



NDA 020220/S-042 and 021425/S-026

**SUPPLEMENT APPROVAL**

Bayer HealthCare Pharmaceuticals, Inc.  
Attention: Delores Fliss  
Associate Director, Global Regulatory Affairs  
100 Bayer Blvd  
P.O Box 915  
Whippany, NJ 07981-0915

Dear Mrs. Fliss:

Please refer to your Supplemental New Drug Application (sNDA) dated January 20, 2017, received January 23, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Ultravist® (iopromide) Injection and Ultravist® (iopromide) Injection Pharmacy Bulk Package.

We also refer to our letter dated December 23, 2016, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for Iodinated Contrast Agents (ICA). This information pertains to the serious risk of Severe Cutaneous Adverse Reactions (SCAR), clinical conditions listed below following the administration of ICA:

- Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis (SJS/TEN)
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
- Acute Generalized Exanthematous Pustulosis (AGEP)

This supplemental new drug application provides for revisions to the labeling for Ultravist, consistent with our December 23, 2016 letter and the agreed upon changes to the language included in our Labeling Discussion Comments emailed March 27, 2017.

**APPROVAL & LABELING**

We have completed our review of this supplemental application, as amended March 30, 2017. 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 [21CFR 314.50(l)] 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 package insert, with the addition of any labeling changes in pending “Changes Being Effectuated” (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 [21 CFR 314.50(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, 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(s) 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.

## **PROMOTIONAL MATERIALS**

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the

revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21CFR 314.70(a)(4) to the address above, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry (available at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf> ).

**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, 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

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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IRA P KREFTING  
04/05/2017