PrZEPOSIA® (ozanimod)

Prescriber’s Checklist

Important points to remember before, during, and after treatment

This material was developed by Celgene Inc., a Bristol Myers Squibb company, as part of the risk minimization plan for ZEPOSIA. This material is not intended for promotional use.

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**ZEPOSIA Prescriber’s Checklist**

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**Treatment Initiation**

Initiate treatment with a titration pack that lasts for 7 days. Start treatment with 0.23 mg once daily on Days 1-4, then increase the dose to 0.46 mg once daily on Days 5-7. Following the 7-day dose escalation, the maintenance dose is 0.92 mg once daily, starting on Day 8.

**Re-initiation of Therapy Following Treatment Interruption**

Use the same dose escalation regimen as initial treatment when treatment is interrupted for:
- 1 day or more during the first 14 days of treatment
- More than 7 consecutive days between Day 15 and Day 28 of treatment
- More than 14 consecutive days after Day 28 of treatment

If the treatment interruption is of shorter duration than the above, continue treatment with the next dose as planned.

**Treatment Initiation Monitoring**

- **Before first dose:**
  - Obtain a baseline electrocardiogram (ECG) to determine whether any pre-existing cardiac abnormalities are present.
  - Determine whether the patient is receiving concomitant medications that reduce heart rate or AV conduction.
  - Obtain recent (within last 6 months) liver function test results for transaminase and bilirubin levels.
  - Obtain recent (within last 6 months or after discontinuation of prior multiple sclerosis [MS] therapy) complete blood cell count (CBC) results, including lymphocyte count.
  - Arrange an ophthalmological assessment before starting ZEPOSIA treatment in patients with diabetes mellitus, uveitis or a history of retinal disease.
  - I confirm that an ophthalmological assessment is not applicable for this patient.
  - Confirm a negative pregnancy test result in women of childbearing potential prior to starting treatment. It must be confirmed at suitable intervals.
  - I confirm that a pregnancy test is not applicable to this patient.

- **Until 6 hours after first dose for patients requiring first dose observation:**
  - Monitor for signs and symptoms of symptomatic bradycardia, with hourly pulse and blood pressure measurement for patients with:
    - A resting heart rate <55 bpm
    - First or second-degree [Mobitz type I] AV block
    - A history of MI or heart failure
  - Perform an ECG prior to and at the end of this 6-hour period.
  - I confirm that this patient does not have applicable pre-existing cardiac conditions.

  Extended monitoring after 6 hours may be required in the following situations:
  - Heart rate <45 bpm
  - Heart rate is the lowest value post-dose, suggesting that the maximum decrease in heart rate may not have occurred yet
  - Evidence of a new onset second-degree or higher AV block at the 6-hour post-dose ECG
  - QTc interval >450 msec in males, >470 msec in females
Prior to Treatment Initiation

Consult a cardiologist before initiating treatment to assess suitability of treatment and to determine if ZEPOSIA can safely be initiated and to determine the most appropriate monitoring strategy, when initiating ZEPOSIA in patients with:

- Pre-existing significant QT prolongation (QTcF >450 msec in males, >470 msec in females)
- A history of cardiac arrest, cerebrovascular disease, uncontrolled hypertension or severe untreated sleep apnea
- A history of recurrent syncope or symptomatic bradycardia
- Concurrent treatment with heart rate lowering drugs

Caution should be taken when initiating ZEPOSIA in patients taking medicines known to decrease heart rate.

I confirm that a cardiology consult is not applicable to this patient.

ZEPOSIA is contraindicated in patients with the following:

- Immunodeficient state predisposing to systemic opportunistic infections
- Severe active infections, active chronic infections such as hepatitis and tuberculosis
- Active malignancies, except localized basal cell carcinoma
- Experienced in the last 6 months myocardial infarction (MI), unstable angina, stroke, transient ischaemic attack (TIA), decompensated heart failure requiring hospitalisation or New York Heart Association (NYHA) Class III/IV heart failure
- History or presence of second-degree atrioventricular (AV) block Type II or third-degree AV block or sick sinus syndrome or sinoatrial block unless the patient has a functioning pacemaker
- Pregnancy and in women (including female adolescents) of childbearing potential not using effective contraception
- Hypersensitivity to the active substance or to any of the excipients
- Concomitant MAO inhibitors: ZEPOSIA should not be administered with other MAO inhibitors because of the increased risk of non-selective MAO inhibition that may lead to a hypertensive crisis.

I confirm that none of these contraindications are applicable to this patient.

