

Tyramine and ZEPOSIA food and drug interaction information

Certain foods that may contain high amounts (more than 150 mg) of tyramine could cause severe hypertension in patients taking recommended doses of ZEPOSIA due to potential tyramine interaction. Because of an increased sensitivity to tyramine, patients should be advised to avoid foods containing high amounts of tyramine while taking ZEPOSIA.¹

Clinical impact of food and drug interaction

MAO in the gastrointestinal tract and liver (primarily type A) provides protection from exogenous amines (eg, tyramine). If tyramine were absorbed intact, it could lead to severe hypertension, including hypertensive crisis. Foods containing high amounts of exogenous amines may cause release of norepinephrine resulting in a rise in blood pressure (tyramine reaction).¹

Foods and beverages your patients should avoid while taking ZEPOSIA

Foods and beverages that are aged, fermented, cured, smoked, or pickled (eg, aged cheese, pickled herring) may be high in tyramine and should be avoided. It's recommended that patients taking ZEPOSIA **avoid foods and beverages that have more than 150 mg of tyramine.**^{1,2}

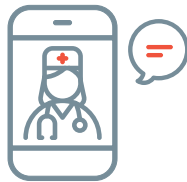
See next page for a list of common foods and beverages that are high in tyramine. The list includes the amount of tyramine per serving, as well as the amount of each food and beverage that could contain 150 mg of tyramine.

Discuss this information with your patients before they make any changes to their diet.

Additional information your patients should know about tyramine and ZEPOSIA

Today's food processing and handling methods have lowered the amount of tyramine in many processed foods (except for certain cheeses and sauces). But tyramine can still be high in certain foods and beverages, and it's important for your patients to be aware of this while taking ZEPOSIA.^{1,2}

Encourage your patients to speak with a Nurse Navigator or a member of your staff if they have any additional questions about tyramine and ZEPOSIA.



If your patients have questions, they can call a Nurse Navigator* at **1-833-ZEPOSIA (1-833-937-6742)** Monday to Friday, 8 AM-8 PM ET

*Nurse Navigators do not provide medical advice.
 MAO=monoamine oxidase.

INDICATIONS

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

1. Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
2. Moderately to severely active ulcerative colitis (UC) in adults.

IMPORTANT SAFETY INFORMATION

Contraindications:

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

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

For additional safety information, please see the full [Prescribing information](#) and [Medication Guide](#).

See next page for a list of common foods and beverages that are high in tyramine

Common foods that are high in tyramine

It's recommended that your patients avoid food and beverages that have more than 150 mg of tyramine while taking ZEPOSIA. Another thing your patients should keep in mind: the amount of tyramine they consume from different foods and beverages can add up. In other words, some tyramine from one food plus some tyramine from another food plus some tyramine from a beverage could add up to a possibly dangerous amount of tyramine.¹⁻³

Below is a list of foods and beverages that may contain high amounts of tyramine, along with the amount of tyramine in a typical serving, and the amount of each that could contain 150 mg of tyramine. This is not an exhaustive list of foods and beverages containing high amounts of tyramine. The amounts listed below are estimates, and different people can react to tyramine differently. Please note that some of the foods and beverages listed below have a wide range of tyramine content. Discuss this information with your patients before they make any changes to their diet.¹⁻⁴

Foods to avoid ^{2,4}	Amount of tyramine per serving ^{2,4} (serving size=tyramine content)	Amount that could contain 150 mg of tyramine ^{2,4a}
CHEESES		
Bel Paese, Emmental (a type of aged Swiss), goat cheese (ripened), Grana Padano, pecorino, provolone, Taleggio	1 oz=5.7 mg	26.3 oz (≈1.6 lb)
Cheddar (young), commercial cheeses	1 oz=5.7 mg	26.3 oz (≈1.6 lb)
Edam	1 oz=3.4 mg	44.1 oz (≈2.76 lb)
Feta (aged)	1 oz=7.1 mg	21.1 oz (≈1.3 lb)
Gouda (young), Gruyère	1 oz=2.8 mg	53.6 oz (≈3.3 lb)
Highly aged artisanal cheeses <i>These may have a high amount of tyramine</i>	1 oz=28.4 mg	5.3 oz (≈0.3 lb)
Parmigiano-Reggiano	1 oz=4.25 mg	35.3 oz (≈2.2 lb)
SAUSAGE, FISH AND SEAFOOD, SAUCES, SPREADS, VEGETABLES, WINE, BEER		
Beer <i>Tyramine content can vary greatly</i> LOWER LEVELS: Most canned or bottled standard (and non-alcoholic) commercial beers are lower in tyramine.	12 oz=less than 3.6 mg	500 oz (about 42 x 12-oz bottles)
HIGHER LEVELS: Draft beers, craft, "micro-brew," Belgian, homemade beers, and beer made with natural yeast may have a higher amount.	12 oz=36 mg	As little as 50 oz (as few as 4 x 12-oz bottles)
Budu, cinalok (Malaysian fish and seafood appetizers)	1 oz=12.76 mg	11.8 oz (≈0.7 lb)
Dried tuna roe (salted)	1 oz=2.55 mg	58.8 oz (≈3.7 lb)
Fermented yeast (Marmite, Vegemite)	1 tbsp=4.43 mg	33.9 tbsp (≈2 cups)
Fish sauce (eg, nam pla)	1 tbsp=7.39 mg	20.3 tbsp (a little over 1 cup)
Kimchi	4 oz=13.6 mg	44.1 oz (≈11 four-oz servings)
Sauerkraut <i>This may have a high amount of tyramine. A 4-oz serving could have as much as 102 mg. That means just a 5.9 oz portion could contain 150 mg.</i>	4 oz=22.7 mg (at a minimum)	26.5 oz (about 6.5 x 4-oz servings)
Sausage (fermented; eg, chorizo, fuet, sobrasada, salchichón) <i>This may have a high amount of tyramine. A 1-oz serving could have as much as 17.01 mg. That means just over a half-pound portion could contain 150 mg.</i>	1 oz=5.7 mg (at a minimum)	26.3 oz (≈1.6 pounds)
Soy sauce (commercial)	1 tbsp=3.0 mg	50 tbsp (a little over 3 cups)
Soy sauce (specialty) <i>This may have a high amount of tyramine</i>	1 tbsp=13.9 mg	10.8 tbsp (≈0.7 cups)
Wine	5 oz=less than 1.48 mg	500 oz (≈100 five-oz glasses)

