HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Fingolimod (Gilenya)-Risks related to immunosuppressive effects

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) advised that healthcare professionals and patients be informed of product information (Summary of Product Characteristics (SmPC) and Package Leaflet (PL)) changes in relation to the immunosuppressive effect of fingolimod and to reiterate some important recommendations for use.

Fingolimod is a sphingosine-1-phosphate receptor modulator, metabolised by sphingosine kinase to the active metabolite fingolimod-phosphate. It is indicated as single disease modifying therapy in adult patients with highly active relapsing remitting multiple sclerosis despite a full and adequate course of treatment with at least one disease-modifying therapy. It has been approved in the US since September 2010 and for use across the EU since March 2011.

Due to its potent immunosuppressive effects, patients are at risk of serious adverse reactions and healthcare professionals are advised as follows:

Advice to Healthcare Professionals

Basal Cell Carcinoma (BCC)

- Cases of BCC have been reported in patients receiving fingolimod from both the clinical trial setting and post-marketing surveillance.
- Healthcare professionals and patients should be aware that vigilance for skin lesions is warranted.
- Medical evaluation of the skin is recommended at initiation, after at least one year and then at least yearly taking into consideration clinical judgement.
- Patients should be referred to a dermatologist if suspicious lesions are detected.
- Patients with active malignancies (including BCC) should not be treated with fingolimod.

Opportunistic Infections

The immunosuppressive effects of fingolimod may increase the risk of CNS infections including opportunistic infections such as viral (e.g. herpes simplex virus, varicella zoster virus), fungal infections (e.g. cryptococcal meningitis) or bacterial infections (e.g. atypical mycobacterium). Prescribers are therefore reminded that:

- Initiation of treatment with fingolimod should be delayed in patients with severe active infection until the infection is completely resolved;
- The benefit-risk balance of using fingolimod should be considered for each individual patient prior to initiation of treatment and also prior to re-initiation of treatment;
- Suspension of treatment should be considered if a patient develops a serious infection;
- Following discontinuation of treatment, fingolimod may take up to two months to be eliminated from the body and healthcare professionals and patients should be alert for symptoms of infection during this period.

Lymphoma

- Cases of lymphoma have been reported in patients treated with fingolimod.

Progressive Multifocal Leukoencephalopathy (PML)

- PML is an opportunistic infection which may be fatal or result in severe disability and cases of PML have been reported in association with fingolimod;
- Before initiating treatment with fingolimod, a baseline MRI should be available (usually within 3 months as a reference).
- During routine MRI scans, healthcare professionals should pay attention to PML suggestive lesions;
- Patients and carers should be informed of the early symptoms suggestive of PML (e.g. change in behaviour/mood, memory lapses, speech difficulties) and recommended to seek immediate medical attention if any of these symptoms are experienced;
- If PML is suspected, treatment with fingolimod should be suspended until PML has been excluded.
- PML only occurs in the presence of a JCV infection. If JCV testing is undertaken however, it should be considered that the influence of lymphopenia on the accuracy of the anti-JCV antibody test has not been studied in fingolimod treated patients. Therefore a negative JCV antibody test does not preclude the possibility of subsequent JCV infection.

Complete Blood Count (CBC) Monitoring

- A recent (i.e. within the last six months or after discontinuation of prior therapy) complete blood count (CBC) should be available to healthcare professionals prior to initiating treatment with fingolimod to ensure that immune effects of previous therapy have resolved.
- Assessment of CBC is also recommended periodically during treatment i.e. three months after starting treatment and at least annually thereafter. CBC should also be measured in case of signs of infection.

Key Message

- In patients receiving fingolimod, medical evaluation of the skin before treatment initiation and during treatment is recommended due to a risk of BCC.
- Healthcare professionals/carers should be alert to the risk of PML and should inform patients/carers of early symptoms suggestive of PML recommending they seek medical advice if any experienced. During routine MRI scans, healthcare professionals should pay close attention to lesions suggestive of PML.
- Treatment with fingolimod should not be initiated in patients with severe active infection and suspension of treatment should be considered if a patient develops a serious infection.
- A CBC should be available prior to initiating treatment and regular CBC is recommended (i.e. 3 months after commencing treatment and at least annually thereafter).
- This information was highlighted in the HPRA's Drug Safety Newsletter (74th edition) and a Direct Healthcare Professional Communication (DHPC) was circulated to relevant healthcare professionals by the marketing authorisation holder in January 2016. Both documents are available from the HPRA website (www.hpra.ie).
- The product information for fingolimod (SmPC and PL) has been updated with this information.

*Further details on Gilenya are available on www.hpra.ie and www.ema.europa.eu

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