Sphingosine 1-phosphate receptor modulators (siponimod, ponesimod, ozanimod, and etrasimod)

FDA INDICATIONS AND USAGE[1,3,4,7]

Siponimod, ponesimod, and ozanimod are indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Ozanimod is also indicated for the treatment of moderately to severe ulcerative colitis. Etrasimod is indicated for the treatment of moderately to severely active ulcerative colitis in adults.

APPROVAL CRITERIA

Multiple Sclerosis Diagnosis[1,2,3,4,5]

1. Patient is 18 years of age or older **AND;**
2. Patient has a diagnosis of relapsing MS, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease **AND**;
3. Is being prescribed by or in consultation with a neurologist or a provider that specializes in MS **AND**;
4. The patient has had an electrocardiogram, complete blood cell count, liver enzyme testing, and an ophthalmic evaluation, showing results deemed appropriate for treatment within the last 6 months **AND**;
5. The Patient has not had a myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, or Class III/IV heart failure with in the last 6 months **AND**;
6. The patient has no presence or history of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker **AND**;
7. The patient has had an adequate trial and failure of at least two disease modifying drugs indicated for MS.

Ulcerative Colitis Diagnosis[4,6,7]

1. Patient is 18 years of age or older **AND;**
2. Patient has the diagnosis of ulcerative colitis and the request is for ozanimod or etrasimod **AND;**
3. The medication is prescribed by or in consultation with a gastroenterologist **AND;**
4. The patient has had an electrocardiogram, complete blood cell count, liver enzyme testing, and an ophthalmic evaluation, showing results deemed appropriate for treatment within the last 6 months **AND;**
5. The Patient has not had a myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, or Class III/IV heart failure with in the last 6 months **AND;**
6. The patient has no presence or history of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker **AND;**
7. The patient has had an adequate trial and failure of at least two systemic agents to include

at least one biologic

DENIAL CRITERIA[1,3,4]

1. Failure to meet approval criteria **OR;**
2. Will be used concurrently with other MS disease modifying agents **OR;**
3. Patient is pregnant **OR;**
4. Request is for ozanimod and the patient has severe sleep apnea.

CAUTIONS[1,2,3,4,7]

- Sphingosine 1-phosphate receptor modulators may increase the risk of infection.
- Patients with a history of uveitis and patients with diabetes mellitus are at increased risk of macular edema when taking sphingosine 1-phosphate receptor modulators.
- Rare cases of Posterior Reversible Encephalopathy Syndrome (PRES) have been reported.
- Cases of basal cell carcinoma and other skin malignancies have been reported in patients.
- May cause Bradyarrhythmia and Atrioventricular Conduction Delays
- Live attenuated vaccines should be avoided for up to 4 weeks after treatment.
- Concomitant use of moderate CYP2C9 and moderate to strong CYP3A4 inhibitors and inducers is not recommended.

DURATION OF APPROVAL

- Initial Approval: up to 6 months
- Reauthorization Approval: up to 12 months

QUANTITY LIMIT

- 34 days supply

REFERENCES / FOOTNOTES:

1. Mayzent® (siponimod) [package insert]. East Hanover, NJ. Novartis Pharmaceuticals Corporation; August 2023. Available at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/mayzent.pdf
2. Olek, M., & Mowry, E. (June 2019) Disease-modifying treatment of relapsing-remitting multiple sclerosis in adults. In J. F. Dashe (Ed.), *UpToDate*. Retrieved July 7, 2019 from https://www.uptodate.com/contents/disease-modifying-treatment-of-relapsing-remitting-multiple-sclerosis-in-adults#H35
3. Ponvory (ponesimod) [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2023. Available at: https://www.ponvory.com.
4. Zeposia® capsules [prescribing information]. Summit, NJ: Celgene; August 2023. Available at: https://packageinserts.bms.com/pi/pi_zeposia.pdf.

5. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. September 2019. Available at: http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Accessed on December 20, 2021.
6. Feuerstein JD, Isaac s KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology. 2020;158:1450-1461.
7. Velsipity™ (etrasimod) [prescribing information]. New York, NY: Pfizer; October 2023