29th January 2011

Circular No. P02/ 2011

Dear Healthcare Professional,

Re: European Medicines Agency's review makes recommendations to minimise risk of nephrogenic systemic fibrosis with gadolinium-containing contrast agents.

Gadolinium-containing contrast agents are used in patients undergoing magnetic resonance imaging (MRI) or magnetic resonance angiography (MRA) scans. The Agency's Committee for Medicinal Products for Human Use (CHMP) reviewed these agents because of the association between the use of gadolinium-containing contrast agents and NSF, a rare, serious and sometimes life-threatening condition that is characterised by formation of connective tissues in the skin, joints, muscles and internal organs, in patients with severe kidney problems.

Because the risk of developing NSF depends on the type of gadolinium-containing contrast agent used, the active substances are classified into three categories of risk (high-, medium-, and low-risk groups). The CHMP's recommendations for the different agents vary according to their risk classification. In Malta, the only licensed medicinal product containing gadolinium is Gadovist 1.0 mmol/ml solution for injection presented in a pre-filled syringe that is authorised in line with article 126a. It is currently being used in our local hospitals. Gadovist is considered as carrying a **low risk** for causing NSF.

For **high-risk** gadolinium-containing contrast agents (Optimark, Omniscan, Magnevist, Magnegita and Gado-MRT ratiopharm) the Committee recommended contraindications in patients with severe kidney problems, in patients who are scheduled for or have recently received a liver transplant and in newborn babies up to four weeks of age. To minimise the risk of using these high-risk agents in patients with unknown kidney problems, the CHMP advised that patients should always be screened for kidney problems using laboratory tests before use. The CHMP also recommended that women should discontinue breastfeeding for at least 24 hours after a scan.

For **medium**- (Vasovist, Primovist and MultiHance) and **low-risk** agents (Dotarem, ProHance and Gadovist), the CHMP recommended adding new warnings in the prescribing information concerning

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their use in patients with severe kidney problems and patients receiving a liver transplant. The CHMP advised that screening patients for kidney problems using laboratory tests is generally recommended before administration of these gadolinium-containing contrast agents and that the decision to continue or suspend breastfeeding for at least 24 hours after a scan should be taken by the doctor and the mother.

The CHMP recommended that the prescribing information of all gadolinium-containing contrast agents should include:

- a warning that the elderly may be at particular risk of NSF due to impaired ability of their kidneys to clear gadolinium from the body;
- a statement that there is no evidence to support the initiation of haemodialysis to prevent or treat NSF in patients not already undergoing haemodialysis
- a statement that the type and dose of contrast agent used should be recorded.

Based on currently available data, and with these risk minimisation measures in place, the CHMP considers that the balance of benefits and risks of these agents is acceptable

Finally, the CHMP recommended that further studies should be carried out on the long-term retention of gadolinium in human tissues.European Commission decisions on this opinion will be issued in due course

The Medicines Authority has participated in the discussions held at the EMA and is in agreement with the full **press release** issued by the EMA, attached here for your perusal. A **question-and-answer** document with more information about the outcome of this assessment is also available.

Healthcare professionals are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis

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