MEDICATION GUIDE

ZEPOSIA® (zeh-poe'-see-ah)
(ozanimod)
capsules, for oral use

Read this Medication Guide before you start taking ZEPOSIA and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your healthcare provider about your medical condition or treatment.

What is the most important information I should know about ZEPOSIA?
ZEPOSIA may cause serious side effects, including:

1. **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 the following symptoms of an infection during treatment with ZEPOSIA and for 3 months after your last dose of ZEPOSIA:

   - fever
   - feeling very tired
   - flu-like symptoms
   - cough
   - painful and frequent urination (signs of a urinary tract infection)
   - 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.

2. **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 1 side of your body
   - loss of coordination in your arms or legs
   - decreased strength
   - problems with balance
   - changes in your vision
   - changes in your thinking or memory
   - confusion
   - changes in your personality

3. **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 that you take ZEPOSIA. 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:

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

   Follow directions from your healthcare provider when starting ZEPOSIA and when you miss a dose. See **"How should I take ZEPOSIA?".**

See "**What are possible side effects of ZEPOSIA?**" for more information about side effects.

What is ZEPOSIA?
ZEPOSIA is a prescription medicine used to treat:

- adults with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease.
- adults with moderately to severely active ulcerative colitis.

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

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.

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

- have a fever or infection, or you 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.
- Before you start treatment with ZEPOSIA, your healthcare provider may give you a chicken pox (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 for chickenpox and then wait 1 month before you start taking ZEPOSIA.
- have a slow heart rate.
- have an irregular or abnormal heartbeat (arrhythmia).
- have a history of a stroke.
- have 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.
- had or now have any types of skin cancer, including basal cell carcinoma (BCC), melanoma, or squamous cell carcinoma (SCC).
- have diabetes.
- are pregnant or plan to become pregnant. ZEPOSIA may harm your unborn baby. Talk with your healthcare provider if you are pregnant or plan to become pregnant. If you are a female who can become pregnant, you should use effective birth control during your treatment with ZEPOSIA and for 3 months after you stop taking ZEPOSIA. Talk with your healthcare provider about what birth control method is right for you during this time. Tell your healthcare provider right away if you become pregnant while taking ZEPOSIA or if you become pregnant within 3 months after you stop taking ZEPOSIA.

  Pregnancy Registry for MS patients: There is a pregnancy registry for women with multiple sclerosis who become pregnant during treatment with ZEPOSIA. If you become pregnant while taking ZEPOSIA, tell your healthcare provider right away. Talk to your healthcare provider about registering with the ZEPOSIA Pregnancy Registry. The purpose of this registry is to collect information about your health and your baby's health. Either you or your healthcare provider can enroll you in this registry by calling 1-877-301-9314 or visiting www.zeposiapregnancyregistry.com.

  Information regarding registration of pregnant women with UC will be made available in the future.
- 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 heart beat
- 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
- 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.

Talk with your healthcare provider if you are not sure if you take any of these medicines.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take ZEPOSIA?

You will receive a 7-day starter pack. You must start ZEPOSIA by slowly increasing doses over the first week. Follow the dose schedule in the table below. This may reduce the risk of slowing of the heart rate.

Days 1-4	Take 0.23 mg (capsule in light grey color) 1 time a day
Days 5-7	Take 0.46 mg (capsule in half-light grey and half-orange color) 1 time a day
Days 8 and thereafter	Take 0.92 mg (capsule in orange color) 1 time a day, or as directed by your healthcare provider

- Take ZEPOSIA exactly as your healthcare provider tells you to take it.
- Swallow ZEPOSIA capsules whole.
- Take ZEPOSIA with or without food.
- Avoid certain foods that are high (over 150 mg) in tyramine such as aged, fermented, cured, smoked and pickled foods. Eating these foods while taking ZEPOSIA may increase your blood pressure.
- Do not stop taking ZEPOSIA without talking with your healthcare provider first.
- Do not skip a dose.
- Start taking ZEPOSIA with a 7-day starter pack.
- If you miss 1 or more days of your ZEPOSIA dose during the first 14 days of treatment, talk to your healthcare provider. You will need to begin with another ZEPOSIA 7-day starter pack.
- If you miss a dose of ZEPOSIA after the first 14 days of treatment, take the next scheduled dose the following day.

What are the possible side effects of ZEPOSIA?

ZEPOSIA may cause serious side effects, including:

- See **"What is the most important information I should know about ZEPOSIA?"**
- **liver problems.** ZEPOSIA may cause 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:
    - unexplained nausea
    - vomiting
    - stomach area (abdominal) pain
    - tiredness
    - loss of appetite
    - yellowing of the whites of your eyes or skin
    - 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. See "**How should I take ZEPOSIA?**" section for more information.
- **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.** Macular edema can cause some of the same vision symptoms as a multiple sclerosis (MS) attack (optic neuritis). You may not notice any symptoms with macular edema. Your healthcare provider should test your vision around the time you start taking ZEPOSIA, periodically while you continue taking ZEPOSIA, and at any time you notice vision changes during treatment with ZEPOSIA. Your risk for macular edema is higher if you have diabetes or have had an inflammation of your eye called uveitis. Call your healthcare provider right away if you have any of the following symptoms:

- blurriness or shadows in the center of your vision
- a blind spot in the center of your vision
- sensitivity to light
- unusually colored vision

- **types of skin cancer, including basal cell carcinoma, melanoma, and squamous cell carcinoma.** Tell your healthcare provider if you have any changes in the appearance of your skin, including changes in a mole, a new darkened area on your skin, a sore that does not heal, or growths on your skin, such as a bump that may be shiny, pearly white, skin-colored, or pink. Your doctor should check your skin for any changes at the start of and during treatment with ZEPOSIA. Limit the amount of time you spend in sunlight and ultraviolet (UV) light. Wear protective clothing and use a sunscreen with a high sun protection factor.
- **swelling and narrowing of blood vessels in your brain**. A condition called PRES (Posterior Reversible Encephalopathy Syndrome) 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 a 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:
  - sudden severe headache
  - sudden loss of vision or other changes in your vision
  - sudden confusion
  - 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
- low blood pressure when you stand up (orthostatic hypotension)
- back pain
- headache
- elevated liver enzymes
- painful and frequent urination (signs of urinary tract infection)
- high blood pressure

These are not all of the possible side effects of ZEPOSIA. For more information, ask your healthcare provider or pharmacist. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store ZEPOSIA?

- Store ZEPOSIA at room temperature between 68°F to 77°F (20°C to 25°C).

Keep ZEPOSIA and all medicines out of the reach of children.

General information about the safe and effective use of ZEPOSIA.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not take ZEPOSIA for conditions for which it was not prescribed. Do not give ZEPOSIA to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for information about ZEPOSIA that is written for health professionals.

What are the ingredients in ZEPOSIA?

Active ingredient: ozanimod

Inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, and microcrystalline cellulose.

The capsule shell contains: black iron oxide, gelatin, red iron oxide, titanium dioxide, and yellow iron oxide.

Marketed by: Bristol-Myers Squibb Company, Princeton, NJ 08543 USA.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 6/2024

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