
FDA
U.S. Food and Drug Administration
Department of Health and Human Services
CENTER FOR DRUG EVALUATION AND RESEARCH

Public Health Advisory

Gadolinium-containing Contrast Agents for Magnetic Resonance Imaging (MRI): Omniscan, OptiMARK, Magnevist, ProHance, and MultiHance

This information is not current.
The FDA has issued new information about this safety issue, please see
http://www.fda.gov/cder/drug/infopage/gcca/default.htm

The FDA is evaluating important safety information about gadolinium-containing contrast agents and a disease known as Nephrogenic Systemic Fibrosis or Nephrogenic Fibrosing Dermopathy (NSF/NFD) that occurs in patients with kidney failure. New reports have identified a possible link between NSF/NFD and exposure to gadolinium containing contrast agents used at high doses for a procedure called Magnetic Resonance Angiography (MRA). An MRA test uses magnetic resonance imaging to take pictures of blood vessels. During an MRA test, a drug known as a gadolinium-contrast agent is injected into a patient's vein so blood vessels can be distinguished from other nearby tissues.

The FDA has learned of 25 cases of NSF/NFD in patients with kidney failure who received Omniscan®, a gadolinium-containing contrast agent, and took the MRA test. The FDA is actively investigating whether exposure to a gadolinium-contrast agent for MRA is associated with the development of NSF/NFD. While FDA conducts its investigation, the following recommendations are being provided to health care providers and patients:

- Gadolinium-containing contrast agents, especially at high doses, should be used only if clearly necessary in patients with advanced kidney failure (those currently requiring dialysis or with a Glomerular Filtration Rate (GFR) = 15 cc/min or less).
- It may be prudent to institute prompt dialysis in patients with advanced kidney dysfunction who receive a gadolinium contrast MRA. Although there are no data to determine the utility of dialysis to prevent or treat NSF/NSD in patients with decreased kidney function, average excretory rates of gadolinium are 78%, 96%, and 99% in the first to third hemodialysis sessions, respectively (Okada, et al, Acta Radiologica, vol 42 p. 339, May 2001).

Five gadolinium-containing contrast agents are FDA-approved for use during magnetic resonance imaging (MRI), a test that can look at internal body organs and tissues. The trade names of the U.S. approved gadolinium-containing contrast agents are: Omniscan, OptiMARK, Magnevist, ProHance, and MultiHance. None of these drugs are FDA approved for MRA. The dose of gadolinium-containing contrast agent given to patients undergoing an MRA test is often higher (up to three times) than the approved dose for MRI.

NSF/NFD appears to occur in patients with kidney failure along with high levels of acid in body fluids a condition known as acidosis that is common in patients with kidney failure. Patients with NSF/NFD have tight and rigid skin making it difficult to bend joints. NSF/NFD may also result in fibrosis, or scarring, of body organs resulting in the inability of body organs to work properly and can lead to death. Diagnosis of NSF/NFD is done by looking at a sample of skin under a microscope.

Scientists first identified NSF/NFD in 1997 and the cause of NSF/NFD is unknown. Worldwide, there are approximately 200 reports of NSF/NFD.

The 25 cases of NSF/NFD were reported on May 29, 2006, by the Danish Medicines Agency. Among these, 20 cases occurred in Denmark and five cases occurred in Austria. The patients developed NSF/SFD within 3 months (range 2 weeks to 3 months) after receiving the gadolinium-containing contrast agent. The five patients from Austria are described in a publication: Grobner T. Gadolinium – a specific trigger for the development of nephrogenic fibrosing dermopathy and nephrogenic systemic fibrosis Nephrol dial Transplant. 21(4):1104-8.

The FDA has not yet determined whether exposure by patients with kidney failure to gadolinium-containing contrast agents during an MRA test causes NSF/NFD. The FDA is gathering additional information about NSF/NFD and investigating whether other patients who received gadolinium-containing contrast agents developed NSF/NFD.

The FDA urges health care providers and patients to report adverse event information to the FDA via the MedWatch program by phone (1-800-FDA-1088), by fax (1-800-FDA-0178), or by the Internet at http://www.fda.gov/medwatch/index.html.

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