For adult patients with moderately to severely active ulcerative colitis (UC)[1]

WHEN DISEASE ACTIVITY HAS PROGRESSED TO MODERATE...

MEET LEAH

Diagnosed with ulcerative colitis in 2015

- Female
- 35 years old
- Married, with 2 small children
- Profession: Dental hygienist

Not an actual patient.

once-daily ZEPOSIA® (ozanimod) | 0.92 mg capsules

INDICATION

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

IMPORTANT SAFETY INFORMATION

Contraindications:

- Patients who in the last 6 months, experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III/IV heart failure or have a presence of Mobitz type II second or third-degree atrioventricular (AV) block, sick sinus syndrome, or sino-atrial block, unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients taking a monoamine oxidase (MAO) inhibitor

Infections: ZEPOSIA may increase the susceptibility to infections. Life-threatening and rare fatal infections have occurred in patients receiving ZEPOSIA. Obtain a recent (i.e., within 6 months or after discontinuation of prior UC therapy) complete blood count (CBC) including lymphocyte count before initiation of ZEPOSIA. Delay initiation of ZEPOSIA in patients with an active infection until the infection is resolved. Consider interruption of treatment with ZEPOSIA if a patient develops a serious infection. Continue monitoring for infections up to 3 months after discontinuing ZEPOSIA.

- Herpes zoster was reported as an adverse reaction in ZEPOSIA-treated patients. Herpes simplex encephalitis and varicella zoster meningitis have been reported with sphingosine 1-phosphate (S1P) receptor modulators. Patients without a healthcare professional-confirmed history of varicella (chickenpox), or without documentation of a full course of vaccination against varicella zoster virus (VZV), should be tested for antibodies to VZV before initiating ZEPOSIA. A full course of vaccination for antibody-negative patients with varicella vaccine is recommended prior to commencing treatment with ZEPOSIA

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

Patient History & Clinical Evaluation

BACKGROUND

Leah is a 35-year-old female with a husband and two small children. She is active in her community and with her children's activities. She was diagnosed in 2015 with ulcerative colitis. Initially, she was able to manage her disease with diet and 5-ASAs.

SYMPTOMS

- Significant increase in stool frequency (4 stools more than normal) over last 6 weeks
- Obvious blood with stool most of the time
- Increasingly missing days at work due to symptoms
- Fatigue
- Occasional tenesmus
- Increased urgency

CURRENT MEDICATIONS

- 5-ASAs
- One course of oral steroids in last 12 months
- Topical steroids 3 months ago
- Oral contraceptive

ASSESSMENT

- Vitals: within limits of normal
- Comorbidities: none
- Endoscopic evaluation: marked erythema and lack of vascular pattern; friability and erosions
- Extent of disease: left-sided

REASON FOR MOST RECENT VISIT

To discuss treatment options—she is concerned about safety risks associated with medications and somewhat averse to needles.

ADDITIONAL CONSIDERATIONS

- Further dietary modifications
- Aversion to intravenous and subcutaneous administration

ASAs=aminosalicylates.

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

- Cases of fatal cryptococcal meningitis (CM) were reported in patients treated with another S1P receptor modulator. If CM is suspected, ZEPOSIA should be suspended until cryptococcal infection has been excluded. If CM is diagnosed, appropriate treatment should be initiated
- Progressive Multifocal Leukoencephalopathy (PML) is an opportunistic viral infection of the brain that typically occurs in patients who are immunocompromised, and that usually leads to death or severe disability. PML has been reported in patients treated with S1P receptor modulators and other UC therapies and has been associated with some risk factors. If PML is suspected, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued
- In the UC clinical studies, patients who received ZEPOSIA were not to receive concomitant treatment with antineoplastic, non-corticosteroid immunosuppressive, or immune-modulating therapies used for treatment of UC. Concomitant use of ZEPOSIA with any of these therapies would be expected to increase the risk of immunosuppression. When switching to ZEPOSIA from immunosuppressive medications, consider the duration of their effects and their mode of action to avoid unintended additive immunosuppressive effects
- 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

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

Another Day Is Dawning for Leah

ZEPOSIA delivers lasting remission and a demonstrated safety profile in a once-daily capsule.[1]
Your patients with moderately to severely active UC can choose another path forward before biologics.[1a]

