus syndrome unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients who have had a hypersensitivity reaction to ozanimod or are allergic to any of the excipients in ZEPOSIA

WARNINGS AND PRECAUTIONS:

Bradycardia: In all patients, dose escalation is recommended for initiation of ZEPOSIA treatment to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater reductions in heart rate

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, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine, should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Patients with preexisting liver disease may be at increased risk of developing elevated hepatic enzymes when taking ZEPOSIA

Infections: ZEPOSIA may increase the susceptibility to infections. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS 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

- Prior and Concomitant Treatment with Antineoplastic, Immunosuppressive, or Immune-modulating Therapies: In 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. 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
- No cases of Progressive Multifocal Leukoencephalopathy (PML) were identified in active-controlled MS clinical trials with ZEPOSIA. However, PML has been observed in patients treated with other MS therapies. Should symptoms present that are suggestive of PML, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued
- 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

Macular edema: Patients with risk factors for macular edema, such as a history of uveitis or diabetes mellitus, should have an ophthalmologic evaluation prior to treatment with ZEPOSIA. Patients who present with visual symptoms of macular edema should be evaluated and, if confirmed, treatment with ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): PRES is a syndrome characterized by sudden onset of severe headache, confusion, seizures, and visual loss. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. In animals, findings at similar exposure levels included embryo-fetal death, abnormal/delayed ossification, and abnormalities of the viscera and large blood vessels. Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping ZEPOSIA

Most common Adverse Reactions (≥2%): Nasopharyngitis, abnormal liver tests, urinary tract infections, hypertension, pharyngitis, and respiratory tract infections

Most common Adverse Reactions (>5%): Nasopharyngitis and abnormal liver tests (ALT/GGT)

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

DRAFT

Bristol-Myers Squibb

© 2020 Bristol-Myers Squibb Company.
ZEPOSIA is a registered trademark of
Bristol-Myers Squibb Company.
All rights reserved. 01/20 US-ZEP-19-0095

Request a Representative

FIND OUT MORE

Learn about ZEPOSIA prescribing, efficacy and safety, and patient savings. Your representative can also provide ZEPOSIA Starter Kits.

*Required

Has a Bristol-Myers Squibb representative visited your office?

Select a response

Email Address*

Ex: John@email.com

First Name* | Last Name*

Ex: John | Ex: Smith

State License* | Specialty*

Enter a license number | Select a speciality

Office Address*

Enter an address

City* | State*

Enter a city | Select a state

ZIP*

Enter a ZIP code

MAIN CONTACT INFORMATION

Bristol-Myers Squibb Company
86 Morris Avenue, Summit, NJ 07901
1-908-673-9000

MEDICAL INFORMATION

Medical questions or adverse event reports can be directed to Bristol-Myers Squibb Medical Information at:

1-888-771-0141

medinfo@celgene.com

Bristol-Myers Squibb Medical Information

I am a healthcare professional. By checking this box, I authorize Bristol-Myers Squibb, its affiliates, and its agents to analyze and use my information to improve or develop services and programs and contact me about marketing programs or research about ZEPOSIA and other related health topics that may be of interest to me. I would like to receive more information about ZEPOSIA, updates on clinical data on ZEPOSIA, our support program for patients, and more.

Bristol-Myers Squibb values your privacy

Bristol-Myers Squibb, its affiliates, and its agents will not sell or rent your personal information. By providing your information, you acknowledge that you have read and agree to the terms of Bristol-Myers Squibb's privacy policy.

START REQUEST

IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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 history or presence of second-degree atrioventricular (AV) block Type II or third-degree AV block or sick sinus syndrome unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients who have had a hypersensitivity reaction to ozanimod or are allergic to any of the excipients in ZEPOSIA

WARNINGS AND PRECAUTIONS:

Bradycardia: In all patients, dose escalation is recommended for initiation of ZEPOSIA treatment to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater reductions in heart rate

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, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine, should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Patients with preexisting liver disease may be at increased risk of developing elevated hepatic enzymes when taking ZEPOSIA

Infections: ZEPOSIA may increase the susceptibility to infections. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS 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

