



Dear Healthcare Provider,

Lantheus Medical Imaging, Inc., is pleased to announce recent FDA changes to the US Prescribing Information for DEFINITY® (Perflutren Lipid Microsphere) Injectable Suspension. These new changes are specific to DEFINITY® and follow the FDA review of Lantheus' labeling supplement submission dated September 2010, as well as the FDA Safety Advisory Committee meeting held in May 2011.

Please read through the revisions carefully to ensure you understand these changes to the DEFINITY® label and their potential to enhance imaging in your patients with suboptimal echocardiograms.

Revised Indications

Activated DEFINITY® (Perflutren Lipid Microsphere) Injectable Suspension is indicated for use in patients with suboptimal echocardiograms to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border.

Please note that the FDA removed the following disclaimer from the Indications & Usage section of the DEFINITY® label:
"The safety and efficacy of DEFINITY® with exercise stress or pharmacologic stress testing have not been established."

Revised Boxed WARNING

WARNING: Serious Cardiopulmonary Reactions

Serious cardiopulmonary reactions, including fatalities, have occurred during or following perflutren-containing microsphere administration (see WARNINGS AND PRECAUTIONS). Most serious reactions occur within 30 minutes of administration.

- Assess all patients for the presence of any condition that precludes DEFINITY® administration (see CONTRAINDICATIONS)
- Always have resuscitation equipment and trained personnel readily available

Please note that the following statement is newly added to the DEFINITY® label: *"Most serious reactions occur within 30 minutes of administration."*

In addition, the following instruction for monitoring was deleted from the boxed WARNING contained within the DEFINITY® label: *"In patients with pulmonary hypertension or unstable cardiopulmonary conditions, monitor vital sign measurements, electrocardiography, and cutaneous oxygen saturation during and for at least 30 minutes after DEFINITY® administration."*

Furthermore, the revised DEFINITY® label now includes data from the safety registry and pulmonary hypertension studies conducted by Lantheus. A time and events history of label changes to this class of agents, including the current revisions to the DEFINITY® label, is enclosed.

Lantheus is committed to supporting the safe and appropriate use of our products. **For further information, please contact Lantheus Medical Information at 1-800-343-7851 (ext. 4) or medicalinformation@lantheus.com.**

Lantheus would like to thank physicians, sonographers, and global medical societies—including ASE, ICUS, and ICAEL—for supporting the appropriate use of contrast to improve patient management and outcomes.

Sincerely,

A handwritten signature in black ink, appearing to read "Dana S. Washburn".

Dana Washburn, MD
Chief Medical Officer

A handwritten signature in black ink, appearing to read "Mark Hibberd".

Mark Hibberd, MD, PhD
Senior Medical Director,
Global Medical Affairs and Pharmacovigilance

Please see the accompanying full Prescribing Information, including boxed WARNING regarding serious cardiopulmonary reactions.



INDICATIONS

Activated DEFINITY® (Perflutren Lipid Microsphere) Injectable Suspension is indicated for use in patients with suboptimal echocardiograms to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border.

CONTRAINDICATIONS

Do not administer DEFINITY® to patients with known or suspected right-to-left, bi-directional or transient right-to-left cardiac shunts, by intra-arterial injection, or to patients with known hypersensitivity to perflutren.

IMPORTANT SAFETY INFORMATION

WARNING: Serious Cardiopulmonary Reactions

See full prescribing information for complete boxed warning

Serious cardiopulmonary reactions, including fatalities, have occurred uncommonly during or following perflutren-containing microsphere administration (5.1). Most serious reactions occur within 30 minutes of administration.

- Assess all patients for the presence of any condition that precludes DEFINITY® administration (4).
- Always have resuscitation equipment and trained personnel readily available.

In postmarketing use, rare but serious cardiopulmonary or anaphylactoid reactions have been reported during or shortly following perflutren-containing microsphere administration (see ADVERSE REACTIONS). The risk for these reactions may be increased among patients with unstable cardiopulmonary conditions (See Postmarketing Experience). It is not always possible to reliably establish a causal relationship to drug exposure due to the presence of underlying cardiopulmonary disease.

Please see the accompanying full Prescribing Information, including boxed WARNING regarding serious cardiopulmonary reactions.



Time and Events History:

DEFINITY® (Perflutren Lipid Microsphere) Injectable Suspension and the Ultrasound Contrast Agent Class

The FDA has recently provided changes to the US Prescribing Information for DEFINITY®, based on its review of the labeling supplement submission from Lantheus Medical Imaging, Inc., dated September 2010, as well as the FDA Safety Advisory Committee meeting held in May 2011. Below is a timeline that chronicles the label-related events for ultrasound contrast agents, culminating in this most recent change for DEFINITY®.

October 2001

DEFINITY® launched

October 2007

Class label changes for ultrasound contrast agents:

- Contraindications for patients with serious cardiopulmonary conditions
- Boxed **WARNING**
- Mandatory physiologic monitoring

May 2008

Class label changes for ultrasound contrast agents, based on review of new data from Lantheus and the academic community, as well as strident advocacy from physicians and ultrasound societies:

- October 2007 contraindications were removed
- Physiologic monitoring required for patients with pulmonary hypertension and unstable cardiopulmonary syndromes

October 2011

DEFINITY® label changes:

- The following disclaimer was deleted from the Indications & Usage section:
"The safety and efficacy of DEFINITY® with exercise stress or pharmacologic stress testing have not been established."
- The following monitoring information was deleted from the boxed **WARNING**:
"In patients with pulmonary hypertension or unstable cardiopulmonary conditions, monitor vital sign measurements, electrocardiography, and cutaneous oxygen saturation during and for at least 30 minutes after DEFINITY® administration."
- The following statement was added to the boxed **WARNING**:
"Most serious reactions occur within 30 minutes of administration."

Please see the accompanying full Prescribing Information, including boxed WARNING regarding serious cardiopulmonary reactions.

