

Fingolimod (Gilyena®) Criteria for Use

VHA Pharmacy Benefits Management Services, Medical Advisory Panel and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or <http://vawww.pbm.va.gov> for further information.

Exclusion Criteria (if any box is checked the patient DOES NOT qualify for fingolimod)

- Primary progressive multiple sclerosis
- Secondary progressive MS and no clinical or MRI evidence of relapses
- Concurrent use of immune system modifying drugs to treat MS (i.e.: interferon beta-1B, glatiramer acetate, interferon beta 1A, natalizumab, mitoxantrone) unless the previous agent will be discontinued when fingolimod is initiated.
- Evidence of macular edema on ophthalmologic exam (see monitoring section)
- History or exam findings of syncope, sick sinus syndrome, 2nd degree or higher conduction block, ischemic heart disease, resting heart rate <55bpm or congestive heart failure without prior cardiology approval
- No documented baseline testing including (within 30 days prior to fingolimod); CBC with differential, LFT, EKG and skin exam.

Inclusion Criteria

Patient with relapsing MS^a characterized by disease activity defined as one or more relapses in the two years prior to therapy or gadolinium positive lesions on MRI^b, or new T2 lesions on MRI *

AND

- Loss of clinical response to disease modifying therapy (interferon beta 1a, interferon beta 1b or glatiramer

OR

- Acquired intolerance to therapy with glatiramer, interferon beta 1a or interferon beta 1b or natalizumab

*Limited safety and efficacy data are available for use of fingolimod in the treatment naive MS patient.

Dosage Recommendations

- Fingolimod is dosed 0.5 mg ,orally once daily
- There is no dosage adjustment based on renal function or in mild to moderate hepatic impairment.
- Ketoconazole may increase fingolimod blood concentrations by 1.7-fold when given concomitantly, increasing the risk of potential adverse reactions.

Issues for Consideration

- Patients without a documented history of varicella zoster virus infection or vaccination against it should be evaluated for vaccination against varicella prior to fingolimod initiation. Zostavax® should not be used in these individuals. In these patients vaccination with the live varicella virus product (Varivax®) should be undertaken. Consult the CDC website for guidance. (2 doses of the vaccine must be given at least 4 weeks apart) www.cdc.gov/vaccines/recs/schedules/adult-schedule.htm
- Patients on antiarrhythmics, beta-blockers or calcium channel blockers may be more prone to development of symptomatic bradycardia and should be initiated on fingolimod with caution.
- Fingolimod is a pregnancy Category C medication. Elimination of fingolimod can take up to 2 months following discontinuation of the drug. Women of child bearing potential should be counseled regarding appropriate forms of contraception during this period.
- Patients with severe COPD may be at higher risk for development of pulmonary compromise and additional monitoring may be indicated.
- Fingolimod has been associated with development of melanomas although the risk does not appear greater than the general population. Referral of high risk individuals to dermatology may be considered.
- The use of live vaccines after initiation of fingolimod therapy should be discouraged (<http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm>)
- Injectable DMT therapy (interferon beta 1a, beta 1b and glatiramer acetate remain first line agents in MS therapy. In cases of needlephobia local pre-medication, behavioral or graded exposure therapy should be considered to allow use of these agents.
- MS patients with dexterity issues, injection site reactions or travel issues may be considered for fingolimod therapy.

Monitoring

- Patients should be observed in a clinically appropriate area(with emergency support available) for six hours after the initial oral dose with vital signs checked intermittently. A baseline pulse and blood pressure should be taken before the dose is given. If symptoms (hypotension, bradycardia) develop, patients should be triaged as required based on degree of symptoms.
- Ophthalmology evaluation repeated 3- 4 months after fingolimod initiation with subsequent evaluations based on clinical symptoms.
- CBC and LFT's repeated at 3-6 month intervals.
- An annual brain MRI by CMSC Protocol (www.va.gov/ms) is recommended

^a Relapsing Forms of MS include: **Relapsing, remitting MS:** A clinical course of MS characterized by clearly defined, acute attacks with full or partial recovery and no disease progression between attacks. **Secondary progressive MS with superimposed relapses:** A clinical course of MS that shows steady progression but with superimposed acute relapses, after an initial relapsing-remitting course, **Progressive-relapsing MS:** A clinical course of MS that shows disease progression from the beginning, but with clear, acute relapses, with or without full recovery from those relapses. ^b gadolinium should not be used in patients with CrCl ≤30 ml/min or those on dialysis