

Taking ZEPOSIA?

What you need to know about tyramine

If you're taking ZEPOSIA® (ozanimod), it's important that you avoid foods and beverages that are high in *tyramine* (TIE-ruh-meen). Tyramine is a type of compound (monoamine compound) found naturally in the body. It can also be found in high amounts in certain foods and beverages.

Why do I need to avoid foods and beverages that are high in tyramine?

Consuming a large amount of tyramine while taking ZEPOSIA could lead to severe high blood pressure (hypertension).

What foods and beverages should I avoid while taking ZEPOSIA?

Foods and beverages that are aged, fermented, cured, smoked, and pickled may be high in tyramine and should be avoided. It's recommended that people taking ZEPOSIA avoid foods and beverages that have more than 150 mg of tyramine.

See the next page for a list of common high-tyramine foods and beverages. 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. **Speak with your healthcare provider before making any changes to your diet.**

What else do I need to know about tyramine and ZEPOSIA?

Today's food processing and handling methods have lowered the amount of tyramine in many processed foods (with the exception of certain cheeses and sauces). But tyramine can still be high in certain foods and beverages, and it's important to look out for them if you're taking ZEPOSIA.

Speak with a member of your healthcare team if you have any additional questions about tyramine and ZEPOSIA.

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



INDICATIONS

Multiple Sclerosis (MS): ZEPOSIA® (ozanimod) is a prescription medicine used to treat relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Ulcerative Colitis (UC): ZEPOSIA is a prescription medicine used to treat moderately to severely active ulcerative colitis (UC) in adults.

It is not known if ZEPOSIA is safe and effective in children.

Please see Important Safety Information on pages 3-5 and full <u>Prescribing Information</u> and <u>Medication Guide</u>.

Common foods that are high in tyramine



If you're taking ZEPOSIA® (ozanimod), it's recommended that you avoid foods and beverages that have more than 150 mg of tyramine. Below is a list of foods and beverages that may contain high amounts of tyramine, along with the amount of tyramine per serving and what amount could contain 150 mg of tyramine. While this is not an exhaustive list of all foods that include tyramine, it may be used as a guide. Keep in mind, consuming multiple foods and beverages with any level of tyramine in them could result in a high amount of tyramine in the body.

Please note that different people react to tyramine differently. The ranges below are only estimates and can vary greatly even among the same item. **Speak with your healthcare provider before making any changes to your diet.**

Foods to avoid	Amount of tyramine per serving (serving size = tyramine content)	Amount that could contain 150 mg of tyramine*
Cheeses:		
Bel Paese, Emmental (a type of aged Swiss), goat cheese (ripened), Grana Padano, Pecorino, provolone, Taleggio	1 oz = 5.7 mg of tyramine	26.3 oz (about 1.6 pounds)
Cheddar (young), commercial cheeses	1 oz = 5.7 mg of tyramine	26.3 oz (about 1.6 pounds)
Edam	1 oz = 3.4 mg of tyramine	44.1 oz (about 2.76 pounds)
Feta (aged)	1 oz = 7.1 mg of tyramine	21.1 oz (about 1.3 pounds)
Gouda (young), Gruyère	1 oz = 2.8 mg of tyramine	53.6 oz (about 3.4 pounds)
Highly aged artisanal cheeses These may have a high amount of tyramine.	1 oz = 28.4 mg of tyramine	5.3 oz (about 0.3 pounds)
Parmigiano-Reggiano	1 oz = 4.25 mg of tyramine	35.4 oz (about 2.2 pounds)
Sausage, fish and seafood, sauces, spreads, vegetables, wine, beer:		
Beer With beer, tyramine content can vary greatly. LOWER LEVELS: Most canned or bottled standard (and non-alcoholic) commercial beers are lower in tyramine.	12 oz = less than 3.6 mg of tyramine	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 of tyramine	As little as 50 oz (as few as 4 x 12-oz bottles)
Budu, cincalok (Malaysian fish and seafood appetizers)	1 oz = 12.76 mg of tyramine	11.8 oz (about 0.7 pounds)
Dried tuna roe (salted)	1 oz = 2.55 mg of tyramine	58.8 oz (about 3.7 pounds)
Fermented yeast (Marmite, Vegemite)	1 tbsp = 4.43 mg of tyramine	33.9 tbsp (almost 2 cups)
Fish sauce (eg, nam pla)	1 tbsp = 7.39 mg of tyramine	20.3 tbsp (a little over 1 cup)
Kimchi	4 oz = 13.6 mg of tyramine	44.1 oz (about 11 x 4-oz servings)
Sauerkraut 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.	4 oz = 22.7 mg of tyramine (at a minimum)	26.5 oz (about 6.5 x 4-oz servings)
Sausage (fermented; eg, chorizo, fuet, sobrasada, salchichón) 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.	1 oz = 5.7 mg of tyramine (at a minimum)	26.3 oz (about 1.6 pounds)
Soy sauce (commercial)	1 tbsp = 3.0 mg of tyramine	50 tbsp (a little over 3 cups)
Soy sauce (specialty) This may have a high amount of tyramine.	1 tbsp = 13.9 mg of tyramine	10.8 tbsp (about 0.5 cups)
Wines	5 oz = less than 1.48 mg of tyramine	500 oz (about 100 x 5-oz glasses)

