



GE Healthcare

101 Carnegie Center
Princeton, NJ 08540
USA

November 19, 2012

Dear Healthcare Professional:

GE Healthcare is committed to helping meet the needs of you and your patients and to providing you with timely information related to product supply issues. We are writing to share with you an update regarding current availability of Optison™ (Perflutren Protein-Type A Microspheres Injectable Suspension, USP) ultrasound contrast media.

We are very pleased to inform you that our issue related to the allocation of our product supply has been alleviated, and we no longer need to allocate Optison. Additionally, our plans to manufacture Optison internally at our plant in Oslo, Norway are continuing as we conduct our facility certification activities. This transition to in-house manufacturing is scheduled for completion in 2013 and demonstrates GE Healthcare's commitment to ultrasound contrast agents, as we will be the only company in the United States with internal manufacturing for these products.

GE Healthcare's first priority is to help enable you to make confident medical decisions for your patients. We are ready to work with you to ensure that your ultrasound contrast media needs are addressed as well as possible. To that end, if you are experiencing any delays or issues related to securing supply of your contrast media, please contact us at one of the numbers below:

Healthcare institutions can inquire about ordering Optison by contacting the GE Healthcare Customer Services Team at 800 292 8514.

Healthcare professionals wishing to learn more about Optison can contact the GE Healthcare Medical Information service at 800 654 0118.

We also encourage you to visit our website at www.optisonimaging.com.

Sincerely,

Thomas Koenig

General Manager, US Cardiology
Medical Diagnostics
Email: thomas.c.koenig@ge.com
Phone: 609 514 6787

Please see Important Risk and Safety Information at the end of this letter and Full Prescribing Information enclosed.

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

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

BOXED 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. Assess all patients for the presence of any condition that precludes Optison administration. Always have resuscitation equipment and trained personnel readily available.

INDICATIONS: Optison is indicated for use in patients with suboptimal echocardiograms to opacify the left ventricle and to improve the delineation of the left ventricular endocardial borders.

CONTRAINDICATIONS: Do not administer Optison to patients with known or suspected: (1) Right-to-left, bi-directional, or transient right-to-left cardiac shunts, or (2) Hypersensitivity to perflutren, blood, blood products, or albumin. Do not administer Optison by intra-arterial injection. **WARNINGS: Anaphylactoid**

Reactions: In postmarketing use, uncommon but serious anaphylactoid reactions were observed during or shortly following perflutren-containing microsphere administration, including in patients with no prior exposure to perflutren-containing microsphere products. **High Ultrasound Mechanical Index:** High ultrasound mechanical index values may cause microsphere cavitation or rupture and lead to ventricular arrhythmias. Additionally, end-systolic triggering with high mechanical indices has been reported to cause ventricular arrhythmias. The safety of Optison at mechanical indices greater than 0.8 and the safety of Optison with the use of end-systolic triggering have not been evaluated. **PRECAUTIONS:**

General: Optison 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 and Creutzfeldt-Jakob disease (CJD), no cases of which have ever been identified for albumin. **Pregnancy:**

Adequate or well-controlled studies were not conducted in pregnant women. Optison should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nursing Mothers:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Optison is administered to a nursing woman. **Pediatric Use:**

Safety and efficacy have not been established in pediatric patients, or in patients with congenital heart disease. **ADVERSE REACTIONS:** 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 non-fatal adverse reactions, were uncommonly reported. Most of these uncommon reactions included cardiopulmonary symptoms and signs such as cardiac or respiratory 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.

Prior to Optison administration, please read the Full Prescribing Information.



OPTISON[™]
(Perflutren Protein-Type A Microspheres
Injectable Suspension, USP)



OPTISON™

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

WARNING: SERIOUS CARDIOPULMONARY REACTIONS

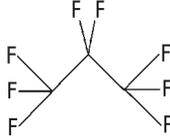
Serious cardiopulmonary reactions, including fatalities, have occurred uncommonly during or following perflutren-containing microsphere administration. Most serious reactions occur within 30 minutes of administration (see WARNINGS and PRECAUTIONS).

