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PRAC confirms restrictions on the use of linear gadolinium agents

Benefit-risk balance of certain linear gadolinium agents no longer favourable

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has confirmed its previous conclusion from March 2017 that there is convincing evidence of gadolinium deposition in brain tissues following use of gadolinium contrast agents.

No specific conditions linked to gadolinium deposition in the brain have been identified, but the clinical consequences are unknown.

As a result of the review, the PRAC recommends that the intravenous linear agents gadoxetic acid and gadobenic acid should only be used for liver scans in the situations where they meet an important diagnostic need. In addition, gadopentetic acid should only be used for joint scans as the gadolinium concentration in the formulation used for joint injections is very low.

All other intravenous linear agents (gadodiamide, gadopentetic acid and gadoversetamide) should be suspended in line with the PRAC's March 2017 recommendation.

Another class of gadolinium agents known as macrocyclic agents (gadobutrol, gadoteric acid and gadoteridol) are more stable and have a lower propensity to release gadolinium than linear agents. These 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.

The PRAC's recommendation will now be sent to the Committee for Medicinal Products for Human Use (CHMP), which will adopt the Agency's final opinion.

More about the medicines

Gadolinium contrast agents are used as contrast enhancers to improve image quality with magnetic resonance (MR) scans. These body scans rely on the magnetic fields produced by water molecules in the body. Once injected, gadolinium interacts with the water molecules. As a result of this interaction, the water molecules give a stronger signal, helping to obtain a brighter image.

This review covers agents containing the following active substances: gadobenic acid, gadobutrol, gadodiamide, gadopentetic acid, gadoteric acid, gadoteridol, gadoversetamide and gadoxetic acid.

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Most gadolinium-containing contrast agents have been authorised nationally in the European Union (EU). OptiMARK (gadoversetamide) is the only gadolinium contrast agent that was authorised centrally in the EU.

More about the procedure

The review of gadolinium contrast agents was initiated on 17 March 2016 at the request of the European Commission, under Article 31 of Directive 2001/83/EC.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which made a set of recommendations in March 2017.

Following a request from companies concerned, the PRAC re-examined its initial recommendation. The PRAC's final recommendations will now be sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's opinion.

The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.