

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**NDA 22-090**

**OFFICE DIRECTOR MEMO**

Memorandum:

Date: June 30, 2008  
From: Karen Weiss M.D., Deputy Director, OODP  
Subject: Tertiary Review, NDA 22-090  
To: File

This memorandum serves as a tertiary review of a new drug application (NDA) for Gadoxetate Disodium (Eovist®), a gadolinium contrast agent for use to detect and characterize liver lesions. Bayer Healthcare Pharmaceuticals submitted the NDA on June 21, 2007. FDA determined it was a standard review. The review team and division recommend approval; I concur for reasons described below. When approved, Eovist® will be the sixth FDA-approved gadolinium contrast agent, though indications for the agents vary (see the division director memo for brief description of the all gadolinium contrast agent indications).

Eovist® was evaluated in 4 clinical studies; two identical trials liver lesion 'detection' trials and two identical trials for liver lesion 'characterization.' The detection studies were designed to show that Eovist® improved sensitivity for detecting liver lesions compared to non-contrast MRI. In these studies, all patients were scheduled to undergo surgical resection; therefore, pathology was the standard of truth (gold standard). The characterization studies were designed to show better agreement with the standard of truth (based on surgical resection or another gold standard if pathological evaluation was not appropriate).

All studies showed Eovist® improved imaging performance relative to the non-contrast scan.

The safety assessment on 1755 Eovist® exposed subjects, did not reveal any differences in type or severity of adverse event when considering the agency's experience with other gadolinium based contrast agents. As Dr. Marzella noted in his secondary review, approximately 2/3 of all patients exposed were only followed for 24 hours, the remainder, up to 72 hours; thus, long(er) term adverse events could have been missed. This product has been marketed in Europe for 4 years; post-marketing surveillance reports do not suggest new safety signals. Patients with renal impairment have developed systemic fibrosis (NSF), a rare but serious/life threatening systemic fibrotic disease, after exposure to gadolinium contrast agents (<http://www.fda.gov/cder/drug/infopage/gcca/default.htm>). While NSF was not reported in Eovist® pre or post marketing safety databases, the manufacture will conduct a required post-marketing study in patients with moderate to severe renal impairment to assess safety in this population. Eovist® labeling will include the same language (class boxed warning) about the risk of NSF.

The other required post marketing study will be a safety and efficacy study in pediatric patients.

-----  
**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
-----

/s/

-----  
Karen Weiss  
7/1/2008 03:23:03 PM  
MEDICAL OFFICER