Direct Healthcare Professional Communication

May 2024

Medicines containing omega-3 fatty acids: dose-dependent increased risk of atrial fibrillation in patients with established cardiovascular diseases or cardiovascular risk factors

Dear Healthcare Professional,

The General Administration for Pharmaceutical Vigilance of the Central Administration for Pharmaceutical Care at The Egyptian Drug Authority would like to inform you **about omega-3 fatty acids: dose-dependent increased risk of atrial fibrillation**

Summary:

reviews and meta-analyses of randomized controlled trials demonstrated a dose-dependent increased risk of atrial fibrillation in patients with established cardiovascular disease or cardiovascular risk factors treated with omega-3 fatty acid-containing drugs compared to placebo.

- The observed risk of atrial fibrillation was at a dose of 4 g/day the highest
- Healthcare professionals should advise patients to seek medical attention if they develop symptoms of atrial fibrillation.
- If atrial fibrillation develops, treatment with these Medicines should be permanently discontinued

Background information on the safety concerns:

Medicines containing omega-3 fatty acids are approved in different formulations and predominantly contain the polyunsaturated fatty acids (PUFAs) eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DPA). Omega-3 acid ethyl esters 60 and 90 Ph. Eur. are ethyl esters of PUFAs with EPA and DHA as the main component of the active ingredient.

If atrial fibrillation develops, treatment should be permanently discontinued.

Drugs containing omega-3 acid ethyl esters are indicated for lowering triglyceride levels (hypertriglyceridemia) when the response to diet and other non-pharmacological measures has proven inadequate.

Medicines that contain omega-3 fatty acids, for example as fish oil rich in omega-3 fatty acids or in the form of triglycerides, are approved for various areas of application. On the one hand, to

lower severely elevated blood fat (triglyceride) levels when diet alone is not enough to lower blood fat levels. On the other hand, also in various drugs for parenteral nutrition when oral or enteral nutrition is not possible, inadequate or contraindicated.

The Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) assessed data from several systematic reviews and meta-analyses of large randomized controlled trials (RCTs) involving a total of more than 80,000 patients, mostly with cardiovascular disease or cardiovascular risk factors , were included and examined treatment with omega-3 fatty acids on cardiovascular outcomes compared to placebo.

Data from these studies showed a dose-dependent increased risk of atrial fibrillation (AF) in patients with established cardiovascular disease or cardiovascular risk factors treated with omega-3 fatty acid-containing medicines compared to patients treated with placebo. The risk observed was highest at a dose of 4 g/day.

The most relevant evidence for an increased AF risk with omega-3 fatty acids comes from three Meta Analysis

- A meta-analysis by Lombardi et al. (1) showed that supplementation of omega-3 Fatty acids were associated with an increased risk of incident AF compared with placebo [IRR 1.37, 95% CI(1.22-1.54), P < 0.001].

- A systematic review and meta-analysis by Gencer et al. (2) showed that omega-3 Fatty acid preparations are associated with an increased risk of AF (HR 1.25, 95% CI 1.07–1.46, P = 0.013).HR was higher in studies testing more than 1 g/day of omega-3 fatty acids (HR 1.49, 95% CI 1.04-2.15, P =0.042) than in those testing ÿ 1 g/day (HR 1.12, 95% CI 1.03-1.22, P = 0.024, P for interaction < 0.001).

- A meta-analysis by Yan et al. (3), which examined the clinical benefit of omega-3 fatty acid supplementation, showed that omega-3 fatty acid supplementation is associated with an increased risk of AF (RR 1.32 95%CI 1.11-1.58; P = 0.002).

- Healthcare professionals should advise patients to seek medical attention if they experience symptoms of atrial fibrillation such as dizziness, asthenia, palpitations or shortness of breath If atrial fibrillation develops, treatment should be permanently discontinued.

Reference:

BfArM:https://www.bfarm.de/SharedDocs/Risikoinformationen/Pharmakovigilanz/DE/RHB/2023/rhb-omega-3-fettsaeure.html?nn=591002

Call for reporting

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

Name: General Administration for Pharmaceutical Vigilance

Email: pv.followup@edaegypt.gov.eg

Online reporting: https://primaryreporting.who-umc.org/EG
QR Code:

Hotline: 15301