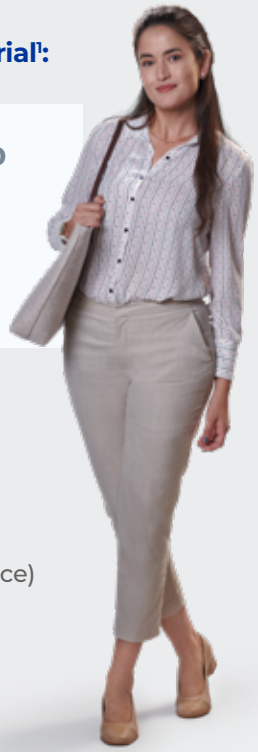
ZEPOSIA achieved significantly higher clinical remission rates vs placebo in the pivotal trial[1]:

18% ZEPOSIA (79/429) **vs** **6%** Placebo (13/216)

Week 10 ($p<0.0001$)

37% ZEPOSIA (85/230) **vs** **19%** Placebo (42/227)

Week 52 ($p<0.0001$)



Not an actual patient.

[a]ZEPOSIA demonstrated higher rates of clinical remission vs placebo in TNFi-naïve patients at Week 10 (22% [66/299] vs 7% [10/151]); and at Week 52 (41% [63/154] vs 22% [35/158], respectively).[1bc]

[b]Efficacy analysis by prior TNFi therapy was prespecified, but not powered to detect a difference in the treatment effect in these subgroups.[2]

[c]In UC Study 1 and UC Study 2, of the ZEPOSIA-treated patients who were TNFi-naïve, 288 and 145 were also biologic-naïve, respectively.[3]

TNFi=tumor necrosis factor inhibitor.

Clinical Trial: the efficacy and safety of ZEPOSIA were evaluated in 2 multicenter, randomized, double-blind, placebo-controlled clinical studies [UC Study 1 (induction) and UC Study 2 (maintenance) (NCT02435992)] in adult patients with moderately to severely active ulcerative colitis defined as a Mayo score of 6-12 at baseline.[1]

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

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

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

IMPORTANT SAFETY INFORMATION (cont'd)

Bradyarrhythmia and Atrioventricular Conduction Delays: Since initiation of ZEPOSIA may result in a transient decrease in heart rate and atrioventricular conduction delays, dose titration is recommended to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater decreases in heart rate. If treatment with ZEPOSIA is considered, advice from a cardiologist should be sought for those individuals:

- with significant QT prolongation
- with arrhythmias requiring treatment with Class 1a or III anti-arrhythmic drugs
- with ischemic heart disease, heart failure, history of cardiac arrest or myocardial infarction, cerebrovascular disease, and uncontrolled hypertension
- with a history of Mobitz type II second-degree or higher AV block, sick sinus syndrome, or sino-atrial heart block

Liver Injury: Elevations of aminotransferases may occur in patients receiving ZEPOSIA. Obtain liver function tests, if not recently available (i.e., within 6 months), before initiation of ZEPOSIA. Patients who develop symptoms suggestive of hepatic dysfunction should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Caution should be exercised when using ZEPOSIA in patients with history of significant liver disease

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IMPORTANT SAFETY INFORMATION (cont'd)

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. Based on animal studies, ZEPOSIA may cause fetal harm. Women of childbearing potential should use effective contraception to avoid pregnancy during treatment and for 3 months after stopping ZEPOSIA

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

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

Macular edema: S1P modulators have been associated with an increased risk of macular edema. Patients with a history of uveitis or diabetes mellitus are at increased risk. Patients with a history of these conditions should have an ophthalmic evaluation of the fundus, including the macula, prior to treatment initiation and regular follow-up examinations. An ophthalmic evaluation is recommended in all patients at any time if there is a change in vision. Continued use of ZEPOSIA in patients with macular edema has not been evaluated; potential benefits and risks for the individual patient should be considered if deciding whether ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): Rare cases of PRES have been reported in patients receiving a S1P receptor modulator. If a ZEPOSIA-treated patient develops unexpected neurological or psychiatric symptoms or any symptom/sign suggestive of an increase in intracranial pressure, a complete physical and neurological examination should be conducted. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. Delay in diagnosis and treatment may lead to permanent neurological sequelae. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Unintended Additive Immunosuppressive Effects From Prior Immunosuppressive or Immune-Modulating Drugs: When switching from drugs with prolonged immune effects, the half-life and mode of action of these drugs must be considered to avoid unintended additive immunosuppressive effects while at the same time minimizing risk of disease reactivation. Initiating treatment with ZEPOSIA after treatment with alemtuzumab is not recommended

