# SAMPLE FORMULARY EXCEPTION REQUEST

[Date]

[Health plan name] ATTN: [Department]

[Medical/pharmacy director’s name (if available)] [Health plan address]

[City, State ZIP]

[Patient’s name]

[Patient’s plan-specific member ID] [Date of birth]

[Case number] [Dates of service]

Dear [Medical/pharmacy director’s name],

I am writing this letter on behalf of [patient’s name] to request coverage for MAYZENT® (siponimod) tablets. Currently, MAYZENT is not listed on your formulary for [relapsing multiple sclerosis (RMS), including active secondary progressive multiple sclerosis (aSPMS)] [ICD-10 code].

I am requesting an exception to your formulary so the prescription for MAYZENT can be filled.

[Patient’s name] has been previously treated with other [RMS/aSPMS] medications. The main reasons for requesting this exception are [insert main medical necessity points, which may include worsening of patient’s RMS/aSPMS symptoms]. These reasons are supported by the information attached.

Considering [patient’s name]’s history and diagnosis, I believe treatment with MAYZENT is appropriate and medically necessary. I can be contacted at [physician’s phone number] or via email at [physician’s email] to answer any additional questions or to participate in a peer-to-peer review discussing the necessity of MAYZENT in the treatment of this patient’s [RMS/aSPMS]. Thank you for your time and consideration.

Sincerely, [Physician’s signature]

Enclosures

[List and attach additional documents, which may include a denial letter, Letter of Medical Necessity, prescribing information, clinical notes/medical records, U.S. Food and Drug Administration approval letter, or clinical practice guidelines.]

This letter is provided as an example and is meant for educational purposes only. Novartis cannot guarantee insurance coverage or reimbursement. Coverage and reimbursement may vary significantly by payer, plan, patient, and setting of care. It is the sole responsibility of the health care provider to include the proper information and ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient.

**Click** [**here**](https://www.novartis.com/us-en/sites/novartis_us/files/mayzent.pdf) **for full Prescribing Information, including Medication Guide.**

# INDICATION AND IMPORTANT SAFETY

## INDICATION

MAYZENT® (siponimod) is 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.

## IMPORTANT SAFETY INFORMATION

**Contraindications**

* Patients with a CYP2C9\*3/\*3 genotype
* In the last 6 months, experienced myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, or Class III/IV heart failure
* Presence of Mobitz type II second-degree, third-degree atrioventricular block, or sick sinus syndrome, unless patient has a functioning pacemaker

**Infections:** MAYZENT may increase risk of infections with some that are serious in nature. Life-threatening and rare fatal infections have occurred. Before starting MAYZENT, review a recent complete blood count (CBC) (ie, within 6 months or after discontinuation of prior therapy).

Delay initiation of treatment in patients with severe active infections until resolved. Employ effective treatments and monitor patients with symptoms of infection while on therapy. Consider discontinuing treatment if patient develops a serious infection.

Cases of fatal cryptococcal meningitis (CM) were reported in patients treated with another sphingosine 1-phosphate (S1P) receptor modulator. Rare cases of CM have occurred with MAYZENT. If CM is suspected, MAYZENT should be suspended until cryptococcal infection has been excluded. If CM is diagnosed, appropriate treatment should be initiated. Cases of herpes viral infection, including cases of meningitis or meningoencephalitis caused by VZV reactivation, have been

reported. Patients without a confirmed history of varicella zoster virus (VZV) or without vaccination should be tested for antibodies before starting MAYZENT. If VZV antibodies are not present or detected, then VZV immunization is recommended and MAYZENT should be initiated 4 weeks after vaccination.

Use of live vaccines should be avoided while taking MAYZENT and for 4 weeks after stopping treatment.

Caution should be used when combining treatment (ie, anti-neoplastic, immune-modulating, or immunosuppressive therapies) due to additive immune system effects.

**Progressive Multifocal Leukoencephalopathy (PML):** Cases of PML have occurred in patients with MS treated with S1P receptor modulators, including MAYZENT. PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. PML has occurred in MAYZENT-treated patients who had not been treated previously with natalizumab (which has a known association with PML), were not taking any other immunosuppressive or immunomodulatory medications concomitantly, and did not have any ongoing systemic medical conditions resulting in compromised immune system function. The majority of cases of PML associated with S1P receptor modulators, including MAYZENT, have occurred in patients treated for at least 2 years. The relationship between the risk of PML and the duration of treatment is unknown.

At the first sign or symptom suggestive of PML, withhold MAYZENT and perform an appropriate diagnostic evaluation. Typical symptoms associated with PML are diverse, progress over days to weeks and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. MRI findings may be apparent before clinical signs or symptoms. Cases of PML, diagnosed based on MRI findings and the detection of JCV DNA in the cerebrospinal fluid in the absence of clinical signs or symptoms specific to PML, have been reported in patients treated with MS medications associated with PML, including S1P receptor modulators. Many of these patients subsequently became symptomatic with PML. Therefore, monitoring with MRI for signs that may be consistent with PML may be useful, and any suspicious findings should lead to further investigation to allow for an early diagnosis of PML, if present. Lower PML-related mortality and morbidity have been reported following discontinuation of another MS medication associated with PML in patients with PML who were initially asymptomatic compared to patients with PML who had characteristic clinical signs and symptoms at diagnosis. It is not known whether these differences are due to early detection and discontinuation of MS treatment or due to differences in disease in these patients.

