



To: Department of Radiology, University of Wisconsin, Madison, WI
From: Scott B. Reeder, MD, PhD; Howard A. Rowley, MD; Elizabeth A. Sadowski, MD
on behalf of the University of Wisconsin MRI Safety Committee
Re: Updated NSF Screening Procedure at the University of Wisconsin
Date: 12/9/16, new guidelines effective 1/1/27

Purpose: This document describes modified screening procedures for mitigating the risk of nephrogenic systemic fibrosis (NSF) in patients with renal failure undergoing gadolinium-enhanced MRI.

Background: In 2006-2007, it was recognized that patients with renal failure who were exposed to gadolinium based contrast agents (GBCAs) were at increased risk of developing a potentially fatal disorder known as nephrogenic systemic fibrosis (NSF). As a result, the FDA issued a black box warning on the use of all GBCAs in patients with renal failure. Through intense international effort it has been determined that some GBCAs are strongly associated with NSF, while others are not. The three agents most associated with NSF include gadodiamide (Omniscan), gadopentetate dimeglumine (Magnevist) and gadoversetamide (Optimark).

At the University of Wisconsin, Sadowski et al (Radiology 2007) reported 14 cases of NSF. All of these patients were inpatients with renal failure, a pro-inflammatory condition, and exposure to gadodiamide. In patients with this risk profile (inpatients, renal failure, pro-inflammatory condition), it was determined that there was an approximate risk of 3-5% of developing NSF after exposure to gadodiamide.

Based on these data, screening procedures to identify inpatients with renal failure and pro-inflammatory conditions were developed. Dedicated screening of all inpatients using the "yellow NSF form" was required. Inpatients with renal failure and a pro-inflammatory condition were flagged as high risk. In these patients, ad hoc review for the need to use gadolinium was necessary. If deemed necessary a discussion with the referring physician and documentation of this communication in the radiology report was required. In many cases this led to significant delays, and a gadolinium-based contrast agent was ultimately administered to most patients.

Since that time, gadodiamide, the only agent used at UW-Madison known to be related to NSF, has been dropped from UW formulary. Further, there are no unconfounded cases of NSF associated with gadobenate dimeglumine (MultiHance) reported anywhere in the world, despite tens of millions of doses. Recently, a publication by Bruce et al (Invest Radiol 2016), reported the absence of NSF in over 1400 high-risk inpatients at UW-Madison injected with gadobenate dimeglumine. Nandwana et al (Emory group, Radiology 2015) also found no cases of NSF in a group of 401 patients with renal impairment (303 dialysis-dependent) who received gadobenate dimeglumine. Based on changes in practice and the avoidance of specific GBCAs, there are no reported cases of NSF with any agent anywhere in the world since 2008.

The following agents are available on the UW formulary: gadobenate dimeglumine (MultiHance), gadoterate meglumine (Dotarem), and gadoexetic acid (Eovist). None of these agents have been associated with NSF when administered as the sole agent. Despite the high safety profile of these GBCAs, the FDA black box warning remains for all agents. Mindful of the FDA warning, the high safety profile of the agents currently on the UW formulary, and also the need to obtain important diagnostic information in our patients, the MRI Safety Committee has modified the UW NSF screening procedure, as follows.



Modified Procedures for Administering Gadolinium in Patients with Renal Failure:

1. The following procedures only apply to the three agents currently on the formulary: gadobenate dimeglumine, gadoterate meglumine, and gadoxetic acid. Should other agents be introduced on an *ad hoc* basis, please review with the Chair of the MRI Safety Committee or Chief of MRI prior to use in patients with renal failure. Should new GBCAs be added to the formulary in the future, this document will be modified / amended.
2. We continue to recommend caution when considering administration of GBCAs to patients with risk factors for NSF. As with all MRI exams, the protocolling Radiologist who prescribes a GBCA is verifying that contrast agent administration is indicated given a risk-benefit analysis, considering patient-specific circumstances and clinical indications.
3. Effective immediately, the "yellow" NSF screening form has been discontinued. Screening for pro-inflammatory conditions is no longer required.
4. Effective immediately, a modified process of screening inpatients will be instituted as follows:
 - a. No screening is required for outpatients.
 - b. Screening will consist of a recent estimated glomerular filtration rate (eGFR). It is required that an eGFR be obtained within 48 hours of all gadolinium enhanced MRI performed on inpatients. Any inpatient with an eGFR < 30 will be considered "elevated risk."
 - c. eGFR screening will be performed by the MRI nursing staff and/or MRI technologists as part of the standard MRI Safety Screening procedure. For all inpatients (with or without known renal failure), the eGFR will be recorded on the screening form or within the exam note on Healthlink.
 - d. For those patients at elevated risk, section-specific protocols for gadolinium dose modification, if any, will be performed. All clinical protocols that use gadolinium will have a specified option detailing gadolinium dose modification for patients at elevated risk. These protocols will be in place before implementation of these procedures. For patients at elevated risk, the technologist will follow pre-specified dose modifications. The technologist will document the administered dose in the exam note. There is no need to consult with the radiologist unless there are other questions. The specific dose and type of contrast agent should always be included in the radiology report, but specific mention that dose modification was performed because of low eGFR is not necessary.
 - e. For those patients at elevated risk who are on dialysis, good faith attempts will be made to coordinate MRI with hemodialysis. Ideally, hemodialysis should be performed the same day, following gadolinium enhanced MRI. However, coordination of MRI with dialysis should never delay an MRI exam in a clinically meaningful way. It is important to note that although GBCAs are removed by hemodialysis, there are no data that demonstrate the benefit of dialysis for reduced risk of NSF. It is not necessary to document that the MRI was coordinated with dialysis.
5. No specific documentation, other than eGFR, is required.

It is our goal that the above modified screening procedures will ensure standardization, improve consistency, avoid dosing errors, and create a streamlined and efficient approach that will avoid confusion and delay of important imaging care to our patients. For specific details on changes to gadolinium dosing within the clinical MRI protocols, please contact specific sections or Megan Vadnais (protocol technologist).

Questions: Scott Reeder (Pager 6713), Howard Rowley (Pager 2518), Elizabeth Sadowski (Pager 9036),