Immune System Effects After Stopping ZEPOSIA: After discontinuing ZEPOSIA, the median time for lymphocyte counts to return to the normal range was 30 days with approximately 90% of patients in the normal range within 3 months. Use of immunosuppressants within this period may lead to an additive effect on the immune system, therefore caution should be applied when initiating other drugs 4 weeks after the last dose of ZEPOSIA

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

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

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References: 1. ZEPOSIA. Prescribing information. Bristol-Myers Squibb Company; 2021. **2.** Data on File. OZA 025. Princeton, NJ: Bristol Myers Squibb. **3.** Data on File. OZA 027. Princeton, NJ: Bristol Myers Squibb.

Bristol Myers Squibb is committed to transparency. For information on the list price of ZEPOSIA as well as information regarding average out-of-pocket costs and assistance programs, please visit our pricing information page at ZEPOSIA.com/ulcerative-colitis/cost.

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Bristol Myers Squibb™

For adult patients with moderately to severely active ulcerative colitis (UC)[1]

WHEN CORTICOSTEROIDS BECOME A CONCERN...

MEET JAYDEN

Diagnosed with ulcerative colitis in 2017

- Male
- 29 years old
- Single
- Profession: Construction supervisor

Not an actual patient.

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Patient History & Clinical Evaluation

BACKGROUND

Jayden is a 29-year-old single male. He has a physically demanding job and a busy social life. He was diagnosed in 2017 with ulcerative colitis. Initially, he was managing his disease with 5-ASAs, but in the past year he has become increasingly dependent on corticosteroids for more frequent flares.

SYMPTOMS

- Significant increase in stool frequency (4-6 per day more than normal) over last 3 weeks, accompanied by rectal bleeding and mucous discharge over the last 8-10 days
- Lower abdominal pain
- Malaise and lethargy
- Lost 4 lbs

CURRENT MEDICATIONS

- 5-ASAs
- Three courses of oral steroids in last 14 months with last course extended because of difficulty tapering

ASSESSMENT

- Vitals: within limits of normal
- Laboratory analysis: Hb 11.0 g/dL[2]
- Comorbidities: none
- Abdominal exam: guarding and tenderness on left side[3]
- Endoscopic evaluation: friable mucosa and ulcerations
- Extent of disease: left-sided

REASON FOR MOST RECENT VISIT

To discuss treatment options that address worsening of UC symptoms. He is concerned with the side effects of steroids.

ADDITIONAL CONSIDERATIONS

- Patient's concern with steroid overuse
- Patient's age and general health profile

ASAs=aminosalicylates; Hb=hemoglobin.

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

- Cases of fatal cryptococcal meningitis (CM) were reported in patients treated with another S1P receptor modulator. If CM is suspected, ZEPOSIA should be suspended until cryptococcal infection has been excluded. If CM is diagnosed, appropriate treatment should be initiated
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Week 10 ($p<0.0001$)

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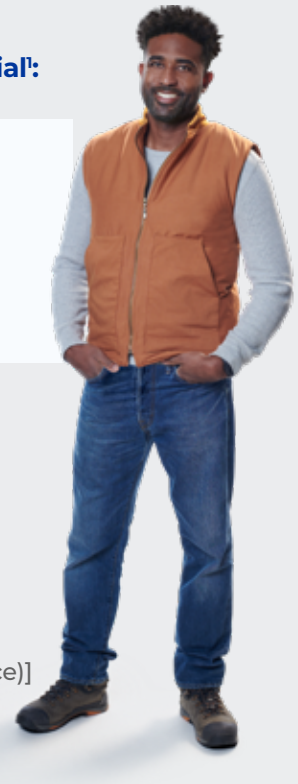
Week 52 ($p<0.0001$)



Not an actual patient.

- **Treatment with ZEPOSIA resulted in a significantly greater corticosteroid-free clinical remission rate vs placebo at Week 52: 32% (N=230) vs 17% (N=227), respectively ($p<0.001$)[1]**
  - Corticosteroid-free remission is defined as clinical remission at Week 52 while off corticosteroids for ≥12 weeks.