If PML is confirmed, treatment with MAYZENT should be discontinued. Immune reconstitution inflammatory syndrome (IRIS) has been reported in patients treated with S1P receptor modulators, including MAYZENT, who developed PML and subsequently discontinued treatment. IRIS presents as a clinical decline in the patient’s condition that may be rapid, can lead to serious neurological complications or death, and is often associated with characteristic changes on MRI. The time to onset of IRIS in patients with PML was generally within a few months after S1P receptor modulator discontinuation. Monitoring for development of IRIS and appropriate treatment of the associated inflammation should be undertaken.

**Macular Edema:** In most cases, macular edema occurred within 4 months of therapy. Patients with history of uveitis or diabetes are at an increased risk. Before starting treatment, an ophthalmic evaluation of the fundus, including the macula, is recommended and at any time if there is a change in vision. The use of MAYZENT in patients with macular edema has not been evaluated; the potential risks

and benefits to the individual patient should be considered.

**Bradyarrhythmia and Atrioventricular Conduction Delays:** Prior to initiation of MAYZENT, an ECG should be obtained to determine if preexisting cardiac conduction abnormalities are present. In all patients, a dose titration is recommended for initiation of MAYZENT treatment to help reduce cardiac effects. MAYZENT was not studied in patients who had:

* In the last 6 months, experienced myocardial infarction, unstable angina, stroke, TIA, or decompensated heart failure requiring hospitalization
* New York Heart Association Class II-IV heart failure
* Cardiac conduction or rhythm disorders, including complete left bundle branch block, sinus arrest or sino-atrial block, symptomatic bradycardia, sick sinus syndrome, Mobitz type II second-degree AV-block or higher-grade AV-block (either history or observed at screening), unless patient has a functioning pacemaker
* Significant QT prolongation (QTc greater than 500 msec)
* Arrhythmias requiring treatment with Class Ia or Class III anti- arrhythmic drugs

Reinitiation of treatment (initial dose titration, monitoring effects on heart rate and AV conduction [ie, ECG]) should apply if ≥4 consecutive daily doses are missed.

**Respiratory Effects:** MAYZENT may cause a decline in pulmonary function. Spirometric evaluation of respiratory function should be performed during therapy if clinically warranted.

**Liver Injury:** Elevation of transaminases may occur in patients taking MAYZENT. Before starting treatment, obtain liver transaminase and bilirubin levels. Closely monitor patients with severe hepatic impairment. Patients who develop symptoms suggestive of hepatic dysfunction should have liver enzymes checked, and MAYZENT should be discontinued if significant liver injury is confirmed.

**Cutaneous Malignancies**: The risk of cutaneous malignancies (including basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma) is increased in patients treated with S1P modulators.

Use of MAYZENT has been associated with an increased risk of BCC and SCC. Cases of other cutaneous malignancies, including melanoma, have also been reported in patients treated with MAYZENT and in patients treated with another S1P modulator.

Skin examinations are recommended at the start of treatment and periodically thereafter for all patients. Monitor for suspicious skin lesions and promptly evaluate any that are observed. Exposure to sunlight and ultraviolet light should be limited by wearing protective clothing and using a sunscreen with high protection factor. Concomitant phototherapy with UV-B radiation or PUVA-photochemotherapy is not recommended.

**Increased Blood Pressure:** Increase in systolic and diastolic pressure was observed about 1 month after initiation of treatment and persisted with continued treatment. During therapy, blood pressure should be monitored and managed appropriately.

**Fetal Risk:** Based on animal studies, MAYZENT may cause fetal harm. Women of childbearing potential should use effective contraception to avoid pregnancy during and for 10 days after stopping MAYZENT therapy. There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to MAYZENT during pregnancy. Healthcare providers are encouraged to enroll pregnant patients, or pregnant women may

register themselves in the MotherToBaby Pregnancy Study in Multiple Sclerosis by calling 1-877-311-8972, sending an email to MotherToBaby@health.ucsd.edu, or visiting [www.mothertobaby.org/join-study.](http://www.mothertobaby.org/join-study)

**Posterior Reversible Encephalopathy Syndrome (PRES):** Rare cases of PRES have been reported in patients receiving an S1P receptor modulator. Such events have not been reported for patients treated with MAYZENT in clinical trials. If patients develop any unexpected neurological or psychiatric symptoms, a prompt evaluation should be considered. If PRES is suspected, MAYZENT should be discontinued.

**Unintended Additive Immunosuppressive Effects From Prior Treatment or After Stopping MAYZENT:** When switching from drugs with prolonged immune effects, the half-life and mode of action of these drugs must be considered to avoid unintended additive immunosuppressive effects.

Initiating treatment with MAYZENT after treatment with alemtuzumab is not recommended.

After stopping MAYZENT therapy, siponimod remains in the blood for up to 10 days. Starting other therapies during this interval will result in concomitant exposure to siponimod.

Lymphocyte counts returned to the normal range in 90% of patients within 10 days of stopping therapy. However, residual pharmacodynamic effects, such as lowering effects on peripheral lymphocyte count, may persist for up to 3-4 weeks after the last dose. Use of immunosuppressants within this period may lead to an additive effect on the immune system, and therefore, caution should be applied 3-4 weeks after the last dose of MAYZENT.

**Severe Increase in Disability After Stopping MAYZENT:** Severe exacerbation of disease, including disease rebound, has been rarely reported after discontinuation of an S1P receptor modulator. The possibility of severe exacerbation of disease should be considered after stopping MAYZENT treatment, thus patients should be monitored upon discontinuation.

After stopping MAYZENT in the setting of PML, monitor for development of immune reconstitution inflammatory syndrome (PML- IRIS).

**Most Common Adverse Reactions:** Most common adverse reactions (>10%) are headache, hypertension, and transaminase increases.

**Please click** [**here**](https://www.novartis.com/us-en/sites/novartis_us/files/mayzent.pdf) **for full Prescribing Information, including Medication Guide.**

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