- Prior and Concomitant Treatment with Antineoplastic, Immunosuppressive, or Immune-modulating Therapies: In 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. 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
- No cases of Progressive Multifocal Leukoencephalopathy (PML) were identified in active-controlled MS clinical trials with ZEPOSIA. However, PML has been observed in patients treated with other MS therapies. Should symptoms present that are suggestive of PML, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued
- 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

Macular edema: Patients with risk factors for macular edema, such as a history of uveitis or diabetes mellitus, should have an ophthalmologic evaluation prior to treatment with ZEPOSIA. Patients who present with visual symptoms of macular edema should be evaluated and, if confirmed, treatment with ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): PRES is a syndrome characterized by sudden onset of severe headache, confusion, seizures, and visual loss. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. In animals, findings at similar exposure levels included embryo-fetal death, abnormal/delayed ossification, and abnormalities of the viscera and large blood vessels. Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping ZEPOSIA

Most common Adverse Reactions (≥2%): Nasopharyngitis, abnormal liver tests, urinary tract infections, hypertension, pharyngitis, and respiratory tract infections

Most common Adverse Reactions (>5%): Nasopharyngitis and abnormal liver tests (ALT/GGT)

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

Bristol-Myers Squibb

© 2020 Bristol-Myers Squibb Company.
ZEPOSIA is a registered trademark of
Bristol-Myers Squibb Company.
All rights reserved. 01/20 US-ZEP-19-0095

DRAFT

Request a Representative

FIND OUT MORE

Learn about ZEPOSIA prescribing, efficacy and safety, and patient savings. Your representative can also provide ZEPOSIA Starter Kits.

*Required

There was a problem with your submission. Errors have been highlighted below.

Has a Bristol-Myers Squibb representative visited your office?

Select a response

Email Address*

Ex: John@email.com

Please enter a valid email address.

First Name*

Ex: John

This field is required.

Last Name*

Ex: Smith

This field is required.

State License*

Enter a license number

Please enter a valid state license.

Specialty*

Select a speciality

This field is required.

Office Address*

Enter an address

This field is required.

City*

Enter a city

This field is required.

State*

Select a state

This field is required.

ZIP*

Enter a ZIP code

Please enter a valid ZIP.

☐ I am a healthcare professional. By checking this box, I authorize Bristol-Myers Squibb, its affiliates, and its agents to analyze and use my information to improve or develop services and programs and contact me about marketing programs or research about ZEPOSIA and other related health topics that may be of interest to me. I would like to receive more information about ZEPOSIA, updates on clinical data on ZEPOSIA, our support program for patients, and more.

Bristol-Myers Squibb values your privacy

Bristol-Myers Squibb, its affiliates, and its agents will not sell or rent your personal information. By providing your information, you acknowledge that you have read and agree to the terms of Bristol-Myers Squibb's privacy policy.

START REQUEST

MAIN CONTACT INFORMATION

Bristol-Myers Squibb Company
86 Morris Avenue, Summit, NJ 07901
1-908-673-9000

MEDICAL INFORMATION

Medical questions or adverse event reports can be directed to Bristol-Myers Squibb Medical Information at:

1-888-771-0141

medinfo@celgene.com

Bristol-Myers Squibb Medical Information

Thank you

Your request has been submitted successfully and a representative will be reaching out shortly.

MAIN CONTACT INFORMATION

Bristol-Myers Squibb Company
86 Morris Avenue, Summit, NJ 07901
1-908-673-9000

MEDICAL INFORMATION

Medical questions or adverse event reports can be directed to Bristol-Myers Squibb Medical Information at:

1-888-771-0141

medinfo@celgene.com

Bristol-Myers Squibb Medical Information

Error 404

The page you're looking for can't be found.

HERE ARE SOME LINKS THAT MIGHT BE HELPFUL

Home

Clinical Endpoints

Safety

IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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 history or presence of second-degree atrioventricular (AV) block Type II or third-degree AV block or sick sinus syndrome unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients who have had a hypersensitivity reaction to ozanimod or are allergic to any of the excipients in ZEPOSIA

WARNINGS AND PRECAUTIONS:

Bradycardia: In all patients, dose escalation is recommended for initiation of ZEPOSIA treatment to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater reductions in heart rate

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, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine, should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Patients with preexisting liver disease may be at increased risk of developing elevated hepatic enzymes when taking ZEPOSIA

