PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrZEPOSIA®

ozanimod capsules

Read this carefully before you start taking **ZEPOSIA** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ZEPOSIA**.

What is ZEPOSIA used for?

ZEPOSIA is used to treat:

- Adult patients with the relapsing and remitting form of multiple sclerosis (RRMS).
- Adult patients with moderately to severely active ulcerative colitis (UC) when other medicines do not work or cannot be used.

ZEPOSIA is not authorized for use in children.

How does ZEPOSIA work?

Ozanimod, the medicinal ingredient in ZEPOSIA, binds to selective receptors on your white blood cells. This keeps the white blood cells in your body's lymph nodes and lowers the number of white blood cells circulating in your body. How ZEPOSIA works is not known, but it may be due to less white blood cells entering your central nervous system where they could cause inflammation and damage to the nerves protective coating. ZEPOSIA helps reduce the inflammation in ulcerative colitis. It works by stopping certain white blood cells from reaching the lining of the intestine.

What are the ingredients in ZEPOSIA?

Medicinal ingredients: ozanimod (as ozanimod hydrochloride)

Non-medicinal ingredients: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose. The capsule is made of black iron oxide (E172), gelatin, pharmaceutical ink, red iron oxide (E172), titanium dioxide (E171), yellow iron oxide (E172).

ZEPOSIA comes in the following dosage forms:

capsules, 0.23 mg, 0.46 mg, 0.92 mg

Do not use ZEPOSIA if:

- you are allergic to ozanimod or any of the other ingredients of ZEPOSIA (see **What are the ingredients in ZEPOSIA?** above)
- you are at an increased risk of opportunistic infection, i.e. if you have a weakened immune system due to:
    - treatments that suppress the immune system (cancer treatments, immunosuppressive or immune modulating therapies, total lymphoid irradiation or bone marrow transplantation)

- disease (immunodeficiency syndrome)

- you have had in the last 6 months:
  - heart attack
  - unstable angina
  - stroke or warning signs of a stroke
  - a sudden worsening of the signs and symptoms of heart failure that required treatment or have been diagnosed with Class III or IV heart failure, or certain types of heart failure in the last 6 months.
- you have or have had a history of certain types of irregular or abnormal heartbeat (arrhythmia) that is not corrected by a pacemaker.
- you currently have an infection, such as hepatitis or tuberculosis.
- you currently have cancer (except for a type of skin cancer called basal cell carcinoma).
- you take certain medicines called monoamine oxidase (MAO) inhibitors (e.g. selegiline, phenelzine, linezolid).
- you are pregnant, think you may be pregnant or plan to get pregnant.
- you are of childbearing age and not using an effective method of birth control.
- you are of childbearing age and your healthcare professional has not performed a pregnancy test to confirm you are pregnant before you start treatment.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ZEPOSIA. Talk about any health conditions or problems you may have, including if you:

- have or have had problems with your heart, such as:
  - an irregular or abnormal heartbeat (arrhythmia)
  - a heart attack
  - severe heart disease
  - uncontrolled high blood pressure
  - a history of stroke or other diseases related to blood vessels in the brain
  - a slow heart rate or you are taking or have recently taken medicines that slow your heart rate (such as beta blockers or calcium channel blockers)
- have untreated severe breathing problems when you sleep (severe sleep apnea)

Your healthcare professional may decide not to use ZEPOSIA if you have or have had one of the above conditions, or may refer you to a cardiologist before you start treatment

- are taking medications:
    - to lower your blood pressure
    - to treat an irregular heartbeat (medicines that cause QT prolongation)
    - that slow your heart rate

Depending on the medications you are taking, your healthcare professional may decide not to use ZEPOSIA or refer you to a cardiologist to change your medication (see **The following may interact with ZEPOSIA** below for more information)

- have an infection. ZEPOSIA lowers your white blood cell count. This may increase your risk of infections including serious and life-threatening infections. This can occur while you are being treated with ZEPOSIA and up to 3 months after you stop treatment. Your healthcare professional should do a complete blood test to check your white blood cell count before you start treatment if you have not had one done within the last 6 months, during treatment and after you stop treatment. Tell your healthcare professional **right away** if you suspect you have an infection while taking ZEPOSIA.

