NOVARTIS

25th January 2012

Direct Healthcare Professional Communication on strengthening the cardiovascular monitoring during treatment initiation with Gilenya (fingolimod) in patients with Relapsing Remitting Multiple Sclerosis

Dear Doctor,

Novartis would like to inform you about important additional recommendations to strengthen the monitoring of cardiovascular status for 6 hours after initiating treatment with Gilenya and to extend it, when necessary.

Gilenya is known to cause a transient bradycardia and might be associated with atrioventricular block, after the first dose as reflected in the current product information. The additional recommendations follow case reports of cardiovascular events including a patient who died of unknown cause after the first dose of Gilenya (fingolimod).

In agreement with the European Medicines Agency, the following recommendations are effective immediately for patients treated with Gilenya:

For all patients starting treatment, monitoring during the first 6 hours after dosing should include:

- A 12-lead ECG at baseline and 6 hours after the first dose
- Continuous 6-hour ECG monitoring
- Blood pressure and heart rate measurement every hour

In those patients with evidence of clinically important cardiac effects, monitoring should be extended until resolution. The following criteria for extended monitoring are recommended:

- The presence at the 6-hour time point after first dose of:
    - Heart rate less than 40 beats per minute
    - Decrease in heart rate of more than 20 beats per minute compared with baseline
    - Persistent new-onset 2nd degree atrioventricular block, Mobitz Type I (Wenckebach)
- The occurrence at anytime during the 6-hour monitoring of:
    - Symptomatic bradycardia
    - New onset 2nd degree atrioventricular block, Mobitz Type II
    - New onset 3rd degree atrioventricular block

Further information on the safety concern

Novartis has received case reports of cardiovascular events including a spontaneous report of a 59 year-old female patient with multiple sclerosis who died within 24 hours of taking the first dose of Gilenya. The patient was being treated with metoprolol and amlodipine for hypertension. The exact cause of death in this patient remains unknown at present. The updated recommendations aim to minimise the cardiovascular risk with Gilenya.

At the request of the European Medicines Agency, Novartis is conducting a complete review of cardiovascular events including data from clinical trials and post-marketing experience.

The content of this letter has been agreed with the European Medicines Agency and the Irish Medicines Board.

Call for Reporting

Please report any suspected adverse events associated with the use of fingolimod (Gilenya) to the Novartis Ireland Limited, Drug Safety and Epidemiology Desk at 01 2080612 or to the Irish Medicines Board.

Communication Information

Should you have any questions or require additional information regarding the use of fingolimod (Gilenya) please contact Dr. Greg Hays, Medical Director, Novartis Ireland Limited at 01-2601255.

Dr. Greg Hays
Medical Director
Novartis Ireland Limited