MODEL APPEAL LETTER – FINGOLIMOD (Gilenya)

Today's Date

Plan Name
Plan Address
Plan Address:

Dear Sir or Ms.:

This is a request for a reconsideration of your denial **(*of coverage/pre-authorization*)** of Fingolimod (Gilenya) for my patient **_____(name) _____,** who received a diagnosis of relapsing-remitting multiple sclerosis in **_____(month, year)_____.** Fingolimod received market approval from the FDA in October 2010 for the "treatment of patients with relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability". Significantly, fingolimod is the first oral disease-modifying therapy for people with MS, and the approved label makes no recommendation that it be used only after other forms of treatment have been tried.

Fingolimod 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 in to the brain and spinal cord. In a two-year phase III trial known as FREEDOMS involving 1,272 people with relapsing-remitting MS, fingolimod significantly reduced relapse rates (the primary endpoint of the study) and slowed disability progression (a secondary endpoint) when compared to inactive placebo.[i]

In a second one-year clinical trial, called the TRANSFORMS study, comparing two different doses of fingolimod with Avonex® (interferon beta-1a, 30mcg IM once weekly) involving 1,292 individuals with relapsing-remitting MS, both doses of fingolimod significantly reduced relapse rates (the primary endpoint of the study), and disease activity on MR brain imaging in comparison to the group taking interferon beta-1a...[ii]

I have recommended that my patient **_____(name)_____** start treatment with fingolimod for relapsing multiple sclerosis because (IMPORTANT: describe why you recommend this treatment for this patient at this time).

_____

_____

Thank you for your reconsideration of denial of coverage to my patient for this recommended FDA approved therapy.

Sincerely,

[i] Kappos L, Radue EW, O'Connor P, Polman C, Hohlfeld R, Calabresi P, Selmaj K, Agoropoulou C, Leyk M, Zhang-Auberson L, Burtin P; FREEDOMS Study Group, *A placebo-controlled trial of oral fingolimod in relapsing multiple sclerosis,* N Engl J Med. 2010 Feb 4;362(5):387-401

[ii] Cohen JA, Barkhof F, Comi G, Hartung HP, Khatri BO, Montalban X, Pelletier J, Capra R, Gallo P, Izquierdo G, Tiel-Wilck K, de Vera A, Jin J, Stites T, Wu S, Aradhye S, Kappos L; TRANSFORMS Study Group, *Oral fingolimod or intramuscular interferon for relapsing multiple sclerosis,* N Engl J Med. 2010 Feb 4;362(5):402-15.

Fingolimod (Gilenya) Abstract 1 of 2

N Engl J Med. 2010 Feb 4;362(5):387-401. Epub 2010 Jan 20.

A placebo-controlled trial of oral fingolimod in relapsing multiple sclerosis.

Kappos L, Radue EW, O'Connor P, Polman C, Hohlfeld R, Calabresi P, Selmaj K, Agoropoulou C, Leyk M, Zhang-Auberson L, Burtin P; FREEDOMS Study Group.

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Abstract

BACKGROUND: Oral fingolimod, a sphingosine-1-phosphate-receptor modulator that prevents the egress of lymphocytes from lymph nodes, significantly improved relapse rates and end points measured on magnetic resonance imaging (MRI), as compared with either placebo or intramuscular interferon beta-1a, in phase 2 and 3 studies of multiple sclerosis.

METHODS: In our 24-month, double-blind, randomized study, we enrolled patients who had relapsing-remitting multiple sclerosis, were 18 to 55 years of age, had a score of 0 to 5.5 on the Expanded Disability Status Scale (which ranges from 0 to 10, with higher scores indicating greater disability), and had had one or more relapses in the previous year or two or more in the previous 2 years. Patients received oral fingolimod at a dose of 0.5 mg or 1.25 mg daily or placebo. End points included the annualized relapse rate (the primary end point) and the time to disability progression (a secondary end point).