Infections: ZEPOSIA may increase the susceptibility to infections. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS 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

- Prior and Concomitant Treatment with Antineoplastic, Immunosuppressive, or Immune-modulating Therapies: In 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. 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
- No cases of Progressive Multifocal Leukoencephalopathy (PML) were identified in active-controlled MS clinical trials with ZEPOSIA. However, PML has been observed in patients treated with other MS therapies. Should symptoms present that are suggestive of PML, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued
- 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

Macular edema: Patients with risk factors for macular edema, such as a history of uveitis or diabetes mellitus, should have an ophthalmologic evaluation prior to treatment with ZEPOSIA. Patients who present with visual symptoms of macular edema should be evaluated and, if confirmed, treatment with ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): PRES is a syndrome characterized by sudden onset of severe headache, confusion, seizures, and visual loss. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. In animals, findings at similar exposure levels included embryo-fetal death, abnormal/delayed ossification, and abnormalities of the viscera and large blood vessels. Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping ZEPOSIA

Most common Adverse Reactions (≥2%): Nasopharyngitis, abnormal liver tests, urinary tract infections, hypertension, pharyngitis, and respiratory tract infections

Most common Adverse Reactions (>5%): Nasopharyngitis and abnormal liver tests (ALT/GGT)

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

DRAFT

Bristol-Myers Squibb

© 2020 Bristol-Myers Squibb Company.
ZEPOSIA is a registered trademark of
Bristol-Myers Squibb Company.
All rights reserved. 01/20 US-ZEP-19-0095

Site Map

Home

Study Design

Clinical Endpoints

- ARR
- Relapse-free Data
- GdE | T2
- Disability Progression
- SDMT Data
- Whole Brain Volume Loss
- Cortical Grey Volume Loss
- Thalamic Volume Loss

Safety

- Adverse Events
- Discontinuation Rates
- Serious Infections and Malignancies
- ALC Profile

MOA

Initiation and Dosing

Support

- ZEPOSIA 360 Support™ Program
- Resources
- Specialty Pharmacy

IMPORTANT SAFETY INFORMATION

INDICATION

ZEPOSIA® (ozanimod) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsingremitting 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 history or presence of second-degree atrioventricular (AV) block Type II or third-degree AV block or sick sinus syndrome unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients who have had a hypersensitivity reaction to ozanimod or are allergic to any of the excipients in ZEPOSIA

WARNINGS AND PRECAUTIONS:

Bradycardia: In all patients, dose escalation is recommended for initiation of ZEPOSIA treatment to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater reductions in heart rate

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, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine, should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Patients with preexisting liver disease may be at increased risk of developing elevated hepatic enzymes when taking ZEPOSIA

Infections: ZEPOSIA may increase the susceptibility to infections. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS 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

- Prior and Concomitant Treatment with Antineoplastic, Immunosuppressive, or Immune-modulating Therapies: In 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. 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
- No cases of Progressive Multifocal Leukoencephalopathy (PML) were identified in active-controlled MS clinical trials with ZEPOSIA. However, PML has been observed in patients treated with other MS therapies. Should symptoms present that are suggestive of PML, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued
- 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

Macular edema: Patients with risk factors for macular edema, such as a history of uveitis or diabetes mellitus, should have an ophthalmologic evaluation prior to treatment with ZEPOSIA. Patients who present with visual symptoms of macular edema should be evaluated and, if confirmed, treatment with ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): PRES is a syndrome characterized by sudden onset of severe headache, confusion, seizures, and visual loss. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. In animals, findings at similar exposure levels included embryo-fetal death, abnormal/delayed ossification, and abnormalities of the viscera and large blood vessels. Women of childbearing potential should use effective contraception during treatment and for 3 months after stopping ZEPOSIA

Most common Adverse Reactions (≥2%): Nasopharyngitis, abnormal liver tests, urinary tract infections, hypertension, pharyngitis, and respiratory tract infections

Most common Adverse Reactions (>5%): Nasopharyngitis and abnormal liver tests (ALT/GGT)

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

Bristol-Myers Squibb

© 2020 Bristol-Myers Squibb Company.
ZEPOSIA is a registered trademark of
Bristol-Myers Squibb Company.
All rights reserved. 01/20 US-ZEP-19-0095

DRAFT