ZEPOSIA Prescriber's Checklist

☐ 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) o 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 has been ruled out 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 liver function (transaminase and bilirubin levels) at months 1, 3, 6, 9 and 12 during ZEPOSIA 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.

For reporting any side effects via the national reporting system :

Bristol Myers Squibb™

Bristol Myers Squibb, Saudi Arabia:
At: medinfo.saudiarabia@bms.com
or call: 800 844 7710

The National Pharmacovigilance Centre (NPC)
Saudi Food and Drug Authority (SFDA):
SFDA call center: 19999
Toll free phone: 8002490000
E-mail: npc.drug@sfda.gov.sa
Website: http://ade.sfda.gov.sa/
Fax: +966-11-2057662

ZEPOSIA®
(ozanimod)

Prescriber's Checklist

This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA.

Important points to remember before, during, and after treatment

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via Medinfo.SaudiArabia@bms.com

Please note that in accordance with applicable laws and regulations, BMS has the obligation to disclose to Saudi Food and Drug Authority (SFDA) name, contact details and any transfer of value to Healthcare professional or Healthcare Organization.

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ZEPOSIA®

Healthcare Professional Information

ZEPOSIA®
Prescriber's Checklist

Patient identification	Prescriber details
Name:	Name: Signature: Date:

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
- Severe hepatic impairment (Child-Pugh class C)
- 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 unless the patient has a functioning pacemaker
- Pregnancy and in women of childbearing potential not using effective contraception
- Hypersensitivity to the active substance or to any of the excipients

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

Prior to Treatment Initiation

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

- History of cardiac arrest, cerebrovascular disease, uncontrolled hypertension, or severe untreated sleep apnoea, history of recurrent syncope or symptomatic bradycardia
- Pre-existing significant QT interval prolongation (QTc greater than 500 msec) or other risks for QT prolongation, and patients on medicinal products other than beta-blockers and calcium-channel blockers that may potentiate bradycardia
- Current class Ia (e.g. quinidine, disopyramide) or class III (e.g. amiodarone, sotalol) antiarrhythmic medicinal products

or

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

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

Before first dose:

☐ Obtain a baseline electrocardiogram (ECG) to determine whether any pre-existing cardiac abnormalities are present
☐ 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 therapy) complete blood cell count (CBC) results, including lymphocyte count
☐ 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
☐ Arrange an ophthalmological assessment before starting ZEPOSIA treatment in patients with diabetes mellitus, uveitis or a history of retinal disease

or

☐ I confirm that an ophthalmological assessment is not applicable for this patient

Pregnancy Counselling

☐ Give the pregnancy-specific reminder card to women of childbearing potential and use it to Counsel them on the risk teratogenicity.
☐ 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
☐ Counsel women of childbearing potential about the possible return of disease activity when stopping ZEPOSIA therapy due to pregnancy or 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 foetus associated with ZEPOSIA treatment and ultrasonography examinations should be performed.
☐ Confirm a negative pregnancy test result in women of childbearing potential prior to starting treatment. It must be confirmed at suitable intervals

OR

☐ I confirm that a pregnancy test and counselling on pregnancy precautions is not applicable to this patient

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

OR

☐ Provision of pregnancy-specific patient reminder card is not applicable to this patient

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

OR

☐ Provision of pregnancy-specific patient reminder card is not applicable to this patient

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 once daily dose is 0.92 mg, starting on Day 8.

"Patients with mild or moderate chronic hepatic impairment (Child-Pugh class A or B) are recommended to complete the 7-day dose escalation regimen and then take 0.92 mg once every other day."

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

First dose monitoring for 6 hours after first dose is required for certain patients.

☐ Patients with any of the following pre-existing conditions should be monitored for signs and symptoms of symptomatic bradycardia, with hourly pulse and blood pressure measurement for 6 hours after the first dose:

- A resting heart rate <55 bpm
- Second-degree [Mobitz type I] AV block
- A history of myocardial infarction or heart failure

☐ In these patients, perform an ECG prior to and at the end of this 6-hour monitoring period.

OR

☐ 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 if at hour 6 post dose:

- 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 ≥500 msec

During Treatment and After Treatment Monitoring

ZEPOSIA reduces peripheral blood lymphocyte counts.

Complete blood cell count (CBC) should be checked in all patients prior to initiation (within 6 months or after discontinuation of prior therapy) and monitored periodically during ZEPOSIA treatment. Interrupt treatment if 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 has an immunosuppressive effect that 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.
- Anti-neoplastic, immunomodulatory, or non-corticosteroid immunosuppressive therapies should not be co-administered due to the risk of additive immune system effects
- 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

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