



NDA 022090/S-016 and 201277/S-016

## **SUPPLEMENT APPROVAL**

Bayer HealthCare Pharmaceuticals Inc.  
Attention: Dolores Fliss  
Deputy Director, Global Regulatory Affairs  
100 Bayer Blvd., P.O. Box 915  
Whippany, NJ 07981

Dear Ms. Fliss:

Please refer to your Supplemental New Drug Application (sNDA) dated August 1, 2018, received August 1, 2018, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Eovist® (gadoxetate disodium) Injection, Gadavist® (gadobutrol) Injection and Gadavist® (gadobutrol) Injection Pharmacy Bulk Package.

This “Changes Being Effected” supplemental new drug application provides for the revision to the HIGHLIGHTS OF PRESCRIBING INFORMATION regarding use of GBCAs during pregnancy.

### **APPROVAL & LABELING**

We have completed our review of this supplemental application. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

### **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21CFR314.50(1)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the prescribing information and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21CFR314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

### **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21CFR 314.80 and 314.81).

If you have any questions, call Rene’ Tyson, Safety Regulatory Project Manager, at (301) 796-1476.

Sincerely,

*{See appended electronic signature page}*

Ira Krefting, M.D.  
Deputy Director for Safety  
Division of Medical Imaging Products  
Office of Drug Evaluation IV  
Center for Drug Evaluation and Research

ENCLOSURE(S):  
Content of Labeling

-----  
**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
-----

/s/  
-----

IRA P KREFTING  
11/02/2018