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An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

New warning on the risk of depression and related events associated with Kalydeco, Orkambi, Symkevi and Kaftrio

Key Message

- Depression (including suicidal ideation and suicide attempt) has been reported in patients treated with these medicines, usually within three months of treatment initiation, and in patients with a history of psychiatric disorders.
- In some cases, symptom improvement was reported after dose reduction or treatment discontinuation.
- Patients (and caregivers) should be alerted to the need to monitor for depressed mood, any suicidal thoughts, or unusual changes in behaviour.

Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor), Symkevi (tezacaftor/ivacaftor), and Kaftrio (elexacaftor/tezacaftor/ivacaftor) are cystic fibrosis transmembrane conductance regulator (CFTR) modulators authorised in the EU for the treatment of cystic fibrosis*. The European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) has recommended updates to the product information** for these medicines to include a new warning on the risk of depression.

The recommendation follows a review of the available data on the risk of depression and related events, including cases from spontaneous reports in post-marketing surveillance, some with a close temporal relationship and a positive de-challenge and re-challenge, and based on which the PRAC considered that a causal relationship is at least a reasonable possibility.

Depression (including suicidal ideation and suicide attempt) has been reported in patients, usually occurring within three months of treatment initiation and in patients with a history of psychiatric disorders. In some cases, symptom improvement was reported after dose reduction or treatment discontinuation.

Patients (and caregivers) should be alerted to the need to monitor for depressed mood, suicidal thoughts, or unusual changes in behaviour, and to seek medical advice immediately if these symptoms present.

The summary of product characteristics and package leaflet for these medicines will be updated accordingly.

*Please refer to product information for further details on authorised indications, available at www.ema.europa.eu.

** The approved product information comprises the Summary of Product Characteristics (SmPC) and Package Leaflet (PL) and is available at www.ema.europa.eu.

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