- have never had chickenpox or have not been vaccinated against chickenpox (varicella zoster virus). You may develop an infection with the varicella zoster virus while taking ZEPOSIA. This may cause herpes viral infections, such as herpes zoster (shingles) and other serious complications including an infection of the membranes covering your brain (meningitis). Your healthcare professional will check your antibody levels and may decide to vaccinate you if you do not have enough antibodies against the virus. If you get the vaccine, you will start treatment 1 month after the full course of the vaccination is completed.

- have not been vaccinated against:
    - Human Papilloma Virus (HPV). Your healthcare professional will decide if you need to be vaccinated against Human Papilloma Virus (HPV) before starting treatment. For female patients, your healthcare professional may recommend HPV screening. HPV infection, including papilloma, dysplasia, warts and HPV-related cancer, has been reported in patients treated with medicines similar to ZEPOSIA.

- plan to receive a vaccine:
    - you should not receive certain types of vaccines (called “live attenuated vaccines”) while you are being treated with ZEPOSIA and for up to 3 months after stopping treatment.

- have a weakened immune system due to a disease or from medicines that suppress the immune system. You may get infections more easily or an infection you already have may get worse. ZEPOSIA lowers your white blood cell count during treatment and for up 3 month after you stop taking it.

- have not had a test to check your liver function within the last 6 months

- have breathing problems. ZEPOSIA can have a slight effect on your lung function

- have or have had:
    - changes in your vision or other signs of swelling in the central vision area at the back of the eye - a condition known as macular edema
    - disease of the retina

- inflammation or infection of the eye (uveitis).

The macula is a small area of the retina at the back of the eye. It allows you to see shapes, colours, and details clearly and sharply. ZEPOSIA may cause swelling in the macula and it can happen anytime during treatment.

Your chance of developing macular edema is higher if you have diabetes, have had an inflammation or infection of the eye or are on long-term treatment with ZEPOSIA.

Your healthcare professional may want you to undergo an eye examination:

- before you start ZEPOSIA
- during treatment and
- at anytime throughout your treatment if you notice changes in your vision. Tell your healthcare professional **right away** about any changes in your vision, which include:
  - blurry vision
  - blurry or wavy vision near or in the center of you field of vision
  - a blind spot in the center of your vision
  - sensitivity to light
  - colours may appear washed out or faded
  - unusually coloured vision

- have liver problems. ZEPOSIA may affect your liver function. If you notice any of the following symptoms, tell your healthcare professional **right away**:
  - yellowing of your skin or the whites of your eyes
  - abnormally dark urine
  - unexplained nausea or vomiting
  - tiredness
  - upper abdominal pain
  - loss of appetite

Your healthcare professional may carry out blood tests to check your liver function and may consider stopping ZEPOSIA treatment if your liver problem is serious.

Other warnings you should know about:

AFTER YOU STOP TREATMENT

- ZEPOSIA will stay in your body for about 3 months after you stop taking it. Your white blood cell count

may remain low during this time. The side effects described in this leaflet may still occur.

- your symptoms of MS can return and may become worse compared to before you started treatment or during treatment. Tell your healthcare professional if MS symptoms become worse after you stop taking ZEPOSIA.

Cancer risk: you could be at an increased risk for developing cancer, particularly skin cancer. Basal cell carcinoma was reported with patients on ZEPOSIA therapy. Your healthcare professional should check for any abnormal skin growths before you start treatment and regularly during your treatment with ZEPOSIA especially if you are at a higher risk for skin cancer. During treatment you should:

- check your skin regularly for unusual changes

- limit how much time you are exposed to the sun and UV rays. Wear protective clothes and regularly apply sunscreen with a high degree of UV protection.

Depression, thoughts of suicide and suicidal behaviour: are known to occur in patients with MS. Thoughts of suicide and suicidal behaviour have been reported with patients taking ZEPOSIA. Tell your family you are taking this medicine. If you, your caregiver or family members notice changes in your mood, or you start to have thoughts about hurting yourself, **contact your healthcare professional right away**.

Pregnancy: You should avoid becoming pregnant while taking ZEPOSIA and for at least 3 months after you stop taking it before planning a pregnancy. ZEPOSIA may harm your unborn baby. Female patients who might become pregnant should use effective birth control methods during treatment and for at least 3 MONTHS after stopping ZEPOSIA. Ask your healthcare professional about options of effective birth control (see **Do not use ZEPOSIA if**).

- If you become pregnant or think you are pregnant, tell your healthcare professional right away. You and your healthcare professional will decide what is best for you and your baby.