Initiation of Treatment, During Treatment, and After Treatment

ZEPOSIA reduces peripheral blood lymphocyte counts. Peripheral lymphocyte count should be checked in all patients prior to initiation (within 6 months or after discontinuation of prior therapy). Monitor peripheral lymphocyte count periodically during ZEPOSIA treatment. Interrupt treatment if absolute lymphocyte count is confirmed as <0.2 x 10^9/L and the re-initiation of ZEPOSIA can be considered if the level reaches >0.5 x 10^9/L.

ZEPOSIA predisposes patients to a risk of infection, including opportunistic infections, and may increase the risk of developing malignancies, particularly those of the skin.

- Carefully monitor patients, especially those with concurrent conditions or known factors, such as previous immunosuppressive therapy. If this risk is suspected, consider discontinuation of treatment on a case-by-case basis.
- Delay treatment initiation in patients with any severe active infection until the infection is resolved.
- Consider interruption of treatment during serious infections.
- Avoid co-administration of anti-neoplastic, immunomodulatory, or non-corticosteroid immunosuppressive therapies due to the risk of additive immune system effects.
- Physicians should be vigilant for clinical symptoms that may be suggestive of serious herpetic infections.
- Vigilance for basal cell carcinoma and other cutaneous neoplasms is recommended:
  - Caution patients against exposure to sunlight without protection
  - Ensure patients are not receiving concomitant phototherapy with UV-B radiation or PUVA-photochemotherapy

Instruct patients to report signs and symptoms of infections promptly to their prescriber during and for up to 3 months after discontinuation of treatment with ZEPOSIA.

- Perform prompt diagnostic evaluation in patients with symptoms of infection while receiving or within 3 months of stopping treatment with ZEPOSIA.
- Be vigilant for clinical symptoms including unexpected neurological or psychiatric symptoms or MRI findings that may be suggestive of progressive multifocal leukoencephalopathy (PML):
  - If PML is suspected, a complete physical and neurological examination (including the possibility of performing an MRI) should be performed and withhold treatment with ZEPOSIA until PML has been excluded.

If PML is confirmed, discontinue treatment with ZEPOSIA.
Avoid administration of live attenuated vaccines during and for 3 months after discontinuation of treatment with ZEPOSIA. Check varicella zoster virus (VZV) antibody status in patients without a healthcare professional confirmed history of varicella or documentation of a full course of varicella vaccination. If negative, VZV vaccination is recommended at least 1 month prior to treatment initiation with ZEPOSIA.

Patients treated with ZEPOSIA should be advised to report immediately any symptoms of depression and/or suicidal ideation to their prescribing physicians.

Counsel women of childbearing potential about the serious potential risks of ZEPOSIA to the fetus, facilitated by the pregnancy reminder card and provide to appropriate patient and caregiver.

Counsel women of childbearing potential to use effective contraception during treatment with ZEPOSIA and for at least 3 months following treatment discontinuation.

Counsel women of childbearing potential to stop ZEPOSIA at least 3 months before planning a pregnancy.

While on treatment, women must not become pregnant. If a woman becomes pregnant while on treatment, ZEPOSIA must be discontinued. Medical advice should be given regarding the risk of harmful effects to the fetus associated with ZEPOSIA treatment and ultrasonography examinations should be performed.

Counsel women of childbearing potential when stopping ZEPOSIA therapy due to pregnancy or planning a pregnancy.

I confirm that counselling on pregnancy precautions is not applicable to this patient.

Check liver function (transaminase and bilirubin levels) before initiation of ZEPOSIA therapy, within the first 3 months of initiating therapy and periodically thereafter.

Blood pressure should be regularly monitored during treatment with ZEPOSIA.

Patients who present with visual symptoms of macular oedema should be evaluated and, if confirmed, treatment with ZEPOSIA should be discontinued. Patients with diabetes mellitus, uveitis or a history of retinal disease should undergo an ophthalmological evaluation prior to treatment initiation with ZEPOSIA and have follow-up evaluations while receiving therapy.

Provide all patients/caregivers with the patient/caregiver guide, and with the pregnancy reminder card if appropriate.

**Reporting Side Effects:**

Celgene Inc. encourages healthcare professionals to report any suspected adverse reactions. This will allow quick identification of new safety information. More information regarding how to report side effects can be found in the Canadian Product Monograph: [https://www.bms.com/assets/bms/ca/documents/productmonograph/ZEPOSIA_EN_PM.pdf](https://www.bms.com/assets/bms/ca/documents/productmonograph/ZEPOSIA_EN_PM.pdf). For more information or to obtain a copy of this document, please contact medical information by calling 1-866-463-6267.