^{*}Amounts shown in this column are approximate and for illustrative purposes only.



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IMPORTANT SAFETY INFORMATION

Do not take ZEPOSIA if you:

- have had a heart attack, chest pain (unstable angina), stroke or mini-stroke (transient ischemic attack or TIA), or certain types of heart failure in the last 6 months
- have or have had a history of certain types of an irregular or abnormal heartbeat (arrhythmia) that is not corrected by a pacemaker
- have untreated, severe breathing problems during your sleep (sleep apnea)
- take certain medicines called monoamine oxidase (MAO) inhibitors (such as selegiline, phenelzine, linezolid)

Talk to your healthcare provider before taking ZEPOSIA if you have any of these conditions or do not know if you have any of these conditions.

ZEPOSIA may cause serious side effects, including:

- Infections. ZEPOSIA can increase your risk of serious infections that can be life-threatening and cause death. ZEPOSIA lowers the number of white blood cells (lymphocytes) in your blood. This will usually go back to normal within 3 months of stopping treatment. Your healthcare provider may do a blood test of your white blood cells before you start taking ZEPOSIA.
 - Call your healthcare provider right away if you have any of these symptoms of an infection during treatment with ZEPOSIA and for 3 months after your last dose of ZEPOSIA:
 - o fever
 - o feeling very tired
 - o flu-like symptoms
 - o cough
 - painful and frequent urination (signs of a urinary tract infection)
- o rash
- headache with fever, neck stiffness, sensitivity to light, nausea, or confusion (these may be symptoms of meningitis, an infection of the lining around your brain and spine)

Your healthcare provider may delay starting or may stop your ZEPOSIA treatment if you have an infection.

- Progressive multifocal leukoencephalopathy (PML). ZEPOSIA can increase your risk for PML, which is a rare brain infection that usually leads to death or severe disability. If PML happens, it usually happens in people with weakened immune systems but has happened in people who do not have weakened immune systems. Symptoms of PML get worse over days to weeks. Call your doctor right away if you have any new or worsening symptoms of PML that have lasted several days, including: weakness on one (1) side of your body, changes in your vision, changes in your thinking or memory, confusion, changes in your personality, loss of coordination in your arms or legs, decreased strength, and/or problems with balance.
- Slow heart rate (also known as bradyarrhythmia) when you start taking ZEPOSIA. ZEPOSIA may cause your heart rate to temporarily slow down, especially during the first 8 days. You will have a test to check the electrical activity of your heart called an electrocardiogram (ECG) before you take your first dose of ZEPOSIA.

Call your healthcare provider if you experience the following symptoms of slow heart rate:

- o dizziness
- o lightheadedness
- feeling like your heart is beating slowly or skipping beats
- o shortness of breath
- o confusion
- o chest pain
- o tiredness

Follow directions from your healthcare provider when starting ZEPOSIA and when you miss a dose.

Continue reading for additional possible serious side effects of ZEPOSIA.

Before taking ZEPOSIA, tell your healthcare provider about all of your medical conditions, including if you:

- have a fever or infection, or are unable to fight infections due to a disease, or take or have taken medicines that lower your immune system
- received a vaccine in the past 30 days or are scheduled to receive a vaccine. ZEPOSIA may cause vaccines to be less effective



IMPORTANT SAFETY INFORMATION (cont'd)

