VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

Gilenya™ (fingolimod)

Effective Date: 1/31/12

Date Developed: 12/20/11 by Albert Reeves MD

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19

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Gilenya™ (Fingolimod) is a Sphingosine 1-Phosphate (S1P) Receptor Modulator.

Pre-Authorization Criteria: treatment of relapsing forms of multiple sclerosis (MS) to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

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VCHCP requires that Gilenya™ (Fingolimod) be prescribed by a Neurologist or MS Specialist. .

Dosing: Adult

Multiple sclerosis: Oral: 0.5 mg once daily; doses >0.5 mg/day associated with increased adverse events and no additional benefit

Dosing: Geriatric

Refer to adult dosing.

Dosage Forms: U.S.

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Capsule, oral: Gilenya™: 0.5 mg

Administration

May be administered with or without food.

WARNINGS / PRECAUTIONS

Concerns related to adverse effects:

AV block: May result in transient AV conduction delays which typically resolve within 24 hours of treatment initiation; recurrence may be observed following discontinuation (>2 weeks) and subsequent resumption of therapy.

Bradycardia: Decreased heart rate (mean: 13 beat per minute) may occur with initiation of therapy. Following the first dose, heart rate may decrease as soon as 1 hour postdose with the maximal decrease occurring ~6 hours postdose. Heart rate typically returns to baseline after 1 month of therapy. All patients should be monitored for 6 hours after the first dose (or in patients where therapy has been interrupted for >2 weeks) for signs and symptoms of bradycardia; in patients who develop bradycardia, initiate appropriate treatment and continue to monitor until symptoms have resolved.

Hypertension: Increased blood pressure may occur ~2 months after initiation of therapy; monitor blood pressure throughout treatment.

Immune suppression: May increase risk of infection due to dose-dependent reduction of lymphocytes; lymphocyte counts may be decreased for up to 2 months following discontinuation of therapy. Monitor for signs and symptoms of infection; consider therapy interruption in patients who develop an infection during therapy. Do not initiate treatment in patients with acute or chronic infections until the infection has resolved. Use with caution in patients receiving concomitant immunosuppressant, immune modulating, or antineoplastic medications.

Macular edema: Macular edema may occur typically in the first 3-4 months of treatment. Patients may present with blurred vision, decreased visual acuity, or without symptoms. Signs and symptoms generally improve or resolve with discontinuation of treatment. Use with caution in patients with a history of diabetes mellitus or uveitis. Ophthalmologic exams should be performed prior to therapy and 3-4 months after treatment initiation; more frequent examination is warranted in patients with diabetes or a history of uveitis.

Respiratory effects: Reductions of FEV_1 and diffusion lung capacity for carbon monoxide (DLCO) are dose-dependent and may occur within the first month of therapy. FEV_1 changes may be reversible with drug discontinuation. Use in MS patients with compromised respiratory function has not been evaluated. If clinically necessary, spirometric evaluation of respiratory function and evaluation of DLCO should be performed during therapy.

Disease-related concerns:

Cardiovascular: Due to the risk of bradycardia and AV conduction delays, ECG is recommended prior to initiation of therapy in patients receiving concomitant antiarrhythmics including beta blockers and calcium channel blockers, patients with a slow or irregular heart beat, or with other cardiac risk factors (eg, AV block [second degree or greater], sick sinus syndrome, prolonged QT interval, ischemic cardiac disease, heart failure). If treatment is discontinued for >2 weeks, repeat ECG is recommended prior to reinitiation.

Hepatic impairment: Use with caution and closely monitor patients with severe hepatic impairment (contraindicated in the Canadian labeling). Increased risk of adverse effects may occur, including elevated liver enzymes. Obtain baseline liver enzymes in all patients prior to therapy initiation; monitor liver enzymes in patients who develop symptoms of hepatic dysfunction (eg, nausea, vomiting, abdominal pain, fatigue, anorexia, jaundice, dark urine). Discontinue treatment with confirmation of liver injury; transaminases tend to return to normal within 2 months of discontinuation.

DRUG Interactions

Antiarrhythmic Agents (Class Ia): Fingolimod may enhance the arrhythmogenic effect of Antiarrhythmic Agents (Class Ia). Management: Obtain baseline ECG (if not recently available) if initiating fingolimod during treatment with class Ia antiarrhythmic agents. Monitor for bradycardia and AV block. The Canadian labeling recommends avoiding concomitant use of these agents. *Risk C: Monitor therapy*

Antiarrhythmic Agents (Class III): Fingolimod may enhance the arrhythmogenic effect of Antiarrhythmic Agents (Class III). Management: Obtain baseline ECG (if not recently available) if initiating fingolimod during treatment with class III antiarrhythmic agents. Monitor for bradycardia and AV block. The Canadian labeling recommends avoiding concomitant use of these agents. *Risk C: Monitor therapy*

BCG: Immunosuppressants may diminish the therapeutic effect of BCG. *Risk X: Avoid combination*

Beta-Blockers: May enhance the bradycardic effect of Fingolimod. *Risk C: Monitor therapy*

Coccidioidin Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioidin Skin Test. *Risk C: Monitor therapy*

Conivaptan: May increase the serum concentration of CYP3A4 Substrates (Low risk). *Risk C: Monitor therapy*

Cyproterone: May decrease the serum concentration of CYP2E1 Substrates. *Risk C: Monitor therapy*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Diltiazem: May enhance the bradycardic effect of Fingolimod. *Risk C: Monitor therapy*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Ketoconazole: May increase serum concentrations of the active metabolite(s) of Fingolimod. Ketoconazole may increase the serum concentration of Fingolimod. *Risk C: Monitor therapy*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Peginterferon Alfa-2b: May decrease the serum concentration of CYP2D6 Substrates. *Risk C: Monitor therapy*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). *Risk C: Monitor therapy*

Vaccines (Inactivated): Fingolimod may diminish the therapeutic effect of Vaccines (Inactivated). *Risk C: Monitor therapy*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Vaccinial infections may develop. Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Vaccines (Live): Fingolimod may enhance the adverse/toxic effect of Vaccines (Live). Vaccinial infections may develop. Fingolimod may diminish the therapeutic effect of Vaccines (Live). *Risk X: Avoid combination*

Verapamil: May enhance the bradycardic effect of Fingolimod. *Risk C: Monitor therapy*

REFERENCES

1. Brinkmann V, "FTY720 (Fingolimod) in Multiple Sclerosis: Therapeutic Effects in the Immune and the Central Nervous System," *Br J Pharmacol*, 2009, 158(5):1173-82. [PubMed 19814729]
2. Chun J and Hartung HP, "Mechanism of Action of Oral Fingolimod (FTY720) in Multiple Sclerosis," *Clin Neuropharmacol*, 2010, 33(2):91-101. [PubMed 20061941]

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