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

DESCRIPTION

OPTISON™ (Perflutren Protein-Type A Microspheres Injectable Suspension, USP) is a sterile non-pyrogenic suspension of microspheres of human serum albumin with perflutren for contrast enhancement during the indicated ultrasound imaging procedures. The vial contains a clear liquid lower layer and a white upper layer that, after resuspension by gentle mixing, provides a homogeneous, opaque, milky-white suspension for intravenous injection.

Perflutren is chemically characterized as 1,1,1,2,2,3,3,3-perflutren with a molecular weight of 188, an empirical formula of C₈F₁₈, and it has the following structural formula:



Each mL of OPTISON contains 5.0-8.0x10⁸ protein-type A microspheres, 10 mg Albumin Human, USP, 0.22 ± 0.11 mg/mL perflutren, 0.2 mg N-acetyltryptophan, and 0.12 mg caprylic acid in 0.9% aqueous sodium chloride. The headspace of the vial is filled with perflutren gas. The pH is adjusted to 6.4-7.4. The protein in the microsphere shell makes up approximately 5-7% (w/w) of the total protein in the liquid. The microsphere particle size parameters are listed in Table 1.

Parameter	Value
Mean diameter (range)	3.0-4.5µm (max. 32.0µm)
Percent less than 10µm	95%

CLINICAL PHARMACOLOGY

General

The OPTISON microspheres create an echogenic contrast effect in the blood.

Pharmacokinetics

Studies in humans have evaluated the pharmacokinetics of the perflutren component of the OPTISON microspheres. After injection of OPTISON, diffusion of the perflutren gas out of the microspheres is limited by the low partition coefficient of the gas in blood that contributes to the persistence of the microspheres. The diffusion rate has not been studied.

In an anesthetized dog model, the acoustic properties of OPTISON were established at 0.6 mechanical index and 2.5 MHz frequency.

Neither the pharmacokinetics of the intact microspheres or of the human albumin component have been evaluated in humans.

Metabolism

Perflutren is a stable gas that is not metabolized. The human albumin component of the microsphere is expected to be handled by the normal metabolic routes for human albumin.

Perflutren Elimination

Following a single intravenous dose of 20 mL OPTISON to 10 healthy volunteers (5 men and 5 women), most of the perflutren was eliminated through the lungs within 10 minutes. The recovery was 96% ± 23% (mean ± SD), and the pulmonary elimination half-life was 1.3 ± 0.69 minutes (mean ± SD). The perflutren concentration in expired air peaked approximately 30-40 seconds after administration.

Perflutren Protein Binding

The binding of perflutren to plasma proteins or its partitioning into blood cells have not been studied. However, perflutren protein binding is expected to be minimal due to the low partition coefficient of the gas in blood.

Special Populations

The pharmacokinetics of OPTISON have not been studied in patients with hepatic or respiratory diseases.

Gender, Age, Race

The effects of gender, age, or race on the pharmacokinetics of OPTISON have not been studied.

Drug-Drug Interactions

Drug-drug interactions for OPTISON have not been studied.

Pediatrics

The pharmacokinetics of OPTISON in pediatric patients have not been studied.

Pharmacodynamics

The general acoustic properties of OPTISON are similar to those of ALBUNEX®. The acoustic impedance of the OPTISON microspheres is much lower than that of the blood. Therefore, impinging ultrasound waves are scattered and reflected at the microsphere-blood interface and ultimately may be visualized in the ultrasound image. At the frequencies used in adult echocardiography (2-5 MHz), the microspheres resonate which further increases the extent of ultrasound scattering and reflection.

As assessed by the unblinded investigators in clinical studies, the median duration of OPTISON contrast enhancement for each of the four doses of OPTISON (0.2, 0.5, 3.0, and 5.0 mL) were approximately one, two, four, and five minutes, respectively (see CLINICAL TRIALS section).

