About Gilenya® (fingolimod) & Measures of MS Disease Activity
MEDIA FACT SHEET

What is Gilenya?
- Gilenya® (fingolimod) is a once-daily oral disease-modifying therapy (DMT) approved to treat relapsing forms of multiple sclerosis (MS).

What is Gilenya indicated for?
- In the EU, Gilenya is indicated for adult patients with highly active relapsing-remitting MS (RRMS) defined as either high disease activity despite treatment with at least one DMT (including interferons and newly-approved oral DMTs), or rapidly evolving severe RRMS.
- In the US, Gilenya may be used first line for the treatment of relapsing forms of MS.

What is Relapsing-Remitting Multiple Sclerosis (RRMS)?
- RRMS is characterized by attacks (relapses) with worsening neurological function, followed by periods of remission where they partially or fully recover. 85% of MS patients are initially diagnosed with RRMS.
- In RRMS, patients can experience a cumulative loss of physical (e.g. walking) and/or cognitive (e.g. memory) function over time, which impacts their daily and working lives.
- This loss of function in MS is driven by two types of damage that result in the loss of neurons and brain tissue - distinct inflammatory lesions (referred to as focal damage) which is caused by infiltration of immune cells into the central nervous system (CNS), and more widespread inflammatory neurodegenerative processes (referred to as diffuse damage), which are caused by activation of resident CNS cells.
- Focal damage results in the loss of brain tissue and can clinically present as relapses. Diffuse damage starts early in the disease and often goes unnoticed, it is also associated with loss of brain tissue and accumulated loss of function.
- It is important to address both focal and diffuse damage in RRMS to effectively impact disease activity and help preserve function.

What are 4 key measures of RRMS disease activity?
- Four key measures of RRMS disease activity are relapses, MRI lesions, brain shrinkage (brain volume loss) and disability progression.
- When these four key measures of RRMS disease activity are effectively impacted, the patient is known to have ‘no evidence of disease activity’ (NEDA4) which is ultimately the treatment goal for patients with RRMS.

How does Gilenya work in RRMS?
- Gilenya targets both focal and diffuse CNS damage. Gilenya prevents cells that cause focal inflammation from reaching the brain (referred to as ‘peripheral’ action), but also enters the CNS and reduces the diffuse damage by diminishing the harmful activation of resident cells (referred to as ‘central action’), as evidenced by animal studies and in vitro experiments.
- Gilenya is the only oral DMT to impact the course of RRMS with high efficacy across four key measures of disease activity (relapses, MRI lesions, brain shrinkage and disability progression).
What is the efficacy profile of Gilenya?

1. Reduction of relapses

Three in five patients had no relapses when continuously treated with Gilenya for up to 4.5 years\(^{11,a}\)

*Why this is significant:* Relapses may have a disabling impact on an individual's life, and incomplete recovery from a relapse can significantly advance their level of disability\(^{17}\).

2. Reduction of MRI lesions

Patients treated with Gilenya had five times fewer Gd+ T1 lesions* compared to placebo-treated patients at two years\(^{12,13,b}\)

*Why this is significant:* During the course of RRMS, inflammation driven focal damage can cause lesions (areas of damage) in the brain\(^{18}\). The number and volume of lesions have been shown to be associated with relapses and disability\(^{19}\).

3. Reduced rate of brain shrinkage

Gilenya is the only oral treatment with consistent, early and sustained reduction in brain volume loss\(^{14,15}\)

*Why this is significant:* MS patients lose brain volume up to three to five times faster than people without MS\(^{20-23}\). This acceleration starts early in the course of MS, even before symptoms are apparent. Brain shrinkage is associated with the loss of physical (e.g. walking) and cognitive (e.g. memory) function\(^{24}\) and can predict a patient’s disability over time.
4. Reduced disability progression

Four in five patients remained free of disability progression when continuously treated with Gilenya for up to four years

Why this is significant:
People with RRMS may increasingly lose their independence due to accumulating disability; some people may lose their ability to walk. Only ~50% of people with MS will be employed 10 years after diagnosis and two-thirds say having MS has affected their jobs. Early treatment is key to giving a person with RRMS as much time free of disability progression as possible.

Real-world use and confirmed tolerability of Gilenya

- Gilenya’s efficacy is confirmed both through clinical trials and in the real-world setting.
- Patients can stay on Gilenya for the long term, due to favorable tolerability and once-daily dosing.
- The most common side effects were headache, hepatic enzymes increased, influenza, sinusitis, diarrhea, back pain, and cough.
- Gilenya is approved in over 80 countries, and has been used to treat more than 100,000 patients in clinical trials and the post-marketing setting with more than 147,000 patient years of exposure.
- Accumulation of efficacy and safety data continues to confirm the positive benefit-risk profile of Gilenya.

* GD+ T1 lesions are lesions that are enhanced by gadolinium (GD), a chemical compound given during MRI scans that highlights a

** In patients with high disease activity despite standard interferon treatment.
- a. vs. 1 in 2 patients who were switched from Avonex® to Gilenya at 1 year; (p<0.001; exploratory analysis of core and extension study)
- b. p<0.001, secondary endpoint, ITT population
- c. vs. 7 in 10 patients switched from placebo to Gilenya at 2 years (p=0.012, secondary endpoint, 6m confirmed; n=425 and 418 for Gilenya and placebo-Gilenya patients respectively. Data taken from FREEDOMS extension study)

References:


31. Ziemssen T. et al. Comparison of therapy efficiency and treatment satisfaction of German RRMS patients on baseline therapy, compared to fingolimod-treated patients; results of an interim analysis of 2 non-interventional studies (PANGAEA and PEARL). Poster P595, presented at ECTRIMS, 2–5 October 2013, Copenhagen, Denmark.