^aAmounts shown in this column are approximate and for illustrative purposes only.

For additional safety information, please see the full [Prescribing Information](#) and [Medication Guide](#).

INDICATIONS

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

1. Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
2. Moderately to severely active ulcerative colitis (UC) in adults.

IMPORTANT SAFETY INFORMATION

Contraindications:

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

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

- Herpes zoster was reported as an adverse reaction in ZEPOSIA-treated patients. Herpes simplex encephalitis and varicella zoster meningitis have been reported with sphingosine 1-phosphate (S1P) receptor modulators. Patients without a healthcare professional-confirmed history of varicella (chickenpox), or without documentation of a full course of vaccination against varicella zoster virus (VZV), should be tested for antibodies to VZV before initiating ZEPOSIA. A full course of vaccination for antibody-negative patients with varicella vaccine is recommended prior to commencing treatment with ZEPOSIA.
- 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.
- In the MS and UC clinical studies, patients who received ZEPOSIA were not to receive concomitant treatment with antineoplastic, non-corticosteroid immunosuppressive, or immune-modulating therapies used for treatment of MS and UC. Concomitant use of ZEPOSIA with any of these therapies would be expected to increase the risk of immunosuppression. When switching to ZEPOSIA from immunosuppressive medications, consider the duration of their effects and their mode of action to avoid unintended additive immunosuppressive effects.
- Use of live attenuated vaccines should be avoided during and for 3 months after treatment with ZEPOSIA. If live attenuated vaccine immunizations are required, administer at least 1 month prior to initiation of ZEPOSIA.

Progressive Multifocal Leukoencephalopathy (PML): PML is an opportunistic viral infection of the brain that typically occurs in patients who are immunocompromised, and that usually leads to death or severe disability.

PML has been reported in patients treated with S1P receptor modulators, including ZEPOSIA, and other MS and UC therapies and has been associated with some risk factors. If PML is suspected, withhold ZEPOSIA and perform an appropriate diagnostic evaluation.

If confirmed, treatment with ZEPOSIA should be discontinued.

Bradycardia 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

For additional safety information, please see the full [Prescribing Information](#) and [Medication Guide](#).

IMPORTANT SAFETY INFORMATION (cont'd)

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

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. Based on animal studies, ZEPOSIA may cause fetal harm. Women of childbearing potential should use effective contraception to avoid pregnancy during treatment and for 3 months after stopping ZEPOSIA. Women who become pregnant while taking ZEPOSIA for MS may enroll in the ZEPOSIA pregnancy registry by calling 1-877-301-9314 or visiting www.zeposiapregnancyregistry.com.

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

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

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

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

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

Severe Increase in Multiple Sclerosis (MS) Disability After Stopping ZEPOSIA: In MS, severe exacerbation of disease, including disease rebound, has been rarely reported after discontinuation of a S1P receptor modulator. The possibility of severe exacerbation of disease should be considered after stopping ZEPOSIA treatment so patients should be monitored upon discontinuation.

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

Most Common Adverse Reactions that occurred in the MS clinical trials of ZEPOSIA-treated patients (≥4%): upper respiratory infection, hepatic transaminase elevation, orthostatic hypotension, urinary tract infection, back pain, and hypertension.

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

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

For additional safety information, please see the full [Prescribing Information](#) and [Medication Guide](#).

References: 1. ZEPOSIA. Prescribing Information. Bristol-Myers Squibb Company; 2022. 2. Meyer JM. A concise guide to monoamine oxidase inhibitors: a better understanding of the risks can lead to increased use of these highly effective agents. *Curr Psychiatr*. 2017;16(12):15-47A. 3. Gillman PK. A reassessment of the safety profile of monoamine oxidase inhibitors: elucidating tired old tyramine myths. *J Neural Transm (Vienna)*. 2018;125(11):1707-1717. 4. Gillman PK. Monoamine oxidase inhibitors: a review concerning dietary tyramine and drug interactions. *PsychoTropical Commentaries*. 2017;1:1-102.

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 for MS at ZEPOSIA.com/multiple-sclerosis/cost and for UC at ZEPOSIA.com/ulcerative-colitis/cost.

ZEPOSIA and ZEPOSIA logo are trademarks of Celgene Corporation, a Bristol Myers Squibb company. All other trademarks are the property of their respective owners.

© 2022 Bristol-Myers Squibb Company. 2084-US-2201486 10/22