FINGOLIMOD (GILENYA) – PATIENT INFORMATION

What is the medication?

Generic: Fingolimod

Brand name: Gilenya
First oral medication (taken by mouth) approved by the Food and Drug Administration (FDA) to modify disease activity in multiple sclerosis (MS)

Has the US Food and Drug Administration (FDA) approved the medication?

Yes – A 0.5-mg daily dose was approved by the FDA on September 21, 2010.

If so, what is the recommended use in MS, and for whom is the medication recommended?

- The medication is approved to reduce the frequency of relapses (also called exacerbations or attacks) and to delay physical disability. It is recommended for people with relapsing forms of MS.
- Studies are currently being done to find out if this medication can also help people with primary-progressive MS.

What studies did the FDA look at when deciding whether to approve this medication?

Two large trials have been published so far:


What was the design of the study?
Three groups of people took part in this two-year study – a low-dose (0.5-mg) fingolimod group, a higher-dose (1.25-mg) fingolimod group, and a group that took a placebo (a capsule without active medication).

What questions was the study trying to answer?
This study was designed to answer several questions, including:

- Do people taking fingolimod have fewer relapses (exacerbations or attacks) over the two-year study than the group taking the placebo?
- Is the risk of disability progression over the two-year study lower in people taking fingolimod than in those who are taking placebo?
- Do people taking fingolimod have fewer new lesions (damaged areas related to MS) on magnetic resonance imaging (MRI) scans over the two-year study than people taking placebo?
- Do people taking fingolimod develop less brain tissue loss or shrinkage over the two-year study than people taking placebo?
- Does the group taking the low dose of fingolimod have different results or side effects than the group taking the high dose of fingolimod?

What were the results of the study?
- The annual relapse rate was 0.18 for the group taking the 0.5-mg dose and 0.40 for those on placebo. This means that over the two years of the trial the group taking fingolimod had a 54% lower risk of relapse than the group taking the placebo.
- The risk of disability progression was 30% lower over the two years of the trial in people taking the 0.5-mg dose of fingolimod than in people taking the placebo.
- The people taking fingolimod had fewer new lesions and developed less brain tissue loss, as shown on their MRI scans, than the group taking placebo.
- The group taking the low dose of fingolimod and the group taking the high dose of fingolimod did equally well, but the higher-dose group had more side effects, including two deaths. These findings led to the FDA’s decision to approve only the 0.5-mg dose of fingolimod.


What was the design of the study?
Three groups of people took part in this 12-month trial. All of them had a relapse during the year before entering the study, many while taking an injectable disease modifying treatment for MS. During the study, one group took a weekly injection of interferon beta-1a (Avonex®) and a daily capsule containing a placebo. One group took the daily 0.5-mg dose of fingolimod and a weekly injection containing a placebo. One group took the daily 1.25-mg dose of fingolimod and a weekly injection of placebo.

What questions was the study trying to answer?
This study was designed to answer several questions, including:
- Do people taking fingolimod have fewer relapses over the one-year study than people taking interferon beta-1a (Avonex)?
- Do people taking fingolimod have fewer new lesions (spots) on their MRI over the one-year study than people taking interferon beta-1a (Avonex)?
Is the risk of disability progression over the one-year study lower in people taking fingolimod than in people taking interferon beta-1a (Avonex)?

What were the results of the study?

- The relapse rate during the one-year study was 0.16 per year for the 0.5-mg fingolimod group and 0.33 per year for the group taking Avonex. This means that the group taking fingolimod had a 52% lower risk of having a relapse during the study period than the group taking interferon beta-1a (Avonex).
- 82.5% of people taking the 0.5-mg dose of fingolimod and 70% of people taking interferon beta-1a had no relapses during the 12 months of the study.
- The group taking the 0.5-mg dose of fingolimod had fewer signs of disease activity on MRI than the group taking Avonex.
- There was no difference among the groups in the risk of disease progression over the course of the 12-month study.

How does the medication work?

Fingolimod appears to prevent some potentially damaging T cells (types of white blood cells called T-lymphocytes) from leaving the lymph nodes. The result is that there are fewer T cells traveling into the central nervous system (CNS - the brain and spinal cord) to do damage. It is not known yet whether fingolimod helps or protects the cells in a person’s CNS.

How is this medication taken? What is the dosage and how often is it taken?