CLINICAL TRIALS

Echocardiography:

The efficacy of OPTISON was evaluated in two identical multicenter, dose escalation, randomized, cross-over studies of OPTISON and ALBUNEX®. The test drugs were administered single blind and the image analysis was double blind. Eligible patients were undergoing routine echocardiography and all patients were required to have at least two of six segments of the left ventricular endocardial border that were not well delineated in the apical 4-chamber view. In these studies, the 203 patients (Study A: n=101, Study B: n=102) received at least one dose of study drug had the following characteristics: 79% men, 21% women, 64% White, 25% Black, 10% Hispanic, and 1% other race or ethnic group. The patients had a mean age of 61 years (range: 21 to 83 years), a mean weight of 196 lbs (range: 117 to 342 lbs), a mean height of 68 inches (range: 47 to 78 inches), and a mean body surface area of 2.0m² (range: 1.4 to 2.6m²). Approximately 23% of the patients had chronic pulmonary disease, and 17% had congestive and dilated cardiomyopathy with left ventricular ejection fractions (LVEFs) of between 20% and 40% (by previous echocardiography). Patients with a LVEF of less than 20% or with New York Heart Association Class IV heart failure were not included in the studies.

The study test drugs were four doses of OPTISON (0.2, 0.5, 3.0 and 5.0 mL) and two doses of ALBUNEX® (0.08 and 0.22 mL/kg). The two test drugs were administered to the patients in a random sequence, with two to ten days between each drug. After non-contrast imaging, the test doses were administered in ascending order with at least ten minutes between each dose. Ultrasound settings were optimized for the baseline (non-contrast) apical four-chamber view and remained unchanged for the contrast imaging. Static echocardiographic images and video-

tape segments were interpreted by a reader who was blinded to the patient's clinical history and to the identity and dose of the test drug. The primary efficacy endpoint was left ventricular endocardial border delineation, assessed before and after OPTISON administration, by the measurement of visualized endocardial border length. The six segments of the left ventricular endocardial border were also assessed qualitatively (i.e., not well delineated, average delineation, good delineation, excellent delineation) before and after OPTISON administration.

In comparison to non-contrast ultrasound, OPTISON significantly increased the length of endocardial border that could be visualized both at end-systole and end-diastole (see Table 2). In these patients there was a trend towards less visualization in women. Similarly, in comparison to non-contrast ultrasound, OPTISON significantly improved the qualitative ability to delineate each of the left ventricular segments, though the effect was less for the septal segments. As assessed by videodensitometry, OPTISON increased left ventricular opacification (peak intensity) in the mid-chamber and apical views (see Table 3). In subset analysis, OPTISON tended to enhance the quality of the spectral Doppler signal of the pulmonary veins. The imaging effects of OPTISON on endocardial border delineation and left ventricular opacification tended to be qualitatively similar in patients with and without pulmonary disease or dilated cardiomyopathy.

In these studies, quantitative measures of left ventricular function (e.g., ejection fraction), quantitative measurements of anatomical structures (e.g., wall thickness), or the evaluation of myocardial perfusion were not performed.

OPTISON dose	Length at End-Systole (cm)		Length at End-Diastole (cm)	
	n	mean ± S.D.	n	mean
Study A (n=101)				
0 mL (baseline)	87	7.7 ± 3.0	86	9.3 ± 3.4
0.2 mL	85	11.7 ± 4.3	85	15.7 ± 3.8
0.5 mL	86	12.0 ± 4.9	91	15.8 ± 5.1
3.0 mL	87	12.3 ± 4.4	88	16.7 ± 4.0
5.0 mL	89	12.7 ± 4.9	90	16.6 ± 4.3
Study B (n=102)				
0 mL (baseline)	89	8.1 ± 3.4	89	9.6 ± 3.7
0.2 mL	90	11.3 ± 4.5	95	15.0 ± 5.3
0.5 mL	95	12.4 ± 4.9	97	16.4 ± 4.6
3.0 mL	94	12.6 ± 4.8	99	16.5 ± 4.7
5.0 mL	92	13.0 ± 4.5	95	16.2 ± 5.1

a The differences in the number of enrolled patients and evaluated patients at each dose reflects exclusions based on withdrawal from the trial, or those with technically inadequate or missing images.
b An intent-to-treat analysis, with non-favorable values imputed for missing patients, provided qualitatively similar results.

