SAMPLE APPEAL LETTER

[Date]

[Payer Name]
[Payer Address 1]
[Payer Address 2]
[Payer City], [State] [ZIP]
[Payer Fax Number]

[HCP Name]
[HCP Address 1]
[HCP Address 2]
[HCP City], [State] [ZIP]

Re: Treatment Authorization Request of GILENYA® (fingolimod) capsules 0.5 mg for [Patient First Name Last Name]
Patient ID #: [ID #]
Patient Date of Birth: [Patient DOB MM/DD/YY]
Reference #: [Reference #]
Re: [Appeal Level]

Dear Appeals/Claims Representative:

I have received a denial of [coverage/pre-authorization] for GILENYA (fingolimod) 0.5 mg for [Patient First Name Last Name]. This letter is submitted as an appeal of the denial dated [Month Day, Year]. I have reviewed and understand your current policy on DMTs for the treatment of RRMS; however, based on my experience with RRMS, I continue to recommend GILENYA as the treatment of choice for [Mr/Ms] [Patient Last Name].

[Mr/Ms] [Patient Last Name] received a diagnosis of RRMS in [Month] [Year]. I have prescribed GILENYA for this patient because [Insert specific information regarding patient's history with this disease, including previously attempted treatments and results (ie, outcomes, tolerability, adverse events, etc)].

[Suggestions include:
- Serious skin reactions have occurred with subcutaneous therapy
- Interferon therapy was not successful in controlling disease activity
- Flushing and intolerable GI side effects with alternate RRMS therapy (specify)
- Breakthrough disease activity, including relapses and/or MRI brain lesions
- Inadequate response to, or inability to tolerate, alternate RRMS therapies (specify)]

We request the submission of this appeal to be evaluated on an individual basis by a board-certified neurologist who is currently practicing and is knowledgeable regarding standard treatments related to my patient's diagnosis.

GILENYA received FDA approval in 2010 for the treatment of adult patients with relapsing forms of multiple sclerosis. GILENYA was the first oral DMT for people with RRMS, and is approved as a first-line agent. The approved label makes no recommendation that it be used only after other forms of treatment have been tried.[1-3]

GILENYA is a sphingosine 1-phosphate receptor modulator that is thought to induce some immune cells to remain in the lymph nodes, inhibiting them from migrating into the brain and spinal cord.* In a 2-year phase III trial, known as FREEDOMS, involving 1272 adult patients with RRMS, GILENYA 0.5 mg (n=425) significantly reduced relapse rates (the primary end point of the study), when compared to placebo (n=418) (0.18 vs 0.40; $P<0.001$).[1,4]

In a second 1-year clinical trial, called the TRANSFORMS study, comparing GILENYA 0.5 mg with Avonex® (interferon beta-1a, 30 mcg IM once weekly) and involving 1292 adult patients with RRMS, GILENYA (n=429) significantly reduced relapse rates (the primary end point of the study) in comparison to the group taking Avonex® (n=431) (0.16 vs 0.33; $P<0.001$).[1,5]

*The mechanism by which GILENYA exerts therapeutic effects in MS is unknown but may involve reduction of lymphocyte migration into the CNS. The mechanism of action for GILENYA was observed in animal models.

The American Academy of Neurology (AAN) has a firm position regarding availability of DMTs for the treatment of RRMS. The Academy urges access to all DMTs in treating patients with RRMS "when they have the potential to provide clinical benefit. If step therapy programs are used, these programs should be driven by evidence-based clinical and safety data, and not just cost."[6]

I urge your reconsideration of this determination, and I encourage you to draw on the expertise and resources of the AAN in your review of this information and relevant data. Based on the above information, please provide coverage for these submitted charges. GILENYA is medically necessary for this patient in order to treat [his/her] condition.

Thank you for your reconsideration of denial of coverage to my patient for this recommended FDA-approved therapy. If you have any further questions, please contact me at [HCP Phone #] to discuss this appeal.

Indication

GILENYA is a sphingosine 1-phosphate receptor modulator 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 patients 10 years of age and older.