Pregnancy Registry: Information is being collected on use of ZEPOSIA in pregnant women. This is done in order to track effects of ZEPOSIA treatment on pregnant women and their offspring. Talk to your healthcare professional for more information.

Breast-feeding: You should not breast-feed while you are taking ZEPOSIA. ZEPOSIA can pass into breast milk and there is a risk of serious side effects for a breast-fed baby. Talk with your healthcare professional before breast-feeding while you take ZEPOSIA.

Laboratory Tests:

- Abnormal liver function test results: a high level of an enzymes called alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT) and aspartate aminotransferase (AST) and bilirubin have been reported in MS patients taking ZEPOSIA.

- Lower lung function test results: decreases in lung function (breathing) tests were have been reported in MS patients taking ZEPOSIA.

Tell your healthcare professional right away, if you get any of the following symptoms during your treatment with ZEPOSIA. It could be serious:

- if you believe your MS is getting worse (e.g. weakness or visual changes) or if you notice any new or unusual symptoms (e.g. problems thinking, memory problems, confusion, sudden inability to walk,

severe imbalance, weakness on one side of your body or vision changes). These may be the symptoms of **progressive multifocal leukoencephalopathy** (PML). This is a rare brain disorder caused by an infection. Your healthcare professional may consider an MRI scan to check for this condition. Your healthcare professional will decide whether you need to stop taking ZEPOSIA.

- if you have fever, feel like you have a flu, or have a headache accompanied by stiff neck, sensitivity to light, nausea, and/or confusion. These may be symptoms of meningitis (inflammation of the membranes covering the brain) and/or encephalitis (inflammation of the brain) caused by a fungal (Cryptococcus) or viral (chicken pox) infection.

- if you have symptoms such as the sudden start of a severe headache, confusion, seizures, changes in your behaviour and changes to your vision. These may be symptoms of a condition called **posterior reversible encephalopathy syndrome** (PRES).

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ZEPOSIA:

Serious Drug Interactions

Do not take ZEPOSIA if you:

- are taking or have recently taken any monoamine oxidase inhibitors (MAOIs) such as selegiline, phenelzine, rasagiline, safinamide, linezolid, methylene blue as you may have serious side effects. Ask your healthcare professional if you are unsure.

- **Medicines that treat an irregular heartbeat (medicines that cause QT prolongation)**
    - procainamide
    - amiodarone
    - sotalol

Your healthcare professional may decide to refer you to a cardiologist to change your medicine before you start treatment with ZEPOSIA.

- **Medicines that slow down your heartbeat such as:**
    - beta-blockers (such as atenolol or propranolol)
    - calcium channel blockers (such as verapamil or diltiazem)
    - cholinomimetics
    - other substances that can decrease your heart rate (ivabradine or digoxin)

ZEPOSIA can slow your heartbeat when you first start treatment. Your healthcare professional may decide to refer you to a cardiologist to change your medicine before you start treatment.

- **Medicines that suppress or modulate the immune system, including other medicines used to treat MS and medicines used to treat cancer:**
    - cyclosporine
    - beta-interferons
    - glatiramer acetate
    - natalizumab
    - mitoxantrone
    - dimethyl fumarate
    - terifunomide
    - alemtuzumab
    - corticosteroids
    - ocrelizumab

ZEPOSIA should not be started while you are taking these medicines or you are switching to or from other therapies used to treat MS with immunosuppressive or immune modulating effects. Your healthcare professional may want to wait for several weeks after you stop taking these medicines before starting you on ZEPOSIA to reduce the possible additive effect on your immune system. ZEPOSIA can generally be started immediately after discontinuation of beta interferon or glatiramer acetate.

- **Eltrombopag**, a medicine used to treat abnormally low platelet levels in the blood
- **Gemfibrozil**, a medicine used to help lower fats and raise “good” cholesterol in the blood
- **Rifampin**, a medicine used to treat bacterial infections, including tuberculosis
- **Vaccines:** If you need to receive a vaccine, talk to your healthcare professional first. For more information about vaccines see **To help avoid side effects and ensure proper use** above.
- **Tyramine:** Certain foods that may contain very high amounts of tyramine [aged, fermented, cured, smoked, and pickled foods (e.g., aged cheese, pickled herring)] could cause (tyramine reaction) severe hypertension (rise in blood pressure) in patients taking ZEPOSIA, even at the recommended doses. You should avoid foods containing a very large amount of tyramine while taking ZEPOSIA.

