GE Healthcare
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RP-2121
Wauwatosa, WI 53226
June 6, 2008

Important Drug Warning

for Optison™ (Perflutren Protein-Type A Microspheres Injectable Suspension, USP)

Dear Healthcare Professional;

GE Healthcare would like to inform you of some important class revisions made to the professional labeling for Optison™ and the other perflutren-containing microsphere products since the last labeling revision in November, 2007. The Food and Drug Administration has become aware of published reports,[1,2] and reports from healthcare providers that indicate, in some situations, the information obtained from the use of microbubble-ultrasound contrast agents during an echocardiogram may be life-saving, even in patients who are at potential risk for serious reactions to the contrast agents.

Based on this information, FDA believes that modifications of the label are appropriate. Revisions have been made to the **BOXED WARNING, WARNINGS, CONTRAINDICATIONS and ADVERSE REACTIONS** sections of the package inserts for these products.

Optison is an ultrasound contrast agent intended for use in patients with suboptimal echocardiograms to opacify the left ventricle and to improve the delineation of the left ventricular endocardial borders.

At the request of FDA, the package inserts of all perflutren-containing microsphere products have been revised to include the following.

CHANGES MADE TO THE BOXED WARNING

WARNING: Serious Cardiopulmonary Reactions

Serious cardiopulmonary reactions, including fatalities, have occurred during or following perflutren-containing microsphere administration.

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

CHANGES MADE TO CONTRAINDICATIONS

Most of the contraindications in the previous package insert have been deleted. The following text has been retained within the CONTRAINDICATIONS section.

Do not administer OPTISON to patients with known or suspected:

- o Right-to-left, bi-directional, or transient right-to-left cardiac shunts,
- o Hypersensitivity to perflutren, blood, blood products or albumin (see WARNINGS).

Do not administer OPTISON by intra-arterial injection.

CHANGES MADE TO THE WARNINGS

The Serious Cardiopulmonary Reactions sub-section has been modified to read:

"Serious cardiopulmonary reactions, including fatalities, have occurred during or following perflutren-containing microsphere administration. The risk for these reactions may be increased among patients with pulmonary hypertension or unstable cardiopulmonary conditions (acute myocardial infarction, acute coronary artery syndromes, worsening or unstable congestive heart failure, serious ventricular arrhythmias or respiratory failure, including patients receiving mechanical ventilation). In these patients, monitor vital signs, electrocardiography and cutaneous oxygen saturation during and for at least 30 minutes after Optison administration. In the absence of these underlying conditions, observe patients closely during and following Optison administration.

In postmarketing use, uncommon but serious reactions observed during or shortly following perflutren-containing microsphere administration included fatal cardiac or respiratory arrest, loss of consciousness, convulsions, symptomatic arrhythmias (atrial fibrillation, supraventricular tachycardia, ventricular tachycardia or fibrillation), hypotension, respiratory distress or cardiac ischemia (see ADVERSE REACTIONS).

Always have cardiopulmonary resuscitation personnel and equipment readily available prior to Optison administration and monitor all patients for acute reactions."

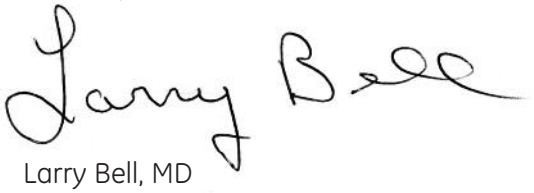
CHANGES MADE TO THE ADVERSE REACTIONS

The Postmarketing Experience sub-section has been slightly modified to say that fatal cardiac arrests have been reported without specifying the number of fatal cardiac arrests.

Further Information

Please contact GE Healthcare Medical and Professional Services directly at 1-800-654-0118 with additional questions or to report adverse events. Healthcare professionals also may report adverse event information to the FDA's MedWatch program by phone (1-800-FDA-1088); on line (https://www.accessdata.fda.gov/scripts/medwatch); or by downloading Form 3500 at http://www.fda.gov/medwatch/getforms.htm and sending it to MedWatch by fax (1-800-FDA-0178) or by mail (5600 Fishers Lane, Rockville, MD 20852-9787).

Sincerely,



Larry Bell, MD
Global Head of
Regulatory and Pharmacovigilance

References: 1. Erb, J. Shanewise, J. Intraoperative contrast echocardiography with intravenous Optison does not cause hemodynamic changes during cardiac surgery. *J Am Soc Echocardiography.* 2001;14:595-600. **2.** Soman, P. Lahiri, A. Senior, R. Safety of an intravenous second generation contrast agent in patients with severe left ventricular dysfunction. *Heart*. 2000;84:634-5.