- before you start ZEPOSIA, your healthcare provider may give you a chickenpox (Varicella Zoster Virus) vaccine if you have not had one before
- have had chickenpox or have received the vaccine for chickenpox. Your healthcare provider may do a blood test for the chickenpox virus. You may need to get the full course of the vaccine and wait 1 month before taking ZEPOSIA
- have a slow heart rate
- have an irregular or abnormal heartbeat (arrhythmia)
- · have a history of stroke
- have or have had heart problems, including a heart attack or chest pain
- have high blood pressure
- have liver problems
- have breathing problems, including during your sleep
- · have eye problems, especially an inflammation of the eye called uveitis
- have diabetes
- are or plan to become pregnant or if you become pregnant within 3 months after you stop taking ZEPOSIA.
 ZEPOSIA may harm your unborn baby. If you are a female who can become pregnant, talk to your healthcare
 provider about what birth control method is right for you during your treatment with ZEPOSIA and for
 3 months after you stop taking ZEPOSIA. If you become pregnant while taking ZEPOSIA for MS, tell your
 healthcare provider right away and enroll in the ZEPOSIA Pregnancy Registry by calling 1-877-301-9314 or
 visiting www.zeposiapregnancyregistry.com
- are breastfeeding or plan to breastfeed. It is not known if ZEPOSIA passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take ZEPOSIA

Tell your healthcare provider about all the medicines you take or have recently taken, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Using ZEPOSIA with other medicines can cause serious side effects. Especially tell your healthcare provider if you take or have taken:

- medicines that affect your immune system, such as alemtuzumab
- medicines to control your heart rhythm (antiarrhythmics), or heartbeat
- CYP2C8 inducers such as rifampin
- CYP2C8 inhibitors such as gemfibrozil (medicine to treat high fat in your blood)
- · opioids (pain medicine), medicines to treat depression, and medicines to treat Parkinson's disease
- medicines to control your heart rate and blood pressure (beta blocker medicines and calcium channel blocker medicines)

You should not receive **live** vaccines during treatment with ZEPOSIA, for at least 1 month before taking ZEPOSIA and for 3 months after you stop taking ZEPOSIA. Vaccines may not work as well when given during treatment with ZEPOSIA.

ZEPOSIA can cause serious side effects, including:

- **liver problems.** Your healthcare provider will do blood tests to check your liver before you start taking ZEPOSIA. Call your healthcare provider right away if you have any of the following symptoms:
 - o unexplained nausea
 - vomiting
 - o stomach area (abdominal) pain
 - o tiredness

- o loss of appetite
- o yellowing of the whites of your eyes or skin
- o dark-colored urine
- **increased blood pressure.** Your healthcare provider should check your blood pressure during treatment with ZEPOSIA. A sudden, severe increase in blood pressure (hypertensive crisis) can happen when you eat certain foods that contain high levels of tyramine.
- **breathing problems.** Some people who take ZEPOSIA have shortness of breath. Call your healthcare provider right away if you have new or worsening breathing problems.
- a problem with your vision called macular edema. Your risk of macular edema is higher if you have diabetes or have had an inflammation of your eye called uveitis. Your healthcare provider should test your vision before you start taking ZEPOSIA if you are at higher risk for macular edema or any time you notice vision changes during treatment with ZEPOSIA. Call your healthcare provider right away if you have any of the following symptoms:
 - o blurriness or shadows in the center of your vision
 - o sensitivity to light

- o a blind spot in the center of your vision
- o unusually colored vision



IMPORTANT SAFETY INFORMATION (cont'd)

- swelling and narrowing of the blood vessels in your brain. Posterior Reversible Encephalopathy Syndrome (PRES) is a rare condition that has happened with ZEPOSIA and with drugs in the same class. Symptoms of PRES usually get better when you stop taking ZEPOSIA. If left untreated, it may lead to stroke. Your healthcare provider will do a test if you have any symptoms of PRES. Call your healthcare provider right away if you have any of the following symptoms:
 - o sudden severe headache

o sudden loss of vision or other changes in your vision

sudden confusion

- o seizure
- severe worsening of multiple sclerosis (MS) after stopping ZEPOSIA. When ZEPOSIA is stopped, symptoms of MS may return and become worse compared to before or during treatment. Always talk to your healthcare provider before you stop taking ZEPOSIA for any reason. Tell your healthcare provider if you have worsening symptoms of MS after stopping ZEPOSIA.

The most common side effects of ZEPOSIA can include:

- · upper respiratory tract infections
- elevated liver enzymes
- low blood pressure when you stand up (orthostatic hypotension)
- painful and frequent urination (signs of urinary tract infection)
- back pain
- · high blood pressure
- headache

These are not all of the possible side effects of ZEPOSIA. For more information, ask your healthcare provider or pharmacist.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see full Prescribing Information, including Medication Guide.