Press release

Gadolinium-based Contrast Agents: update on PRAC recommendations

Villepinte, March 13, 2017 - Guerbet (FR0000032526 GBT), a global specialist in contrast products and solutions for medical imaging, takes note of the recommendations issued by the Pharmacovigilance Risk Assessment Committee (PRAC), on Gadolinium-based Contrast Agents - procedure under Article 31 of Directive 2001/83/EC.

On March 17, 2016, the European Medicines Agency (EMA) initiated a review of the risk of gadolinium deposition in brain tissue following the repeated use of gadolinium contrast agents in patients undergoing magnetic resonance imaging (MRI) scans.[1]

After carrying out an almost year-long in-depth review of the risk of brain deposits and of the overall safety of these products, the PRAC recommendations[2] are as follows:

> *"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.*
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> *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. (…)*
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> *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 PRAC recommends that macrocyclic agents[3] 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*

[1] *http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Gadolinium-containing_contrast_agents/human_referral_prac_000056.jsp&mid=WC0b01ac05805c516f*
[2] *Gadolinium Article-31 referral - PRAC concludes assessment of gadolinium agents used in body scans and recommends regulatory actions, including suspension for some marketing authorisations. 10/03/2017*
[3] *Gadobutrol, gadoteric acid and gadoteridol*

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. (…)"

"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."

Guerbet has read carefully and agrees with the PRAC recommendations. Guerbet does not intend to request a re-examination of their recommendations.

Guerbet markets Dotarem® and Artirem® (gadoteric acid), products belonging to the class of macrocyclic gadolinium-based contrast agents, a class of agents for which PRAC specifies it has a "*much lower propensity to release gadolinium*",[2] and Optimark® (gadoversetamide), a product belonging to the class of linear gadolinium-based contrast agents, a class of agents for which PRAC specifies they have "*a structure more likely to release gadolinium*".[2]

Guerbet is strongly committed to providing healthcare professionals with a comprehensive range of effective and safe contrast media in order to improve diagnosis, prognosis and quality of life for patients.

About Guerbet

Guerbet is a pioneer in the contrast agent field, with 90 years' experience, and is the only pharmaceutical group dedicated to medical imaging worldwide. It offers a comprehensive range of X-Ray, Magnetic Resonance Imaging (MRI) and Interventional Radiology and Theranostics (IRT) products, along with a range of injectors and related medical devices to improve the diagnosis and treatment of patients. To discover new products and ensure future growth, Guerbet invests heavily in R&D on which it spends around 9% of its sales each year. Guerbet (GBT) is listed on Euronext Paris (Segment B – Mid Caps) and generated €776 million in revenue in 2016.

For more information about Guerbet, please visit www.guerbet.com

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