There is a potential for serious adverse reactions, including a sudden, severe increase in blood pressure (hypertensive crisis) and serotonin toxicity, with co-administration of ZEPOSIA and the following medications:

- treatment with opioid medications (e.g., meperidine and its derivatives, methadone, propoxyphene, tramadol or tapentadol) is not recommended.
- treatment with serotonergic medications (e.g., serotonin-norepinephrine reuptake inhibitors (SNRI), selective serotonin reuptake inhibitors (SSRI), tricyclic, tetracyclic or triazolopyridine antidepressants, cyclobenzaprine or St John’s wort) is not recommended.

- treatment with sympathomimetic medications (e.g., pseudoephedrine) may lead to increased blood pressure or heart rate.

Your healthcare professional will regularly monitor your blood pressure while you take ZEPOSIA.

Serotonin Toxicity:

ZEPOSIA may cause serotonin toxicity, a rare but potentially life-threatening condition. It can cause serious changes in how your brain, muscles and digestive system work. You may develop serotonin toxicity if you take ZEPOSIA with certain antidepressants or migraine medications.

Serotonin toxicity symptoms include:

- fever, sweating, shivering, diarrhea, nausea, vomiting;
- muscle shakes, jerks, twitches or stiffness, overactive reflexes, loss of coordination;
- fast heartbeat, changes in blood pressure;
- confusion, agitation, restlessness, hallucinations, mood changes, unconsciousness, and coma.

How to take ZEPOSIA:

Before you start treatment:

Your healthcare professional will:

- conduct an electrocardiogram (ECG) to check for any pre-existing heart conditions. If you have certain heart conditions or risk factors the first dose ZEPOSIA will have to be taken in your healthcare professional's office or hospital where your heart rate and blood pressure can be monitored (hourly blood pressure and pulse measurements, ECG monitoring) for at least 6 hours. The same process may apply if you are starting treatment again after a break from ozanimod therapy.
- perform:
    - liver tests if you have not had one within the last 6 months
    - a complete blood test if you have not had one in the last 6 months or have recently stopped previous treatment for MS.
    - a check of your antibody levels for the chickenpox virus (varicella zoster virus)
    - a pregnancy test if you are a woman of childbearing potential
- check if you currently have a severe infection
- check your medication history
- check your skin for suspicious moles

Your healthcare professional may also:

- have you go for an eye exam if you have or had uveitis (a swelling in the middle layer of tissue in the eye wall) a history of retinal disorders or diabetes

- consider a Magnetic Resonance Imaging (MRI) scan of your brain, if you have received certain previous treatment for MS.

- check that you are vaccinated against the human papilloma virus (HPV). Your healthcare professional will tell you if you need to get vaccinated against HPV before starting treatment.

- recommend that you get screened for HPV if you are a female

Usual dose:

ZEPOSIA capsules are to be taken by mouth once daily according to the following schedules.

On Days 1 to 7 (Initiation Pack):

- When you start treatment with ZEPOSIA you will be given an Initiation Pack. The Initiation Pack contains 7 capsules. Over a period of 7 days you will slowly increase (titrate) your dose. Follow the directions on the Initiation Pack and the table below.

- Take your Initiation doses once a day at about the same time each day with or without food. Swallow the capsules whole with water. Do not open, break, or chew your capsules.

Starter pack dosing schedule:

Day	**Daily Dose**	**Capsule Colour**
Day 1 to Day 4	0.23 mg (1 time per day)	Light grey
Day 5 to Day 7	0.46 mg (1 time per day)	Light grey and orange

On Day 8 and after (Maintenance dose):

- Switch to your maintenance dose.

- The recommended dose is 0.92 mg (orange capsule) once a day.

- If you have mild to moderate liver problems (assessed by your healthcare professional), the recommended dose, after completing the 7-day Initiation Pack, is 0.92 mg **once every other day**.

- Take ZEPOSIA exactly as your healthcare professional tells you to take it.

- Take your maintenance dose once a day **at about the same time each day** with or without food. Swallow the capsules whole with water. Do not open, break, or chew your capsules.

- Continue taking ZEPOSIA every day for as long as your healthcare professional tells you. Do not stop taking this medicine without talking to your healthcare professional.

If you have questions about how long to take ZEPOSIA, talk to your healthcare professional.

Overdose:

If you think you, or a person you are caring for, have taken too much ZEPOSIA, contact a healthcare professional, hospital emergency department, or regional poison control centre or Health Canada's toll-

free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no symptoms.