Important Safety Information

Contraindications

- Patients who in the last 6 months experienced myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure (HF) requiring hospitalization or Class III/IV HF
- History or presence of Mobitz Type II second-degree or third-degree atrioventricular (AV) block or sick sinus syndrome, unless patient has a functioning pacemaker
- Baseline QTc interval ≥500 msec
- Cardiac arrhythmias requiring treatment with Class Ia or Class III anti-arrhythmic drugs
- Patients who have had a hypersensitivity reaction to fingolimod or any of the excipients in GILENYA. Observed reactions include rash, urticaria, and angioedema upon treatment initiation

Bradyarrhythmia and Atrioventricular (AV) Block: Monitor patients during GILENYA initiation because of a risk of bradyarrhythmia and AV block. Prior to dosing and at the end of the observation period, obtain an electrocardiogram (ECG) in all patients (10 years of age and older). Monitor all patients for 6 hours after the first dose for signs and symptoms of bradycardia with hourly pulse and blood pressure (BP) measurement.

Continue monitoring until the abnormality resolves if any of the following is present after 6 hours: (1) The heart rate (HR) 6 hours postdose is <45 bpm in adults, <55 bpm in pediatric patients 12 years of age and older, or <60 bpm in pediatric patients 10 or 11 years of age. (2) The HR 6 hours postdose is at the lowest value postdose suggesting that the maximum pharmacodynamic effect on the heart may not have occurred. (3) The ECG 6 hours postdose shows new onset second degree or higher atrioventricular (AV) block.

Begin continuous ECG monitoring in patients with symptomatic bradycardia until resolution. If pharmacological intervention is required, continue ECG monitoring overnight in a medical facility, and repeat 6-hour monitoring after the second dose. Some patients may experience a second decrease in HR within 24 hours after the first dose.

Patients with pre-existing ischemic heart disease, history of MI or cardiac arrest, CHF, cerebrovascular disease, uncontrolled hypertension, history of symptomatic bradycardia or recurrent syncope, severe untreated sleep apnea, AV block, sinoatrial heart block, or on concomitant drugs that slow HR or AV conduction should be evaluated by a physician and, if treated with GILENYA, monitored overnight with continuous ECG in a medical facility after first dose due to higher risk of symptomatic bradycardia or heart block. Patients with or at risk for QT prolongation or on concomitant QT-prolonging drugs with a known risk of torsades de pointes should also be monitored overnight with continuous ECG.

Repeat first-dose monitoring if GILENYA is interrupted ≥1 day within first 2 weeks or >7 days during weeks 3 and 4, or >14 days after the first month of treatment because effects on HR and AV conduction may occur upon reinitiation. First-dose monitoring is also recommended when the dose is increased in pediatric patients switching from 0.25 mg to 0.5 mg.

Infections: GILENYA may increase risk of infections. Life threatening and fatal infections have occurred in association with GILENYA. A recent CBC should be available before initiating GILENYA. Consider suspending GILENYA if a patient develops a serious infection. Monitor for signs and symptoms of infection during treatment and up to 2 months after discontinuation. Do not start GILENYA in patients with active acute or chronic infections until infection is resolved. Two patients receiving a higher than recommended dose of GILENYA (1.25 mg) in conjunction with high-dose corticosteroid therapy died of herpetic infections. In the postmarketing setting with GILENYA, serious infections, some fatal, have been reported with opportunistic pathogens, including viruses (eg, John Cunningham virus [JCV], herpes simplex viruses 1 and 2, varicella zoster virus [VZV]), fungi (eg, cryptococci), bacteria (eg, atypical mycobacteria), and Kaposi's sarcoma. Patients with signs and symptoms consistent with any of these infections should undergo prompt diagnostic evaluation and treatment. Concomitant use with antineoplastic, immunosuppressive, or immune-modulating therapies are expected to increase the risk of additive immunosuppression. When switching to GILENYA from these types of therapies, consider their duration of effect and mode of action to avoid this risk.

Before initiating GILENYA, patients should be tested for antibodies to VZV. VZV vaccination of antibody-negative patients is recommended prior to starting treatment. GILENYA initiation should be postponed for 1 month after vaccination. It is recommended that pediatric patients, if possible, complete all immunizations in accordance with current immunization guidelines prior to initiating GILENYA.