[a]ZEPOSIA demonstrated higher rates of clinical remission vs placebo in TNFi-naïve patients at Week 10 (22% [66/299] vs 7% [10/151]); and at Week 52 (41% [63/154] vs 22% [35/158], respectively).[1bc]

[b]Efficacy analysis by prior TNFi therapy was prespecified, but not powered to detect a difference in the treatment effect in these subgroups.[4]

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

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Bristol Myers Squibb is committed to transparency. For information on the list price of ZEPOSIA as well as information regarding average out-of-pocket costs and assistance programs, please visit our pricing information page at ZEPOSIA.com/ulcerative-colitis/cost.

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Bristol Myers Squibb™

For adult patients with moderately to severely active ulcerative colitis (UC)[1]

WHEN FACED WITH CHOOSING AMONG UC TREATMENTS...

MEET ANDREW

Diagnosed with ulcerative colitis in 2013

- Male
- 44 years old
- Married, with 2 teenage children
- Profession: Accountant

Not an actual patient.

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INDICATION

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IMPORTANT SAFETY INFORMATION

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Patient History & Clinical Evaluation

BACKGROUND

Andrew is a 44-year-old married male with 2 teenagers. His job is stressful, and when he's not at work, he is busy coaching his kids' high school basketball teams. He was diagnosed with ulcerative colitis in 2013. He has historically used 5-ASAs to control his UC with moderate success, but in 2018, with worsening symptoms, had thiopurine added to his regimen.

SYMPTOMS

- Six to 7 urgent bowel movements per day; diarrhea is mucoid with increasing streaks of blood over the last 2 weeks
- Increasing occurrence of tenesmus
- Disease is impacting his ability to work
- Occasional lower abdominal cramping
- Lost 3 lbs over the last 2 weeks

CURRENT MEDICATIONS

- 5-ASAs
- Thiopurine
- Two courses of corticosteroids in the last 12 months

ASSESSMENT

- Vitals: within limits of normal
- Abdominal exam: diffuse pain and tenderness on deep palpitation[2]
- Endoscopic evaluation: friable and erythematous mucosa extending proximally from the rectum to past the splenic flexure[3,4]
- Extent of disease: extensive

REASON FOR MOST RECENT VISIT

To discuss a new treatment option that would address his worsening symptoms.

ADDITIONAL CONSIDERATIONS

- Effect of patient's busy schedule on treatment choice
- Extent of patient's disease and its potential effect on treatment choice
- Patient's increasing use of over-the-counter products to manage symptoms

ASAs=aminosalicylates.

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

- Cases of fatal cryptococcal meningitis (CM) were reported in patients treated with another S1P receptor modulator. If CM is suspected, ZEPOSIA should be suspended until cryptococcal infection has been excluded. If CM is diagnosed, appropriate treatment should be initiated
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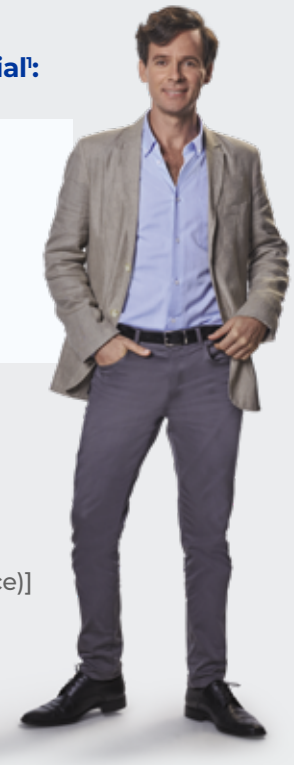
37% ZEPOSIA (85/230) **vs** **19%** Placebo (42/227)

Week 52 ($p<0.0001$)



Not an actual patient.

[a]ZEPOSIA demonstrated higher rates of clinical remission vs placebo in TNFi-naïve patients at Week 10 (22% [66/299] vs 7% [10/151]); and at Week 52 (41% [63/154] vs 22% [35/158], respectively).[1bc]

[b]Efficacy analysis by prior TNFi therapy was prespecified, but not powered to detect a difference in the treatment effect in these subgroups.[5]

[c]In UC Study 1 and UC Study 2, of the ZEPOSIA-treated patients who were TNFi-naïve, 288 and 145 were also biologic-naïve, respectively.[6]

TNFi=tumor necrosis factor inhibitor.