RESULTS: A total of 1033 of the 1272 patients (81.2%) completed the study. The annualized relapse rate was 0.18 with 0.5 mg of fingolimod, 0.16 with 1.25 mg of fingolimod, and 0.40 with placebo ($P<0.001$ for either dose vs. placebo). Fingolimod at doses of 0.5 mg and 1.25 mg significantly reduced the risk of disability progression over the 24-month period (hazard ratio, 0.70 and 0.68, respectively; $P=0.02$ vs. placebo, for both comparisons). The cumulative probability of disability progression (confirmed after 3 months) was 17.7% with 0.5 mg of fingolimod, 16.6% with 1.25 mg of fingolimod, and 24.1% with placebo. Both fingolimod doses were superior to placebo with regard to MRI-related measures (number of new or

enlarged lesions on T(2)-weighted images, gadolinium-enhancing lesions, and brain-volume loss; P<0.001 for all comparisons at 24 months). Causes of study discontinuation and adverse events related to fingolimod included bradycardia and atrioventricular conduction block at the time of fingolimod initiation, macular edema, elevated liver-enzyme levels, and mild hypertension.

CONCLUSIONS: As compared with placebo, both doses of oral fingolimod improved the relapse rate, the risk of disability progression, and end points on MRI. These benefits will need to be weighed against possible long-term risks. (ClinicalTrials.gov number, NCT00289978.)

N Engl J Med. 2010 Feb 4;362(5):402-15. Epub 2010 Jan 20.

Oral fingolimod or intramuscular interferon for relapsing multiple sclerosis.

Cohen JA, Barkhof F, Comi G, Hartung HP, Khatri BO, Montalban X, Pelletier J, Capra R, Gallo P, Izquierdo G, Tiel-Wilck K, de Vera A, Jin J, Stites T, Wu S, Aradhye S, Kappos L; TRANSFORMS Study Group.

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Abstract

BACKGROUND: Fingolimod (FTY720), a sphingosine-1-phosphate-receptor modulator that prevents lymphocyte egress from lymph nodes, showed clinical efficacy and improvement on imaging in a phase 2 study involving patients with multiple sclerosis.

METHODS: In this 12-month, double-blind, double-dummy study, we randomly assigned 1292 patients with relapsing-remitting multiple sclerosis who had a recent history of at least one relapse to receive either oral fingolimod at a daily dose of either 1.25 or 0.5 mg or intramuscular interferon beta-1a (an established therapy for multiple sclerosis) at a weekly dose of 30 microg. The primary end point was the annualized relapse rate. Key secondary end points were the number of new or enlarged lesions on T(2)-weighted magnetic resonance imaging (MRI) scans at 12 months and progression of disability that was sustained for at least 3 months.

RESULTS: A total of 1153 patients (89%) completed the study. The annualized relapse rate was significantly lower in both groups receiving fingolimod--0.20 (95% confidence interval [CI], 0.16 to 0.26) in the 1.25-mg group and 0.16 (95% CI, 0.12 to 0.21) in the 0.5-mg group--than in the interferon group (0.33; 95% CI, 0.26 to 0.42; P<0.001 for both comparisons). MRI findings supported the primary results. No significant differences were seen among the study groups with respect to progression of disability. Two fatal infections occurred in the group that received the 1.25-mg dose of fingolimod: disseminated primary varicella zoster and herpes simplex encephalitis. Other adverse events among patients receiving fingolimod were nonfatal herpesvirus infections, bradycardia and atrioventricular block, hypertension, macular edema, skin cancer, and elevated liver-enzyme levels.

CONCLUSIONS: This trial showed the superior efficacy of oral fingolimod with respect to relapse rates and MRI outcomes in patients with multiple sclerosis, as compared with intramuscular interferon beta-1a. Longer studies are needed to assess the safety and efficacy of treatment beyond 1 year. (ClinicalTrials.gov number, NCT00340834.)