Fingolimod is taken once a day by mouth in capsule form. The dose of the medication is 0.5-mg.

Can this medication be used with other medications?

- **Disease-modifying Therapies:**
  - Has this medication been tested in combination with other medications?
    - No studies have been done to look at the use of fingolimod in combination with other disease-modifying therapies.
    - The FDA has suggested caution when switching from a long-acting therapy such as natalizumab or mitoxantrone to fingolimod. If you are currently taking one of these medications, your doctor will determine if a switch is safe or appropriate for you. See [Product Insert](#).
• **Other Medications**

  - Can fingolimod be taken with other medications a person is taking to manage MS symptoms or other medical problems?
    - Certain medications are known to interact with fingolimod. These include medications that contain quinidine, such as Neudexta®, a combination of dextromethorphan and quinidine that is approved for treating uncontrollable laughing and/or crying (pseudobulbar affect) in people with MS. Other medications that might interact with fingolimod include beta blockers (a type of heart medication) and some medications that are used to treat fungal infections.
    - Live vaccines should not be taken by someone who is taking fingolimod or within two months after a person stops taking fingolimod. The reason for this is that live vaccines can increase a person’s risk of infection.
    - Inactivated (killed) vaccines (such as the seasonal flu vaccine) may not be as effective while a person is taking fingolimod or for 2 months after treatment with fingolimod is stopped.

What results can a person expect from this medication?

- Fingolimod does not cure MS or make the symptoms of MS go away.
- Fingolimod was shown in the clinical trials to reduce the rate of relapses, reduce disease activity (as shown on MRI scans), and slow the progression of disability.
- No data are available yet to show whether fingolimod is effective in the long term.
- Only one comparison trial (the TRANSFORMS trial – see p. 2) has been done so far. More comparison trials must be done to determine if fingolimod is more effective than the other approved MS disease-modifying therapies.

What are the possible short-term side effects of this medication?

- The most commonly-reported side effects of fingolimod are headache, flu, diarrhea, back pain, abnormal liver tests, and cough.
- Fingolimod can cause a person’s heart rate to slow, particularly right after the first dose. The heart rate will be lowest approximately six hours after the first dose, which may cause the person to feel dizzy or tired. The heart rate will generally return to
normal within one month.

- During the course of the two-year FREEDOMS trial two individuals on the higher (1.25-mg) dose of the medication died from herpes virus infections. One patient who had never had chicken pox was infected with the herpes virus that causes chicken pox. The other person was infected with a different kind of herpes virus that caused a brain infection.

Can long-term health problems occur from use of this medication?

- The FDA’s labeling information for fingolimod lists some warnings about health problems that can occur with the use of fingolimod:
  - Increased risk of infections. In clinical trials, a small number of serious herpes infections occurred, including two deaths from herpes infections that occurred in people taking the 1.25-mg dose rather than the 0.5-mg dose that the FDA has now approved.
  - Macular edema (swelling of the center of the retina inside the eye)
  - Decrease in lung function
  - Slight increase in blood pressure
  - Increases in liver enzymes (which indicate liver injury)

- The long-term safety of fingolimod is unknown at this time.

Is training recommended or required for people who are starting this treatment?

There is no specific training required of either provider or patient before beginning fingolimod treatment.

What is known about the effect of this medication on reproduction?

Fingolimod is Pregnancy Category C, which means that animal studies have shown that it may cause harm to the unborn baby. It is recommended that women use effective birth control while taking fingolimod and for two months after stopping the medication.

Does this medication interact or interfere with oral contraceptives (birth control pills)?

Fingolimod is not known to interact with oral contraceptives.

Has the FDA recommended or required a safety-monitoring program?

- The FDA has required Novartis to create a registry that will follow 5000 patients for
five years to track any significant safety problems that may occur.

- Novartis has created a pregnancy registry in order to follow the pregnancies of any women who accidentally become pregnant while taking fingolimod or within two months after stopping the medication. Since all women in the clinical trials were required to be using birth control, this is the most effective way to learn about the impact of fingolimod on a woman’s health during pregnancy and on her unborn baby.

