



NDA 021064/S-025 and S-029

## **SUPPLEMENT APPROVAL**

Lantheus Medical Imaging, Inc.  
Attention: Laura Lee  
Director, Regulatory Affairs  
331 Treble Cove Road  
Building 300-2  
North Billerica, MA 01862

Dear Ms. Lee:

Please refer to your supplemental new drug applications (sNDA) dated August 27, 2020 and March 4, 2021, received August 27, 2020 and March 4, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for DEFINITY®, Vial for (Perflutren Lipid Microsphere) Injectable Suspension and DEFINITY® RT (Perflutren Lipid Microsphere) Injectable.

We also refer to our letter dated February 2, 2021, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for DEFINITY and ultrasound contrast agents with a PEG component. This information pertains to the risk of serious hypersensitivity reactions.

These supplemental new drug applications provide for revisions to the labeling for DEFINITY and DEFINITY RT consistent with our February 2, 2021, March 17, 2021, and March 23, 2021 letters.

### **APPROVAL & LABELING**

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

## **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information), 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 *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

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 Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), 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).

## **CARTON AND CONTAINER LABELING**

Submit final printed carton labeling that is identical to the enclosed carton labeling **and** carton labeling submitted on **March 23, 2021**, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 021064/S-029.**” Approval of this submission by FDA is not required before the labeling is used.

## **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

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

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.

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 [21CFR314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR314.70(a)(4).

### **REPORTING REQUIREMENTS**

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

If you have any questions, please contact 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 Imaging and Radiation Medicine  
Office of Specially Medicine  
Center for Drug Evaluation and Research

#### ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
- Carton Labeling

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**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.**  
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/s/  
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IRA P KREFTING  
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