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VSEM IMETNIKOM DOVOLJENJ ZA PROMET Z ZDRAVILI, KI VSEBUJEJO ESCITALOPRAM

Zahteva za predložitev spremembe tipa IB – dopolnitev povzetka glavnih značilnosti zdravila in navodila za uporabo za zdravila, ki vsebujejo escitalopram

Spoštovani,

Delovna skupina za farmakovigilanco (PhVWP) pri Evropski agenciji za zdravila EMA je v decembru 2011 pregledala oceno študije QT in povezanosti od odmerka odvisno podaljšanje intervala QT. Na osnovi ocene podatkov je zaključila, da je treba informacije v povzetku glavnih značilnosti zdravila in navodilih za uporabo za zdravila, ki vsebujejo escitalopram, ustrezno dopolniti.

Imetnike dovoljenj za promet z zadevnimi zdravili, ki vloge za spremembo dovoljenja za promet še niso vložili, prosimo, da Javni agenciji RS za zdravila in medicinske pripomočke v skladu s Pravilnikom o dovoljenju za promet z zdravilom za uporabo v humani medicini (Uradni list RS, št. 109/2010) predložijo spremembo tipa IB. Vlogo za zadevna zdravila, ki so pridobila dovoljenje za promet po nacionalnem postopku, imetniki dovoljenj za promet predložijo najkasneje v 30 dneh ob objave obvestila, za zdravila, ki so pridobila dovoljenje za promet po mednarodnih postopkih, pa v skladu s časovnico referenčne države članice (RMS). Dodatne informacije in podporna dokumentacija v vlogi niso potrebne.

V nadaljevanju vam podajamo odobreno originalno besedilo spremembe, objavljeno je tudi na spletni strani Vodij agencij za zdravila http://www.hma.eu/222.html.

S spoštovanjem,

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Pripravila:
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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. phenotiazine 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 supratherapeutic 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 rhrythm (called “pronlongation of QT interval”, seen on ECG, electrical activity of the heart).