**Does the FDA recommend or require that people taking this medication be monitored for safety concerns?**

The FDA has recommended that clinicians and patients take certain steps for safety purposes. These steps are intended to lower health risks

- Prior to starting treatment, a person should be evaluated for heart, lung, liver, and eye problems.
- A person with no history of chicken pox should be given a blood test for antibodies to determine if he or she has ever been exposed to the varicella zoster virus. If the test indicates that the person has not previously been exposed, the FDA recommends that the varicella zoster vaccination be considered at least one month prior to starting treatment with fingolimod.
- A person’s pulse and blood pressure should be measured before the first dose. The person should remain in a medical facility for six hours following the first dose so that she or he can be observed for changes in heart rate. If a drop occurs that is significant enough to cause symptoms, those symptoms should be managed before the person leaves the medical facility.
- Blood pressure should be monitored on a regular basis while a person is taking fingolimod.
- People should have their eyes examined 3-4 months after starting treatment and any time that they experience visual symptoms.
- A person who develops breathing problems while taking fingolimod should report them to the doctor so an evaluation can be done.
- A person who develops symptoms of liver problems should report them to the doctor so an evaluation can be done. These symptoms might include yellowing of the skin and whites of the eyes; dark urine; light-colored bowel movements; nausea and vomiting; diarrhea; loss of appetite.

**How long can a person safely take this medication?**

There are no recommended limits for treatment with fingolimod.
What happens if a person stops taking fingolimod?

- **If a person stops this medication, what other treatment options are available for patients after being treated with fingolimod?**
  After taking fingolimod a person may take any of the other disease-modifying therapies.

- **After stopping fingolimod, how long would a person have to wait before starting a different medication?**
  The answer to this question is not known. The numbers of certain types of cells in the body generally return to their normal levels within two months of stopping fingolimod. This means that healthcare providers will probably recommend waiting at least two months before starting another disease-modifying therapy.

- **What would a person do in the meantime?**
  While waiting to begin treatment with another medication, a patient should work with her or his healthcare provider on a plan to manage symptoms.

- **Are there any risks associated with suddenly stopping the use of fingolimod?**
  The answer to this question is not known. It is important for people to talk with their healthcare provider before suddenly stopping any medication that has been prescribed for them.

How can a person tell if the medication is not working?

Fingolimod does not treat long-standing symptoms. This means that symptoms a person has had for some time are likely to continue even if the medication is working. It is possible for relapses to occur even if the person is taking fingolimod as prescribed. If a sudden worsening of symptoms occurs, the person should see her or his healthcare provider for further evaluation.

Is the manufacturer/distributor offering any financial assistance program for patients?

Financial assistance is available from Novartis. Call 1-877-408-4974 for information about their financial assistance program.

Are there any special considerations for this medication?

People with relapsing forms of MS would be considered appropriate candidates for this therapy.
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FOR DISCLOSURES AND OTHER INFORMATION:
Please visit our website at http://www.ms-coalition.org/emergingtherapies or email us at emergingtherapies@ms-coalition.org.
Fingolimod (Gilenya) Update for Clinicians and People Affected by MS

Update Posted on February 10, 2012

Following the report on January 20, 2012 of 11 deaths among patients who received fingolimod (Gilenya) outside of the clinical trials, the European Medicines Agency (EMA) announced a review of the medication. This review is separate from the investigation currently underway by the U.S. Food and Drug Administration (FDA). The FDA issued a statement in December, 2011 concerning a patient who died within 24 hours of receiving a first dose of the medication.

According to Novartis Pharmaceuticals, more than 33,000 people have received fingolimod to date. Although little is known at this time about the 11 reported deaths, they appear to be related to cardiac events. Until the EMA and FDA have completed their reviews, it is impossible to know what role fingolimod may have played in the deaths.

While their review is under way, the EMA has recommended to healthcare professionals in Europe that they increase patient monitoring for the first dose of fingolimod. The recommendations include:

• Electrocardiogram (ECG) monitoring before treatment and then continuously during the first six hours following the first dose
• Measurement of blood pressure and heart rate every hour during the six-hour observation period
• After six hours, any patients with clinically important heart-related effects, such as bradycardia (a slow heart rate) or atrioventricular block (a problem with the conduction of electricity in the heart), should continue to be managed and monitored until their condition has improved.

Pending further investigation, the FDA recommends that healthcare professionals who prescribe Gilenya continue to follow the recommendations on the approved label. The FDA further states that people who are currently taking Gilenya should not stop taking it without talking to their prescriber.

The Emerging Therapies Collaborative will continue to post updated information as it becomes available.

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