OPTISON dose	Mid-Chamber				Apex			
	n	mean ± S.D.	n	mean ± S.D.	n	mean ± S.D.	n	mean ± S.D.
Study A (n = 101)								
0 mL (baseline)	91	39.5 ± 16.9	91	40.0 ± 18.1	91	46.7 ± 19.7	91	46.9 ± 20.1
0.2 mL	91	56.7 ± 26.2	91	55.4 ± 26.6	91	63.2 ± 28.9	91	61.1 ± 28.5
0.5 mL	91	57.3 ± 26.8	90	57.4 ± 26.7	91	67.0 ± 30.1	90	64.1 ± 30.2
3.0 mL	90	53.9 ± 22.5	90	55.8 ± 24.3	90	66.1 ± 28.2	90	61.8 ± 26.8
5.0 mL	89	54.7 ± 24.0	89	57.9 ± 28.3	89	69.1 ± 30.4	89	63.7 ± 28.9
Study B (n = 102)								
0 mL (baseline)	95	40.4 ± 17.4	95	40.9 ± 17.5	95	43.7 ± 19.9	95	45.0 ± 19.6
0.2 mL	97	52.5 ± 21.0	97	51.5 ± 20.6	97	58.4 ± 22.2	97	56.0 ± 22.2
0.5 mL	97	53.3 ± 20.7	96	53.6 ± 21.0	97	64.4 ± 25.3	96	61.6 ± 26.7
3.0 mL	99	51.2 ± 23.6	99	55.6 ± 24.5	99	65.4 ± 26.3	99	62.7 ± 25.7
5.0 mL	95	51.8 ± 23.8	95	55.6 ± 24.8	95	65.2 ± 28.1	95	62.8 ± 28.1

a Intensity measured by videodensitometry in arbitrary gray scale units (0-255).
b The differences in the number of enrolled patients and evaluated patients at each dose reflects exclusions based on withdrawal from the trial, or those with technically inadequate or missing images.
c An intent-to-treat analysis, with non-favorable values imputed for missing patients, provided qualitatively similar results.

Pulmonary Hemodynamic Effects:

The effect of OPTISON on pulmonary hemodynamics was studied in a prospective, open-label study of 30 patients scheduled for pulmonary artery catheterization, including 19 with an elevated baseline pulmonary arterial systolic pressure (PASP) (>35 mmHg) and 11 with a normal PASP (≤35 mmHg). Systemic hemodynamic parameters and ECGs were also evaluated. No clinically important pulmonary hemodynamic, systemic hemodynamic, or ECG changes were observed. This study did not assess the effect of OPTISON on visualization of cardiac or pulmonary structures.

INDICATIONS

OPTISON is indicated for use in patients with suboptimal echocardiograms to opacify the left ventricle and to improve the delineation of the left ventricular endocardial borders.

CONTRAINDICATIONS

Do not administer OPTISON to patients with known or suspected:

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

Do not administer OPTISON by intra-arterial injection.

WARNINGS

Serious Cardiopulmonary Reactions

Serious cardiopulmonary reactions, including fatalities, have occurred uncommonly during or shortly following perflutren-containing microsphere administration, typically within 30 minutes of 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).

The reported reactions to perflutren-containing microspheres include: fatal cardiac or respiratory arrest, shock, syncope, symptomatic arrhythmias (atrial fibrillation, tachycardia, bradycardia, supraventricular tachycardia, ventricular fibrillation, ventricular tachycardia), hypertension, hypotension, hypoxemia, hypoxia, chest pain, respiratory distress, stridor, wheezing, loss of consciousness and convulsions (see ADVERSE REACTIONS).

