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Association of escitalopram (Lexapro®) with dose-dependent QT interval prolongation

Dear Healthcare Professional,

Lundbeck Ireland Limited, in collaboration with the Irish Medicines Board, would like to inform you of important new safety information on escitalopram (Lexapro®).

Summary:

- **Escitalopram is associated with dose-dependent QT interval prolongation**
- **In elderly patients age >65 years the maximum dose of escitalopram is now reduced to 10 mg daily**
- **The maximum dose of escitalopram for adults <65 years remains 20 mg daily**
- **Escitalopram is contraindicated in patients with known QT interval prolongation or congenital long QT syndrome**
- **Use of escitalopram with other medicinal products known to prolong the QT interval is contraindicated**
- **Caution is advised in patients at higher risk of developing Torsade de Pointes; for example, those with uncompensated heart failure, recent myocardial infarction, bradyarrhythmias or a predisposition to hypokalaemia or hypomagnesaemia because of concomitant illness or medicines**
- **Patients should be advised to contact a Healthcare Professional immediately if they experience an abnormal heart rate or rhythm while taking escitalopram.**

Further information on the safety concern

Escitalopram is a selective serotonin reuptake inhibitor (SSRI) indicated for the treatment of major depressive episodes, panic disorder with or without agoraphobia, social anxiety disorder, generalised anxiety disorder and obsessive compulsive disorder. Escitalopram is available as 5 mg, 10 mg, 15 mg and 20 mg film-coated tablets.

The new recommendations for escitalopram are the result of an assessment of a QT

study that revealed a dose-dependent increase of the QT interval observed with ECG. In addition, review of data from spontaneous reporting has identified cases of QT prolongation and ventricular arrhythmias including Torsade de Pointes associated with escitalopram use.

Lately, based on similar considerations, it was recommended to update the product information for the racemate citalopram and related generics with a general dose reduction, a dose reduction in the elderly and in patients with impaired liver function and new contraindications, warnings and precautions for use in patients with cardiovascular diseases.

The product information for escitalopram will be revised to include information about the risk for QT interval prolongation and the following new dosage and usage recommendations:

- A study was conducted assessing the effects of 10 mg and 30 mg escitalopram on the QT interval in healthy adults. Compared to placebo, the mean change from baseline in QTcF (Fridericia correction) was 4.3 ms at the 10 mg daily dose and 10.7 ms at the supratherapeutic 30 mg daily dose

- The recommended maximum dose in elderly patients aged over 65 years is now reduced to 10 mg daily

- The maximum recommended dose for adults <65 years remains unchanged at 20 mg daily

- The product information has also been updated with contraindications, warnings and precautions, and interactions including:
    - Escitalopram has been found to cause a dose-dependent prolongation of the QT interval
    - Cases of ventricular arrhythmia including Torsade de Pointes have been reported during the post-marketing period, predominantly in patients of female gender, with hypokalaemia and with pre-existing QT interval prolongation or other cardiac diseases
    - Escitalopram is contraindicated in patients with known QT interval prolongation and congenital long QT syndrome.
    - Use of escitalopram is also contraindicated in combination with other drugs known to prolong the QT interval. These include:
        - Class IA and III antiarrhythmics
        - antipsychotics (e.g. fentiazine derivatives, pimozide, haloperidol)
        - tricyclic antidepressants
        - some antimicrobial agents (e.g. sparfloxacin, moxifloxacin, erythromycin IV, pentamidine, anti-malarial treatment particularly halofantrine)
        - some antihistamines (e.g. astemizole, mizolastine)
    - Caution is advised in patients at higher risk of developing Torsade de Pointes; for example, those with uncompensated heart failure, recent myocardial

infarction, bradyarrhythmias or a predisposition to hypokalaemia or hypomagnesaemia because of concomitant illness or medicines

Patients should be advised to contact a Healthcare Professional immediately if they experience signs and symptoms of an abnormal heart rate or rhythm while taking escitalopram.

Patients should not stop taking escitalopram or change or reduce the dose without first consulting their Healthcare Professional, as withdrawal symptoms may occur when escitalopram treatment is discontinued, particularly if this is abrupt (Refer to the product information for more information regarding withdrawal symptoms).

Healthcare Professionals are advised to review elderly patients who currently take doses of escitalopram that are above the new recommended maximum dose, and gradually reduce the dose accordingly.

Cases of QT interval prolongation have been reported also in association with some other SSRIs, including the racemate citalopram. For further information, please refer to the respective product information.

Healthcare Professionals and patients are encouraged to report any product-related adverse reactions to the marketing authorisation holder (see contact details below) or to the IMB using a Yellow Card obtained either from the IMB, or electronically via the website at www.imb.ie.

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Yours faithfully,

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