



Direct Healthcare Professional Communication

January 2022

Donepezil-QTc interval extension and Torsade de Pointes

Dear Healthcare Professional,

The Egyptian Pharmaceutical Vigilance Center of the Central Administration for Pharmaceutical Care at The Egyptian Drug Authority would like to inform you of the following:

Summary:

- Cases of QTc interval prolongation and torsade de pointes have been reported in the post-marketing setting with the use of donepezil.
- Caution is advised:
 - in patients with existing or familial QTc interval prolongation
 - in patients concomitantly treated with medicinal products that affect the QTc interval.
 - in patients with relevant pre-existing heart disease (e.g., uncompensated heart failure, recent heart attack, bradyarrhythmia) or electrolyte disorders (hypokalemia, hypomagnesaemia).
- ECG monitoring should be considered in patients at risk.
- Adverse effects newly included in the product information: Polymorphic ventricular tachycardia including torsade de pointes, prolonged QTc interval in the electrocardiogram.

Background on the safety concern

Donepezil is a selective reversible acetylcholinesterase inhibitor which is indicated for the symptomatic treatment of mild to moderate Alzheimer's disease.

The risk of cholinergic effects on heart rate is already known. The product information includes a warning that cholinesterase inhibitors may have vagotonic effects on the heart rate (e.g., bradycardia) and that the potential for this effect in patients with sick sinus syndrome or other supraventricular excitation conditions, such as: B. sinoatrial or atrioventricular block, may be particularly important.

The latest changes to the product information for donepezil are the result of an evaluation of post-marketing data and the scientific literature. Reports of QTc interval extensions and torsade de pointes associated with donepezil use have been identified and assessed by the EMA. It was found that a causal relationship between donepezil and QTc interval extensions and Torsade de Pointes is at least a reasonable possibility. Since the assessment was primarily based on spontaneous reports of adverse events after marketing, the frequency is reported as unknown.





The product information and package leaflet for donepezil-containing medicinal products are updated in the sections Warnings and Precautions, Interactions and Side Effects.

References

Germany

<https://www.bfarm.de/SharedDocs/Risikoinformationen/Pharmakovigilanz/DE/RHB/2021/rhb-donepezil.html;jsessionid=9575B3719F71286DD115E1B4357EE630.internet562?nn=591002>

Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions via the Egyptian reporting system:

Name: Egyptian Pharmaceutical Vigilance Center

Address: 21 Abd El Aziz Al Soud Street, El-Manial, Cairo, Egypt, And PO Box: 11451 Telephone: +202- 25354100, Extension: 1470 Fax: +202 – 23610497

Email: pv.followup@edaegypt.gov.eg

Online reporting: <https://primaryreporting.who-umc.org/EG>

QR Code:

Hotline: 15301