Progressive Multifocal Leukoencephalopathy (PML): Cases of PML occurred in patients with MS who received GILENYA in the postmarketing setting. 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 usually leads to severe disability or death. PML has occurred in patients who had not been treated previously with natalizumab, which has a known association with PML, and who were not taking concomitant immunosuppressive or immunomodulatory medications.

Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body, clumsiness of limbs, visual disturbances, and changes in thinking, memory, and orientation, leading to confusion and personality changes.

MRI findings may be apparent before clinical signs or symptoms. PML, diagnosed based on MRI findings and detection of JCV DNA in the cerebrospinal fluid in the absence of clinical signs or symptoms specific to PML, has been reported in patients treated with MS medications associated with PML, including GILENYA. Therefore, monitoring with MRI for signs that may be consistent with PML may be useful. Any suspicious findings should lead to further investigation to allow for an early diagnosis of PML. Lower PML-related morbidity and mortality 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 differences in disease in these patients.

At the first sign or symptom suggestive of PML, withhold GILENYA and perform an appropriate diagnostic evaluation.

Macular Edema: Fingolimod increases the risk of macular edema, with or without visual symptoms. Perform an exam of the fundus, including the macula, before starting GILENYA, and 3 to 4 months after initiation. Monitor visual acuity at baseline, during routine patient evaluations, and if a patient reports visual disturbances while on GILENYA. Patients with diabetes mellitus or history of uveitis are at increased risk and should have regular ophthalmologic evaluations.

Liver Injury: Clinically significant liver injury has occurred in patients treated with GILENYA in the postmarketing setting. Signs and symptoms of liver injury, including markedly elevated serum hepatic enzymes and elevated total bilirubin, have occurred as early as 10 days after the first dose and also have been reported after prolonged use. Cases of acute liver failure requiring liver transplant have been reported.

Elevation of liver enzymes (ALT, AST, and GGT) 3- and 5-fold the upper limit of normal and greater has occurred with GILENYA. The majority occurred within 6 to 9 months and returned to normal within 2 months after discontinuing GILENYA. Recurrence of liver transaminase elevations occurred with rechallenge in some patients.

Prior to starting treatment with GILENYA (within 6 months), obtain serum transaminases (ALT and AST) and total bilirubin levels, and periodically until 2 months after GILENYA discontinuation. Patients should be monitored for signs and symptoms of any hepatic injury. Treatment with GILENYA should be interrupted if the patient is found to have an ALT greater than 3 times the reference range with serum total bilirubin greater than 2 times the reference range. Patients with severe hepatic impairment should be closely monitored, as their risk of adverse reactions is greater.

Posterior Reversible Encephalopathy Syndrome (PRES): Rare cases of PRES have been reported with GILENYA. Symptoms reported include sudden onset of severe headache, altered mental status, visual disturbances, and seizure. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. Delay in diagnosis and treatment may lead to permanent neurological sequelae. If PRES is suspected, GILENYA should be discontinued.

Respiratory Effects: Dose-dependent reductions in forced expiratory volume over 1 second (FEV1) and diffusion lung capacity for carbon monoxide (DLCO) were observed in GILENYA patients as early as 1 month after initiation. Changes in FEV1 appear to be reversible after discontinuing GILENYA; however, there is insufficient information to determine reversibility of DLCO. Obtain spirometry and DLCO when clinically indicated.

Fetal Risk: GILENYA may cause fetal harm. Women of childbearing potential should use effective contraception during and for 2 months after stopping GILENYA. A registry for women who become pregnant during GILENYA treatment is available. Contact the GILENYA Pregnancy Registry by calling 1-877-598-7237, sending an e-mail to gpr@quintiles.com, or visiting gilenyapregnancyregistry.com.

Severe Increase in Disability After Stopping GILENYA: Severe increase in disability accompanied by multiple new lesions on MRI has been reported following discontinuation of GILENYA in the postmarketing setting. Most of these reported cases did not return to the functional status they had before stopping GILENYA. The increase in disability generally occurred within 12 weeks after stopping GILENYA, but was reported up to 24 weeks after GILENYA discontinuation.

