ZEPOSIA®
(ozanimod)

Healthcare Professional Information

Prescriber's Checklist

Important points to remember before, during, and after treatment

Adverse reactions and pregnancies associated with ozanimod can be reported to Bristol-Myers Squibb Medical Information at:

- Email: MedInfo.Singapore@bms.com
- Phone: 1800 415 5182

For more information or to obtain a copy of this document, please contact Bristol-Myers Squibb Medical Information at:

- Email: MedInfo.Singapore@bms.com
- Phone: 1800 415 5182

Bristol Myers Squibb™

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ZEPOSIA® Healthcare Professional Information

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

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	Ozanimod is contraindicated in patients with the following: • Immunodeficient state • 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 • Taking a monoamine oxidase (MAO) inhibitor
☐	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 ozanimod can safely be initiated and to determine the most appropriate monitoring strategy, when initiating ozanimod in patients with: • Ischemic heart disease, heart failure, history of myocardial infarction, cardiac arrest, cerebrovascular disease, uncontrolled hypertension, or severe untreated sleep apnoea, history of recurrent syncope or symptomatic bradycardia • Pre-existing significant QT interval prolongation (QTcF > 450 msec in males, > 470 msec in females) 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 ozanimod in patients taking medicines known to decrease heart rate, including beta-blockers or calcium-channel blockers.
	Before first dose:
☐	Obtain a baseline electrocardiogram (ECG) to determine whether any pre-existing cardiac abnormalities are present. First dose monitoring is recommended in patients with certain pre-existing conditions (see section "Monitoring at Treatment Initiation" below)
☐	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 ozanimod
☐	Delay treatment initiation in patients with any active infection until the infection is resolved
☐	Arrange an ophthalmological assessment before starting ozanimod 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

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Pregnancy Counselling

- ☐ Give the pregnancy-specific reminder card to women of childbearing potential and use it to counsel them on the risk of teratogenicity
- ☐ Counsel women of childbearing potential on the importance of effective contraception prior to initiation of treatment. Effective contraception must be used without interruption while taking ozanimod and for at least 3 months after treatment discontinuation
- ☐ Counsel women of childbearing potential to stop ozanimod at least 3 months before planning a pregnancy
- ☐ Counsel women of childbearing potential about the possible return of disease activity when stopping ozanimod therapy due to pregnancy or planning a pregnancy
- ☐ While on treatment, women must not become pregnant. If a woman becomes pregnant while on treatment, ozanimod must be discontinued. Medical advice should be given regarding the risk of harmful effects to the foetus associated with ozanimod 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

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.

Monitoring at Treatment Initiation

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 measurement of pulse rate and blood pressure 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 first dose monitoring for 6 hours is not applicable.

- ☐ Extended monitoring after 6 hours is recommended if at hour 6 post dose, the patient presents with any of the following signs:
  - 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
- ☐ Appropriate management should be initiated and observation continued until the symptoms/signs have resolved. If medical treatment is required, monitoring should be continued overnight, and a 6-hour monitoring period should be repeated after the second dose of ozanimod

OR

- ☐ I confirm that further extended monitoring is not required for this patient.

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	Monitoring During and After Treatment
	Ozanimod reduces peripheral blood lymphocyte counts to approximately 45% of baseline values. Complete blood cell count (CBC) should be checked in all patients prior to initiation (i.e., within 6 months or after discontinuation of prior MS therapy) and monitored periodically during ozanimod treatment. Interrupt treatment if absolute lymphocyte count is < 0.2 x 10^9/L. Consider reinitiating ozanimod if the level reaches > 0.5 x 10^9/L.

	Ozanimod 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

☐	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 ozanimod • Perform prompt diagnostic evaluation in patients with symptoms of infection while receiving or within 3 months of stopping treatment with ozanimod • 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, perform a complete physical and neurological examination (including the possibility of performing an MRI) and withhold treatment with ozanimod until PML has been ruled out If PML is confirmed, discontinue treatment with ozanimod
	Avoid administration of live attenuated vaccines during and for 3 months after discontinuation of treatment with ozanimod.
	Check liver function (transaminase and bilirubin levels) at months 1, 3, 6, 9 and 12 during ozanimod therapy and periodically thereafter. If liver transaminases rise above 5 times the ULN, monitor more frequently and interrupt treatment. Only re-commence once values have normalised.
	Blood pressure should be regularly monitored during treatment with ozanimod. Advise patients to avoid consuming food with very high amounts of tyramine.
	Patients who present with visual symptoms of macular oedema should be evaluated and, if confirmed, treatment with ozanimod should be discontinued. Patients with diabetes mellitus, uveitis or a history of retinal disease should undergo an ophthalmological evaluation prior to treatment initiation with ozanimod and have follow up evaluations while receiving therapy.
	Posterior reversible encephalopathy syndrome (PRES) may occur. PRES is characterised by sudden onset of severe headache, confusion, seizures and visual loss. If PRES is suspected, discontinue treatment with ozanimod.

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