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

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

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

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

IMPORTANT SAFETY INFORMATION (cont'd)

Bradyarrhythmia and Atrioventricular Conduction Delays: Since initiation of ZEPOSIA may result in a transient decrease in heart rate and atrioventricular conduction delays, dose titration is recommended to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater decreases in heart rate. If treatment with ZEPOSIA is considered, advice from a cardiologist should be sought for those individuals:

- with significant QT prolongation
- with arrhythmias requiring treatment with Class 1a or III anti-arrhythmic drugs
- with ischemic heart disease, heart failure, history of cardiac arrest or myocardial infarction, cerebrovascular disease, and uncontrolled hypertension
- with a history of Mobitz type II second-degree or higher AV block, sick sinus syndrome, or sino-atrial heart block

Liver Injury: Elevations of aminotransferases may occur in patients receiving ZEPOSIA. Obtain liver function tests, if not recently available (i.e., within 6 months), before initiation of ZEPOSIA. Patients who develop symptoms suggestive of hepatic dysfunction should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Caution should be exercised when using ZEPOSIA in patients with history of significant liver disease

once-daily ZEPOSIA® (ozanimod) 0.92 mg capsules

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

IMPORTANT SAFETY INFORMATION (cont'd)

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. Based on animal studies, ZEPOSIA may cause fetal harm. Women of childbearing potential should use effective contraception to avoid pregnancy during treatment and for 3 months after stopping ZEPOSIA

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

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

Macular edema: S1P modulators have been associated with an increased risk of macular edema. Patients with a history of uveitis or diabetes mellitus are at increased risk. Patients with a history of these conditions should have an ophthalmic evaluation of the fundus, including the macula, prior to treatment initiation and regular follow-up examinations. An ophthalmic evaluation is recommended in all patients at any time if there is a change in vision. Continued use of ZEPOSIA in patients with macular edema has not been evaluated; potential benefits and risks for the individual patient should be considered if deciding whether ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): Rare cases of PRES have been reported in patients receiving a S1P receptor modulator. If a ZEPOSIA-treated patient develops unexpected neurological or psychiatric symptoms or any symptom/sign suggestive of an increase in intracranial pressure, a complete physical and neurological examination should be conducted. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. Delay in diagnosis and treatment may lead to permanent neurological sequelae. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Unintended Additive Immunosuppressive Effects From Prior Immunosuppressive or Immune-Modulating Drugs: When switching from drugs with prolonged immune effects, the half-life and mode of action of these drugs must be considered to avoid unintended additive immunosuppressive effects while at the same time minimizing risk of disease reactivation. Initiating treatment with ZEPOSIA after treatment with alemtuzumab is not recommended

Immune System Effects After Stopping ZEPOSIA: After discontinuing ZEPOSIA, the median time for lymphocyte counts to return to the normal range was 30 days with approximately 90% of patients in the normal range within 3 months. Use of immunosuppressants within this period may lead to an additive effect on the immune system, therefore caution should be applied when initiating other drugs 4 weeks after the last dose of ZEPOSIA

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

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

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

References: 1. ZEPOSIA. Prescribing information. Bristol-Myers Squibb Company; 2021. **2.** Snipelisky DF, Cable CA, Maniaci MJ. 37-year-old man with abdominal pain. *Mayo Clin Proc.* 2014;89(4):558-562. **3.** Kayal M, Shah S. Ulcerative colitis: current and emerging treatment strategies. *J Clin Med.* 2019;9(1):94. **4.** Ungaro R, Mehandru S, Allen PB, Peyrin-Biroulet L, Colombel J-F. Ulcerative colitis. *Lancet*. 2017;389(10080):1756-1770. **5.** Data on File. OZA 025. Princeton, NJ: Bristol Myers Squibb. **6.** Data on File. OZA 027. Princeton, NJ: Bristol Myers Squibb.

Bristol Myers Squibb is committed to transparency. For information on the list price of ZEPOSIA as well as information regarding average out-of-pocket costs and assistance programs, please visit our pricing information page at ZEPOSIA.com/ulcerative-colitis/cost.

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