

Escitalopram and risk of QT prolongation

Final SmPC and PL wording agreed by the PhVWP December 2011

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SUMMARY OF PRODUCT CHARACTERISTICS

4.2 Posology and method of administration

Elderly patients (> 65 years of age)

Initial dosage is 5 mg once daily. Depending on individual patient response the dose may be increased to 10 mg daily (see section 5.2).

(...)

4.3 Contraindications

(...)

Escitalopram is contraindicated in patients with known QT-interval prolongation or congenital long QT syndrome.

Escitalopram is contraindicated together with medicinal products that are known to prolong the QT-interval (see section 4.5).

4.4 Special warnings and precautions for use

(...)

QT interval prolongation

Escitalopram has been found to cause a dose-dependent prolongation of the QT-interval. Cases of QT interval prolongation and ventricular arrhythmia including torsade de pointes have been reported during the post-marketing period, predominantly in patients of female gender, with hypokalaemia, or with pre-existing QT interval prolongation or other cardiac diseases (see sections 4.3, 4.5, 4.8, 4.9 and 5.1).

Caution is advised in patients with significant bradycardia; or in patients with recent acute myocardial infarction or uncompensated heart failure.

Electrolyte disturbances such as hypokalaemia and hypomagnesaemia increase the risk for malignant arrhythmias and should be corrected before treatment with escitalopram is started.

If patients with stable cardiac disease are treated, an ECG review should be considered before treatment is started.

If signs of cardiac arrhythmia occur during treatment with escitalopram, the treatment should be withdrawn and an ECG should be performed.

4.5 Interaction with other medicinal products and other forms of interactions

(...)

Contraindicated combinations

QT interval prolongation

Pharmacokinetic and pharmacodynamic studies of escitalopram combined with other medicinal products that prolong the QT interval have not been performed. An additive effect of escitalopram and these medicinal products cannot be excluded. Therefore, co-administration of escitalopram with medicinal products that prolong the QT interval, such as Class IA and III antiarrhythmics, antipsychotics (e.g. phenothiazine derivatives, pimozide, haloperidol), tricyclic antidepressants, certain antimicrobial agents (e.g. sparfloxacin, moxifloxacin, erythromycin IV, pentamidine, anti-malarian treatment particularly halofantrine), certain antihistamines (astemizole, mizolastine), is contraindicated.

Influence of other medicinal products on the pharmacokinetics of escitalopram

(...)

Co-administration of escitalopram with cimetidine 400 mg twice daily (moderately potent general enzyme-inhibitor) resulted in a moderate (approximately 70%) increase in the plasma concentrations of escitalopram. Caution is advised when administering escitalopram in combination with cimetidine. Dose adjustment may be warranted.

4.8 Undesirable effects

To be added in the table, under “Cardiac disorders”

Frequency unknown:

Ventricular arrhythmia including torsade de pointes

(...)

To be added below the table

QT interval prolongation

Cases of QT interval prolongation and ventricular arrhythmia including torsade de pointes have been reported during the post-marketing period, predominantly in patients of female gender, with hypokalaemia, or with pre-existing QT interval prolongation or other cardiac diseases (see sections 4.3, 4.4, 4.5, 4.9 and 5.1).

To be deleted

~~Cases of QT prolongation have been reported during the post-marketing period, predominantly in patients with pre-existing cardiac disease. In a double-blind, placebo-controlled ECG study in healthy subjects, the change from baseline in QTc (Fridericia correction) was 4.3 msec at the 10 mg/day dose and 10.7 msec at the 30 mg/day dose.~~

4.9 Overdose

Management

(...)

ECG monitoring is advisable in case of overdose, in patients with congestive heart failure/bradyarrhythmias, in patients using concomitant medications that prolong the QT interval, or in patients with altered metabolism, e.g. liver impairment.

5.1 Pharmacodynamic properties

(...)

Pharmacodynamic effects

In a double-blind, placebo-controlled ECG study in healthy subjects, the change from baseline in QTc (Fridericia-correction) was 4.3 msec (90% CI: 2.2, 6.4) at the 10 mg/day dose and 10.7 msec (90% CI: 8.6, 12.8) at the suprathreshold dose of 30 mg/day (see sections 4.3, 4.4, 4.5, 4.8 and 4.9).

PACKAGE LEAFLET

2. BEFORE YOU TAKE <PRODUCT>

Do not take <Product>

(...)

- If you are born with or have had an episode of abnormal heart rhythm (seen at ECG; an examination to evaluate how the heart is functioning)
- If you take medicines for heart rhythm problems or that may affect the heart's rhythm (see section 2 "Taking other medicines")

Take special care with <Product>

(...)

- if you suffer or have suffered from heart problems or have recently had a heart attack
- if you have a low resting heart-rate and/or you know that you may have salt depletion as a result of prolonged severe diarrhoea and vomiting (being sick) or usage of diuretics (water tablets)
- if you experience a fast or irregular heartbeat, fainting, collapse or dizziness on standing up, which may indicate abnormal functioning of the heart rate

Taking other medicines

(...)

DO NOT TAKE <PRODUCT> if you take medicines for heart rhythm problems or medicines that may affect the heart's rhythm, such as Class IA and III antiarrhythmics, antipsychotics (e.g. phenothiazine derivatives, pimozide, haloperidol), tricyclic antidepressants, certain antimicrobial agents (e.g. sparfloxacin, moxifloxacin, erythromycin IV, pentamidine, anti-malarian treatment particularly halofantrine), certain antihistamines (astemizole, mizolastine). If you have any further questions about this you should speak to your doctor.

3. HOW TO TAKE <PRODUCT>

(...)

Elderly patients (above 65 years of age)

The recommended starting dose of <product> is 5 mg taken as one daily dose. The dose may be increased by your doctor to 10 mg per day.

4. POSSIBLE SIDE EFFECTS

(...)

If you experience the following side effects you should contact your doctor or go to the hospital straight away:

- (...)

- Fast, irregular heart beat, fainting which could be symptoms of a life-threatening condition known as Torsades de Pointes.

Some patients have reported (frequency cannot be estimated from the available data):

- (...)
- Alteration of the heart rhythm (called “prolongation of QT interval”, seen on ECG, electrical activity of the heart).