The possibility of severe increase in disability should be considered in patients who discontinue GILENYA, including those who are pregnant or planning for pregnancy.

Monitor patients for development of severe increase in disability following discontinuation of GILENYA and begin appropriate treatment as needed.

Increased Blood Pressure (BP): Monitor BP during treatment with GILENYA. An average increase of 3 mm Hg in systolic and 2 mm Hg in diastolic BP was observed in clinical trials versus placebo.

Malignancies: The risk of basal cell carcinoma (BCC) and melanoma is increased in patients treated with GILENYA. Melanoma and Merkel cell carcinoma have been reported with GILENYA in the postmarketing setting. Monitor and evaluate suspicious skin lesions.

Cases of lymphoma, including both T-cell and B-cell types and CNS lymphoma, have occurred in patients receiving GILENYA. The reporting rate of non-Hodgkin lymphoma with GILENYA is greater than that expected in the general population. Cutaneous T-cell lymphoma (including mycosis fungoides) has also been reported in the postmarketing setting.

Immune System Effects Following Discontinuation: Fingolimod remains in the blood and has pharmacodynamic effects, including decreased lymphocyte counts for up to 2 months following the last dose. Lymphocyte counts generally return to normal range within 1 to 2 months of stopping therapy. Initiating other drugs during this period warrants the same considerations needed for concomitant administration.

Hypersensitivity Reactions: Hypersensitivity reactions including rash, urticaria, and angioedema have been reported with GILENYA.

Drug Interactions: Closely monitor patients receiving systemic ketoconazole. The use of live attenuated vaccines should be avoided during, and for 2 months after stopping GILENYA.

Common Adverse Reactions: The most common adverse reactions with GILENYA 0.5 mg (incidence ≥10% and >placebo) were headache, liver transaminase elevations, diarrhea, nausea, cough, influenza, sinusitis, abdominal pain, back pain, and pain in extremity.

Seizure: Cases of seizures, including status epilepticus, have been reported with the use of GILENYA in clinical trials and in the postmarketing setting in adults. In adult clinical trials, the rate of seizures was 0.9% in GILENYA-treated patients and 0.3% in placebo-treated patients.

Pediatric Patients 10 Years of Age and Older: In the pediatric study, the safety profile in pediatric patients receiving GILENYA 0.25 mg or 0.5 mg daily was similar to that seen in adult patients. Cases of seizures were reported in 5.6%

of GILENYA-treated patients and 0.9% of interferon beta-1a-treated patients.

Click here for full Prescribing Information.

Sincerely,

[HCP First Name Last Name], [Suffix]

Attachments: Denial letter
Supporting documentation

DMT=disease-modifying therapy; GI=gastrointestinal; IM=intramuscular; MRI=magnetic resonance imaging; RRMS=relapsing-remitting multiple sclerosis.

References:
1. Gilenya [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; [August 2019]. **2.** Tecfidera [prescribing information]. Cambridge, MA: Biogen.; December 2017. **3.** Aubagio [prescribing information]. Cambridge, MA: Genzyme Corp; November 2016. **4.** Kappos L, Radue E-W, O'Connor P, et al; for FREEDOMS Study Group. A placebo-controlled trial of oral fingolimod in relapsing multiple sclerosis. *N Engl J Med*. 2010;362(5):387-401. **5.** Cohen JA, Barkhof F, Comi G, et al; for TRANSFORMS Study Group. Oral fingolimod or intramuscular interferon for relapsing multiple sclerosis. *N Engl J Med*. 2010;362(5):402-415. **6.** American Academy of Neurology. Position Statement: Availability of Disease Modifying Therapies (DMT) for Treatment of Relapsing Forms of Multiple Sclerosis. https://www.aan.com/siteassets/home-page/policy-and-guidelines/policy/position-statements/availability-of-disease-modifying-therapies-dmt/diseasemodtherams_posstatement.pdf Accessed August 26, 2019.

NOVARTIS

GILENYA™ (fingolimod) capsules 0.5mg

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