



GE HEALTHCARE ANNOUNCES FDA LABELING CHANGE FOR USE OF OPTISON™ IN PATIENTS WITH CARDIAC SHUNTS

Marlborough, MA, October 3, 2016 – Today, GE Healthcare announced that the U.S. Food and Drug Administration (FDA) has approved a label change for the ultrasound contrast agent Optison™ (Perflutren protein-Type A Microspheres Injectable Suspension, USP). The FDA removed the contraindications for use in patients with cardiac shunts and for administration by intra-arterial injection. Both contraindications have been revised and moved to the WARNINGS AND PRECAUTIONS section (5.3 : Systemic Embolization) of the Full Prescribing Information.

Optison is the first contrast agent available in the United States to receive this contraindication label change.

A cardiac shunt is a pattern of blood flow in the heart that deviates from the normal flow of the circulatory system. Previously, in suspected cardiac shunt populations, an agitated saline procedure was needed to determine if a shunt existed and whether the patient was contraindicated to receive an ultrasound contrast agent.

Sharon L. Mulvagh, MD, Professor of Medicine, Women's Heart Clinic Director, Associate Director, Preventive Cardiology Consultant in Cardiovascular Diseases, Mayo Clinic and Mayo Clinic College of Medicine, said: "I am very pleased that the FDA has approved the removal of the cardiac shunt contraindication from the ultrasound contrast agent Optison. This label change will allow more patients access to a diagnostic imaging tool that has established safety and efficacy. The FDA's decision to remove this contraindication is supported by a body of data from studies demonstrating safety and clinical benefits of all ultrasound contrast agents in patients with cardiovascular diseases."

She added: "This is an important step forward in eliminating barriers to ultrasound contrast use and delivering quality diagnostic care of value to our patients."

Steven Feinstein, MD, Co-President of the International Contrast Ultrasound Society, said: "Up to one-third of our patients have known or suspected cardiac shunts and, thanks to this important FDA decision, they too will now have access to ultrasound contrast agents, which offer an inexpensive and radiation-free option for diagnostic imaging. The International Contrast Ultrasound Society applauds the FDA for its decision, and believes it will benefit individual patients as well as our healthcare delivery system."

Jonathan Lindner, MD, M. Lowell Edwards Professor of Cardiology at the Knight Cardiovascular Center, Oregon Health & Science University, said: "Thanks to the overwhelming weight of evidence from clinical trials, most practitioners in the field of echocardiography already realize the benefits of using contrast agents and understand their capacity to improve diagnostic accuracy, improve outcomes, and streamline care. However, a major obstacle to widespread use has been lack of consensus and confusion regarding how far one needs to go to exclude shunts, no matter how small. The decision by the FDA removes a barrier to using this contrast agent, and may result in an increase in the number of labs that will choose to utilize this important technology, which allows clinicians to provide the best care possible."

Ger Brophy, PhD, Chief Technology Officer at GE Healthcare, said: "We welcome this FDA decision and hope that this will allow more patients access to contrast-enhanced ultrasound procedures and improve the management of their conditions."

Mark Hibberd, Head of Global Medical Services at GE Healthcare, commented: “We are extremely pleased that the FDA has changed the labeling for cardiac shunts with Optison when it is used in the clinically important group of patients who have suboptimal echocardiograms, and a need for left ventricular opacification and delineation of LV borders. Many of these patients have limited options for cardiac imaging, and the FDA’s decision will facilitate their care.”

PRODUCT INDICATION: Optison™ (Perflutren Protein-Type A Microspheres Injectable Suspension, USP) is an ultrasound contrast agent indicated for use in patients with suboptimal echocardiograms to opacify the left ventricle and to improve the delineation of the left ventricular endocardial borders.

**Boxed Warning and Important Risk and Safety Information About Optison™
(Perflutren Protein-Type A Microspheres Injectable Suspension, USP)**

WARNING: SERIOUS CARDIOPULMONARY REACTIONS

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

- **Assess all patients for the presence of any condition that precludes Optison administration [see **CONTRAINDICATIONS (4)**]**
- **Always have resuscitation equipment and trained personnel readily available [see **WARNINGS and PRECAUTIONS (5.1)**]**

CONTRAINDICATIONS: Do not administer Optison to patients with known or suspected hypersensitivity to perflutren, blood, blood products, or albumin. **WARNINGS AND PRECAUTIONS — Serious Cardiopulmonary Reactions:** Serious cardiopulmonary reactions, including fatalities, have occurred uncommonly during or shortly following administration. The risk for these reactions may be increased among patients with unstable cardiopulmonary conditions (acute myocardial infarction, acute coronary artery syndromes, worsening or unstable congestive heart failure, or serious ventricular arrhythmias). Always have cardiopulmonary resuscitation personnel and equipment readily available prior to Optison administration, and monitor all patients for acute reactions. **Hypersensitivity Reactions:** Serious anaphylactic reactions have been observed during or shortly following perflutren-containing microsphere administration, including shock, hypersensitivity, bronchospasm, throat tightness, angioedema, edema (pharyngeal, palatal, mouth, peripheral, localized), swelling (face, eye, lip, tongue, upper airway), facial hypoesthesia, rash, urticaria, pruritus, flushing, and erythema have occurred in patients with no prior exposure to perflutren-containing microsphere products. Always have cardiopulmonary resuscitation personnel and equipment readily available prior to Optison administration, and monitor all patients for hypersensitivity reactions. **Systemic Embolization:** When administering Optison to patients with a cardiac shunt, microspheres can bypass filtering of the lungs and enter the arterial circulation. Assess patients with shunts for embolic phenomena following Optison administration. Optison is only for intravenous administration; do not administer Optison by intra-arterial injection. **Ventricular Arrhythmia Related to High Mechanical Index:** High ultrasound mechanical index values may cause microsphere rupture and lead to ventricular arrhythmias. Additionally, end-systolic triggering with high mechanical indices has been reported to cause ventricular arrhythmias. Optison is not recommended for use at mechanical indices greater than 0.8. **Transmissible Infectious Agents:** This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral disease. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) is also considered extremely remote. No cases of transmission of viral disease or CJD have ever been identified for albumin. **ADVERSE REACTIONS:** Serious adverse reactions related to cardiopulmonary and

hypersensitivity reactions are described in the WARNINGS AND PRECAUTIONS section. The most frequently reported adverse reactions following clinical trial use of Optison were headache, nausea and/or vomiting, warm sensation or flushing, and dizziness. **Postmarketing Experience:** Cardiac arrests and other serious but nonfatal adverse reactions were uncommonly reported. Most of these uncommon reactions included cardiopulmonary symptoms and signs such as cardiac arrest, hypotension, supraventricular and ventricular arrhythmias, respiratory distress, or decreased oxygenation. Reports also identified neurologic reactions (loss of consciousness or convulsions) as well as anaphylactoid reactions. **USE IN SPECIFIC POPULATIONS — Pregnancy:** There are no data on Optison use in pregnant women to inform any drug-associated risks. **Lactation:** There are no data on the presence of perflutren protein-type A microspheres in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for Optison and any potential adverse effects on the breastfed infant from Optison or from the underlying maternal condition. **Pediatric Use:** Safety and effectiveness in pediatric patients have not been established. **Geriatric Use:** No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Prior to Optison administration, please read the [Full Prescribing Information](#).