European Parliament
2019-2024

Committee on Petitions

24.7.2019

NOTICE TO MEMBERS

Subject: Petition No 0104/2019 by Panagiotis Karapanagiotis (Greek) on toxic poisoning by a cross-polarizing substance Dotarem following a medical examination in Greece

1. Summary of petition

The petitioner claims that the medicinal product Dotarem (a gadolinium-based contrast imaging agent), which is marketed in the European Union and used during medical examination procedures with Magnetic Resonance Imaging (MRI), caused him serious toxic poisoning. In particular, he claims that the medication was not removed by the kidneys within one week, as indicated on the medication's instructions, and that 3.5 months after he was administered the medication, it was diagnosed that the amount of gadolinium that exits from his urine is three times the maximum acceptable limit. He also claims that, as a result, he developed systemic fibrosis throughout his body with obvious damage to the skin, eyes, face, and severe physical exhaustion.

2. Admissibility

Declared admissible on 8 May 2019. Information requested from Commission under Rule 227(6).

3. **Commission reply**, received on 24 July 2019

Dotarem belongs to a group of contrast agents that contain the substance gadolinium. Gadolinium contrast agents are given to patients during body scans to help obtain a clear image of the inside of the body. Most of the gadolinium contrast agents, including Dotarem, are authorised at national level through a marketing authorisation granted by the Member State.

Like any other medicinal product, contrast agents are subject to a post-marketing surveillance

for which obligations to marketing authorisation holders and competent authorities are set by the legislation. Among other obligations, the marketing authorisation holders are obliged to submit to the European Medicines Agency (EMA) periodic safety update reports (PSURs) about their medicines including summaries of data relevant to the benefits and risks of the medicinal product and results of all studies with a consideration of their potential impact on the marketing authorisation.

In addition, the marketing authorisation holder is responsible for informing the competent authorities of any new information which might influence the evaluation of the benefits and risks of the medicinal product concerned. This information must be updated regularly on the basis of recent scientific knowledge.

Following new information about the retention of small amounts of gadolinium in the brain after a scan, in March 2016, the Commission requested EMA to conduct a review of those contrast agents under Article 31 of Directive 2001/83/EC[1] in order to investigate the accumulation of gadolinium in different body tissues and the impact on the overall benefit-risk balance of the products concerned.

In 2017 several restrictions and additional measures were put in place as an outcome of this review. These measures differentiated between the two classes of gadolinium contrast agents, i.e. linear and macrocyclic (Dotaram–gadoteric acid belongs to the macrocyclic class).

The EMA scientific review concluded that the macrocyclic agents are more stable and have a lower propensity to release gadolinium than linear agents. Therefore, the macrocyclic agents can continue to be used in their current indications but in the lowest doses that enhance images sufficiently and only when unenhanced body scans are not suitable. To the contrary and subject to some limited exceptions, most of the marketing authorisations for linear products were suspended.

The outcome of this scientific review is also reflected in the patient and prescriber information. As for every authorised product, the relevant patient and prescriber information summarises the current scientific knowledge including benefits, risks and specific warnings. In the case of Dotaram, it should be noted that the risk of systemic fibrosis is reflected in the summary of product characteristics and patient leaflet.

This being said, before using Dotaram, a physician has always to consider whether the proposed testing method is adequate in view of the benefits and risks it involves and in view of the specific patient the doctor is treating.

The Commission is not in a position to comment on the petitioner’s claims with regard to compensation. This is a Member State competence under Article 168 of the Treaty on the

[1] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, *OJ L 311, 28.11.2001, p. 67–128.*

Functioning of the European Union[2].

Conclusion

The Commission believes that the necessary measures to protect European patients are in place. Gadolinium-containing contrast agents have been subject to a recent review in order to take the necessary measures to ensure that the medicines which are made available to patients in the EU correspond to high standards of safety, quality and efficacy.

[2] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:12012E/TXT&from=EN