Missed Dose:

IMPORTANT

If you **miss 1 day between day 1 and day 14** of treatment:

- Contact your healthcare professional right away before you take the next dose.
- You will have to re-start treatment (from Day 1) using a new initiation pack.
- Do not take a double dose to make up for a missed dose.

If you **miss 1 to 7 days after 14 days** of treatment:

- Continue with the treatment as planned

If you miss **more than 7 days after 14 days** of treatment:

- Talk to your healthcare professional about how to re-start your treatment (from day 1) if you have stopped taking ZEPOSIA:
  - for more than 7 consecutive days between day 15 and day 28 of treatment
  - for more than 14 consecutive days after day 28 of treatment.
- Contact your healthcare professional right away if any of these happen so he or she can tell you how to re-start your treatment.
- Do not take a double dose to make up for a missed dose.

What are possible side effects from using ZEPOSIA?

These are not all the possible side effects you may have when taking ZEPOSIA. If you experience any side effects not listed here, tell your healthcare professional.

- headache
- back pain
- infections of the
  - nose or nostrils
  - nasal cavity
  - mouth
  - throat (pharynx), or
  - voice box (larynx)

- respiratory infection
- low blood pressure when you stand up (orthostatic hypotension)

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
COMMON			
Herpes simplex (oral herpes): pain, heat, and itching in area of infection, small red or tiny fluid-filled blisters or sores		✓	
Herpes zoster (chickenpox): rash of small fluid-filled blisters, appearing on reddened skin		✓	
Hypertension (high blood pressure): shortness of breath, fatigue, dizziness or fainting, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse or heart palpitations		✓	
Lymphopenia (low white blood cells - lymphocytes): get infections more easily, fever, sore throat or mouth ulcers due to infections		✓	
Urinary tract infection: pain or burning when urinating, bloody or cloudy or foul smelling urine		✓	
UNCOMMON			
Allergic reaction: rash, red, itchy skin, hives	✓		
Atrioventricular block (irregular heartbeat)		✓	
Bradycardia (low heart rate): feeling dizzy, tired, fainting, chest pain		✓	

Macular edema (swelling and build-up of fluid in the center of the retina): blurry vision, blurry or wavy vision near or in the center of your field of vision, a blind spot in the center of your vision, sensitivity to light, colours may appear washed out or faded, unusually coloured vision		✓	
Melanocytic nevus (a type of tumors - moles)		✓	
Skin Cancer: shiny pearly nodules, moles, patches or open sores that changes in size, shape or colour or do not heal, red or brown blotches or tumours usually on the skin of the legs or face		✓	
RARE			
Posterior reversible Encephalopathy syndrome (PRES) (symptoms may include sudden severe headache, feeling nauseous or throwing up confusion, drowsiness, personality change, paralysis, abnormal speech, convulsions and vision changes)			✓
FREQUENCY NOT KNOWN			
Cerebrovascular accident, ischemic stroke, transient ischemic attack (stroke): Sudden numbness or weakness of your arm, leg or face, especially if only on one side of the body; sudden confusion, difficulty speaking or understanding others; sudden difficulty in walking or loss of balance or coordination; suddenly feeling dizzy or sudden severe headache with no known cause.			✓
Liver problems: yellowing of your skin or the whites of your eyes, abnormally dark urine, unexplained nausea or vomiting, tiredness, upper abdominal pain, loss of appetite		✓	
Meningitis (inflammation of the membranes covering the brain) **and/or**		✓	

encephalitis (inflammation of the brain)**, caused by fungal (Cryptococcus) or viral (chickenpox) infections:** headache accompanied by stiff neck, sensitivity to light, nausea, repeated vomiting, confusion, and/or seizures (fits)			
Progressive multifocal leukoencephalopathy (PML) (a rare brain infection): (progressive weakness on one side of your body, sudden inability to walk, severe imbalance, problems thinking, memory problems, confusion, or vision changes)		✓	
Serotonin Toxicity: agitation or restlessness, loss of muscle control or muscle twitching, tremor, diarrhea			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store between 15°C and 25°C. Do not store above 25°C.

Keep out of reach and sight of children.

Do not take this medicine after the expiry date, which is stated on the box.

Keep in the original package.

Ask your pharmacist how to dispose of medicines you no longer use.

If you want more information about ZEPOSIA:

- Talk to your healthcare professional

- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.bms.com/ca, or by calling number 1-866-463-6267.

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