Gilenya (fingolimod)

What is Gilenya?

Gilenya (fingolimod) is an oral drug treatment approved for relapsing remitting MS (RRMS). It is a disease modifying therapy (DMT) that targets the immune system to reduce relapses.

How does Gilenya work?

Damage incurred from RRMS is thought to be caused by a special type of immune cell called a T cell. Gilenya acts by trapping these T cells from the bloodstream into organs called lymph nodes. In turn, this prevents the T cells from getting into the brain and causing damage to the myelin sheath, which can lead to the symptoms of MS.

Who should take Gilenya?

Gilenya has been approved as a second-line therapy for the treatment of RRMS. It should be considered for individuals with MS that have failed to respond despite treatment with beta-interferon (a current conventional MS treatment) or individuals who have rapidly evolving severe MS (two or more relapses a year).

Gilenya does not cure MS, but it helps to reduce the number of relapses and slows down the progression of physical disabilities due to MS.

How is Gilenya administered?

Gilenya comes in 0.5mg capsules. It is taken by mouth once a day with or without food.

Before the first dose, doctors should check the patient's blood pressure, heart rate, as well as their heart by electrocardiogram (ECG, a test that measures the electrical activity of the heart). After the first dose, the patient's blood pressure and heart rate should be checked every hour for six hours. In addition, doctors may perform ECG continuously during six hours or extend the monitoring period, if considered necessary.

What are the side effects from taking Gilenya?

Clinical studies of over 4000 MS patients showed that the most common side effects are headache, liver enzyme elevations, influenza, diarrhoea, back pain, and cough. Other Gilenya-related side effects include transient, generally asymptomatic, heart rate reduction and atrioventricular block upon treatment initiation, mild blood pressure increase, macular oedema, and mild bronchoconstriction.

The rates of infections overall, including serious infections, were comparable among treatment groups, although a slight increase in lower respiratory tract infections (primarily

bronchitis) was seen in patients treated with Gilenya. The number of malignancies reported across the clinical trial program was small, with comparable rates between the Gilenya and control groups.

Are there serious side effects?

Gilenya is known to cause lowering of the heart rate at the beginning of treatment. Therefore, Gilenya is not recommended for people taking certain anti-arrhythmic medicines (medicines used to restore normal cardiac rhythm) and in patients taking certain medicines that lower the heart rate. Gilenya is also not recommended in patients with certain cardiovascular disease or a history of cardiovascular or cerebrovascular disease (problems with the blood supply to the brain).

In January 2012, the European Medicines Agency started a review of the cardiovascular safety of Gilenya, following receipt of information relating to an unexplained and sudden death of a patient within 24 hours of taking Gilenya for the first time. At the time, temporary recommendations were given, advising doctors to perform ECG monitoring for six hours after taking the first dose, and to consider the need for extended monitoring.

This review assessed all available data on the heart safety of Gilenya, including reports of 15 cases of sudden or unexplained death in patients treated with Gilenya. It was noted that most of the deaths and cardiovascular problems had occurred in patients with a history of cardiovascular problems or taking other medicines. The data reviewed were not conclusive as to whether Gilenya was the cause of the deaths.

It was also noted the maximum effect of Gilenya on decreasing the heart rate occurred within six hours after the first dose in most patients, and that this decrease in heart rate can be reversed if necessary by giving atropine or Isoprenaline.

What are the findings from Gilenya's clinical trials?

Two main studies have provided the evidence to support Gilenya as a treatment for relapsing remitting MS. The FREEDOMS trial compared two doses of Gilenya (fingolimod) with placebo and the TRANSFORMS trial compared two doses of Gilenya with interferon beta-1a.

Gilenya's approval was based on the largest clinical trial program submitted to date for a new MS drug, and included data from clinical studies showing significant efficacy in reducing relapses, the risk of disability progression, and the number of brain lesions detected by magnetic resonance imaging (MRI), a measure of disease activity. In MS, the immune system damages the covering that protects nerve fibres in the central nervous system (CNS), which includes the brain and spinal cord.

The novel mechanism of Gilenya is thought to work by reducing the immune system's attack on the CNS by retaining certain white blood cells (lymphocytes) in the lymph nodes. This prevents the white blood cells from reaching the CNS, where they could potentially attack the protective covering around the nerve fibres, resulting in less inflammatory damage to the nerve cells. The white blood cell retention is reversible if Gilenya treatment is stopped.

How does Gilenya compare to current therapies?

The EU application (the TRANSFORMS trial) included data showing Gilenya 0.5mg reduced by 52% at one year compared with interferon beta-1a (Avonex), one of the most

commonly prescribed treatments for MS. Data from a two-year placebo-controlled study showed a reduction in the risk of disability progression among Gilenya patients (30% reduction confirmed at three-month follow-up visit compared with placebo).

What further Gilenya studies are planned?

Gilenya is also being investigated in phase III clinical trials for primary progressive multiple sclerosis. Laboratory investigations provided evidence that, in addition to its effect on the immune system, Gilenya may have neuroprotective and remyelinating properties in the brain and spinal cord.

This potential is being evaluated by the INFORMS phase III trial (FTY720 in patients with primary progressive multiple sclerosis). This double blind study is testing whether Gilenya (0.5mg capsules, taken daily for three years) is effective in delaying disability progression compared to placebo in 951 people with primary progressive MS. The study is due to finish in September 2014.

When is Gilenya likely to become available?

Gilenya was approved by the European Medicines Agency on 17 March 2011, and then granted a positive Health Technology Assessment (HTA) by the National Centre for Pharmacoeconomics (NCPE). In June 2012, reimbursement of Gilenya was approved allowing for its availability for prescription by neurologists. This was achieved after a new contract between the HSE and the Irish Pharmaceutical Healthcare Association was agreed.

What does MS Ireland say in relation to Gilenya?

MS Ireland is pleased that Gilenya is now available for those deemed suited for its use. It provides another important treatment option for people with MS to consider in consultation with their neurologist.

Links to further information on Gilenya

Gilenya Information MS Trust
http://www.mstrust.org.uk/research/drugsindevelopment/fingolimod.jsp
Gilenya Information Multiple Sclerosis Research Centre UK
http://www.msrc.co.uk/index.cfm/fuseaction/show/pageid/1309/
Gilenya Information MS Society UK
http://www.mssociety.org.uk/what-is-ms/treatments-and-therapies/licensed-disease-modifying-drugs/gilenya
Gilenya – European Public Assessment Report
http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002202/human_med_001433.jsp&mid=WC0b01ac058001d124

Gilenya – Clinical Trials

Long-term Efficacy and Safety of Fingolimod (FTY720) in Patients with RRMS
http://clinicaltrials.gov/show/NCT00662649
Efficacy and Safety of Fingolimod in Patients with RRMS with Optional Extension Phase (TRANSFORMS)
http://clinicaltrials.gov/ct2/show/NCT00340834
FTY720 in Patients with Primary Progressive Multiple Sclerosis (INFORMS)
http://clinicaltrials.gov/show/NCT00731692

Disclaimer:

MS Ireland provides information to the MS Community on an array of topics associated with MS. This information is for reference purposes only and medical advice should always be sought before any treatment or intervention is tried.