

Pressemitteilung des Pharmacovigilance Risk Assessment Committee (PRAC) der European Medicines Agency (EMA) bezüglich gadoliniumhaltiger MR-Kontrastmittel: Was bedeutet dies für die Radiologen in der Schweiz?

In der Pressemitteilung des Pharmacovigilance Risk Assessment Committee (PRAC) vom 10. März 2017 (siehe Seite 2) wird empfohlen vier lineare MR Kontrastmittel ‚vom europäischen Markt‘ zu nehmen. Hierbei handelt es sich um folgende Produkte:

Wirkstoff	Handelsname	Hersteller
Gadobensäure	Multihance	Bracco
Gadodiamid	Omniscan	GE Healthcare
Gadopentetsäure	Magnograf	Berlis
Gadoversetamid	Optimark	Mallinckrodt

Gadoversetamid (Optimark) ist in der Schweiz nicht verfügbar, sodass letztendlich die drei Kontrastmittel Gadobensäure (Multihance), Gadodiamid (Omniscan) und Gadopentetsäure (Magnograf) verbleiben. Bei letzterem ist zu sagen, dass dies lediglich die intravenöse Applikation betrifft; die intraartikuläre Applikation von Gadopentetsäure (Magnevist® 2 mmol/l Injektionslg) ist von dieser Empfehlung ausgenommen, da nach Ansicht der Kommission die Vorteile die potentiellen Nachteile überwiegen. Das gleiche gilt für Gadoxetsäure (Primovist), ebenfalls ein lineares MR-Kontrastmittel: auch hier ist das PRAC der Meinung, dass die Vorteile die potentiellen Nachteile überwiegen.

Vorerst (Zeitpunkt: 10.03.2017) ist es nur eine Empfehlung, die das Pharmacovigilance Risk Assessment Committee (PRAC) ausgesprochen hat. Diese Empfehlung geht nun an das Committee for Medicinal Products for Human Use (CHMP), welches vermutlich die Empfehlung des PRAC übernehmen wird (aber nicht muss!). Es ist dann an den Zulassungsinhabern (sprich Herstellerfirmen) darzulegen, dass die Vorteile allfällige Nachteile überwiegen oder nachzuweisen, dass ihre Produkte kein Gadolinium freisetzen. Hinsichtlich des zeitlichen Ablaufes wird es auch darauf ankommen, ob die Firmen einen aufschiebenden Einspruch einlegen können, oder ob ein Widerruf der Zulassung unabhängig von allfälligen Einsprüchen der Firmen Bestand hat.

Was die Schweiz betrifft, muss dann Swissmedic nachziehen und für die betroffenen Produkte die Zulassung zurückziehen. Es ist aber davon auszugehen, dass Swissmedic den Entscheid der European Medicines Agency (EMA) übernehmen wird.



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PRAC concludes assessment of gadolinium agents used in body scans and recommends regulatory actions, including suspension for some marketing authorisations

Review finds evidence of gadolinium deposits in the brain after MRI body scans but no signs of harm

EMA's Pharmacovigilance and Risk Assessment Committee (PRAC) has recommended the suspension of the marketing authorisations for four linear gadolinium contrast agents because of evidence that small amounts of the gadolinium they contain are deposited in the brain.

The agents concerned are intravenous injections of gadobenic acid, gadodiamide, gadopentetic acid and gadoversetamide, which are given to patients to enhance images from magnetic resonance imaging (MRI) body scans.

The PRAC's review of gadolinium agents found convincing evidence of accumulation of gadolinium in the brain from studies directly measuring gadolinium in brain tissues and areas of increased signal intensity seen on MRI scan images many months after the last injection of a gadolinium contrast agent.

The companies concerned by this review have the right to request the PRAC to re-examine its recommendations.

The PRAC's final recommendations will be sent to the Committee for Medicinal Products for Human Use (CHMP) for its opinion. Further details will be published at the time of the CHMP opinion.

Although no symptoms or diseases linked to gadolinium in the brain have been reported, the PRAC took a precautionary approach, noting that data on the long-term effects in the brain are limited. Deposition of gadolinium in other organs and tissues has been associated with rare side effects of skin plaques and nephrogenic systemic fibrosis,¹ a scarring condition in patients with kidney impairment. Furthermore, non-clinical laboratory studies have shown that gadolinium can be harmful to tissues.

The four agents recommended for suspension are referred to as linear agents. Linear agents have a structure more likely to release gadolinium, which can build up in body tissues. Other agents, known as macrocyclic agents, are more stable and have a much lower propensity to release gadolinium. The

¹ See EMA [review](#) of gadolinium contrast agents in 2010.



PRAC recommends that macrocyclic agents² be used at the lowest dose that enhances images sufficiently to make diagnoses and only when unenhanced body scans are not suitable.

Some linear agents will remain available: gadoxetic acid, a linear agent used at a low dose for liver scans, can remain on the market as it meets an important diagnostic need in patients with few alternatives. In addition, a formulation of gadopentetic acid injected directly into joints is to remain available because its gadolinium concentration is very low – around 200 times lower than those of intravenous products. Both agents should be used at the lowest dose that enhances images sufficiently to make diagnoses and only if unenhanced scans are not suitable.

For those marketing authorisations recommended for suspension, the suspensions can be lifted if the respective companies provide evidence of new benefits in an identified patient group that outweigh its risks or show that their product (modified or not) does not release gadolinium significantly (dechelation) or lead to its retention in tissues.

More about the medicine

Gadolinium contrast agents are used as contrast enhancers to improve image quality with MRI scans.

MRI is an imaging method that relies 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.

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. The PRAC's final recommendations will 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.

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² Gadobutrol, gadoteric acid and gadoteridol