

## **Fingolimod (Gilenya®)**

Gilenya is a once daily pill used to treat relapsing multiple sclerosis.

*Mechanism of Action:* Fingolimod is an S1P1 receptor modulator whose proposed mechanism of action is sequestration of peripheral lymphocytes. It causes immune cells to become trapped in lymph nodes and therefore unavailable to travel from the blood stream into the brain and cause autoimmune inflammatory attacks in the setting of MS. It is not an immunosuppressant.

*Efficacy:* The following information is based on data from the TRANSFORMS and FREEDOMS trials, long term follow-up studies, and the MS centers experience with fingolimod (Gilenya).

*Relapses:* In the TRANSFORMS trial, fingolimod (ARR 0.16) decreased relapse rate 52% compared to IFNβ1a (ARR 0.33). In FREEDOMS fingolimod (ARR 0.18) decreased relapse rate by 54% compared to placebo (ARR 0.40).

*Disability:* Fingolimod decreased risk of disability by 30% over placebo in FREEDOMS.

*NEDA (No evidence of disease activity):* no new relapses, no sustained 3-month disability, no new/enlarged T2 MRI lesions or new Gad+ lesions was seen in 33% of fingolimod treated patients in the two-year FREEDOMS trial, compared to 13% in placebo patients.

*Safety/Tolerability:* Side effects and risks associated with this medication include but not limited to: risk of infection (two deaths in the TRANSFORMS trial and one post-marketing death all secondary to disseminated VZV family infections, a few cases of PML and meningitis have been described), cardiac (1st degree heart block or bradycardia associated with the 1st dose, as well as mild elevation in BP), pulmonary (reversible decrease in PFTs), ocular (risk of macular edema), elevation in liver enzymes.

*Required screening tests:* We must review an EKG and lab testing (VZV titer, CBC and LFTs) before starting this DMT. We must also have a documented normal recent (within 3 months) skin examination and eye examination before starting fingolimod. If you have lung disease a PFT may be required.

*First dose observation:* We discussed how there can be a "1st dose effect" where a patient becomes bradycardic or develops first degree heart block only during the 1st dose of the drug. You must take the 1st dose of fingolimod under our observation here at the clinic. After you start fingolimod, you must remember to take a pill every day without missing any for the first month to avoid a first dose effect that could be dangerous. After the first month you must remember to never miss more than 13 days then restart fingolimod to avoid a first dose effect.

*Poor candidates for fingolimod:* Patients with heart conditions may not be best suited for this DMT. We must review your medications before starting fingolimod and avoid certain drugs such as Celexa, beta blockers, certain calcium channel blockers and others.

*Important Reminders:* Risks associated with fingolimod use can include PML infection, VZV infection, crypto meningitis infection, hypertension, posterior reversible encephalopathy syndrome, reversible decreased pulmonary functions, macular edema, elevation in liver enzymes, first dose cardiac effects (bradycardia, heart block). Patients on (Gilenya) have a 0.4% risk of macular edema. Patient has been asked to promptly alert provider if vision were to become "wavy" or "warped" or dim in the center. It is important to remain adherent to taking fingolimod (Gilenya) EACH DAY. Missing several consecutive

does may place a patient at risk for recurrence of the "first dose cardiac" effects when restarting. This could include the risk of a potentially harmful abnormal heart rhythm. The patient is instructed to promptly report any fever, rash, cough or other signs or symptoms of a possible infection. People taking fingolimod may be at slight risk of basal cell carcinoma and melanoma. We recommend people taking fingolimod have an annual skin examination. Also, we recommend all patients on fingolimod promptly report any suspicious skin changes to PCP or our team.