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

Anaphylactoid Reactions

In postmarketing use, uncommon but serious anaphylactoid reactions were 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 (see ADVERSE REACTIONS).

Systemic Embolization of OPTISON in Patients with Cardiac Shunts

In patients with right-to-left, bi-directional, or transient right-to-left cardiac shunts perflutren-containing microspheres can bypass the pulmonary particle-filtering mechanisms and directly enter the arterial circulation resulting in microvascular occlusion and ischemia. Do not administer OPTISON by intra-arterial injection (see CONTRAINDICATIONS).

High Ultrasound Mechanical Index

High ultrasound mechanical index values may cause microsphere cavitation or rupture and lead to ventricular arrhythmias. Additionally, end-systolic triggering with high mechanical indices has been reported to cause ventricular arrhythmias. The safety of OPTISON at mechanical indices greater than 0.8 has not been evaluated. The safety of OPTISON with the use of end-systolic triggering has not been evaluated.

PRECAUTIONS

General

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) also is considered extremely remote. No cases of transmission of viral disease or CJD have ever been identified for albumin.

Laboratory Tests

Immunologic tests of serum immunoglobulins, cytokines, and complement were monitored in a 3 week study of 20 healthy volunteers and 30 patients who received OPTISON or a 1% albumin control. Clinically relevant changes in the measured parameters were not noted. In another study 5 subjects received a skin test with OPTISON one year after receiving OPTISON. One subject had a positive skin test and was not given a repeat dose of OPTISON.

Information for Patients

Patients receiving OPTISON should be instructed to inform their healthcare provider if they:

1. have a congenital heart defect, or recent worsening of heart or lung conditions;
2. have had reactions to blood, blood products, albumin or a prior OPTISON administration (see CONTRAINDICATIONS and WARNINGS);
3. may be pregnant or are nursing an infant.

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Animal studies were not carried out to determine the carcinogenic potential of OPTISON.

The result of the following genotoxicity studies with OPTISON were negative: 1) Salmonella/Escherichia coli reverse mutation assay, 2) *in vitro* mammalian chromosome aberration assay using Chinese hamster ovary cells (CHO) with and without metabolic activation, 3) CHO/HGPRT forward mutation assay, and 4) *in vivo* mammalian micronucleus assay.

Pregnancy Category C

OPTISON administered intravenously to rats during organogenesis at doses of 0.25, 5.0 and 10.0 mL/kg/day was fetotoxic at 0.25 and 5.0 mL/kg (approximately 0.2 and 5 times the recommended maximum human dose, respectively, based on body surface area). Fetotoxicity was characterized by an increased incidence of reversible delayed pelvic ossification, the incidence of which was not related to dose. Signs of maternal toxicity at 5 mL/kg included respiratory and motor signs. Maternal death occurred at 10 mL/kg. A no observable adverse effect level (NOAEL) for fetotoxicity was not determined. Teratogenic effects were not observed at doses up to 10 mL/kg/day. The NOAEL for maternal toxicity was 0.25 mL/kg.

OPTISON administered intravenously to rabbits during organogenesis at doses of 0.25, 2.5 and 5.0 mL/kg/day was embryofetal toxic at 2.5 and 5.0 mL/kg (approximately 5 and 10 times the recommended maximum human dose, respectively, based on body surface area). Embryofetal toxicity was characterized by a decrease in fetal body weight and an increase in embryofetal death. Teratogenic effects (cleft palates and dilation of the lateral ventricles of the brain associated with skull abnormalities and compression deformities) were observed at 2.5 mL/kg but not 5 mL/kg. Neither the incidence nor the severity of embryofetal toxicity and teratogenicity exhibited a dose-dependent relationship. Maternal toxicity (significant suppression of body weight gain, abnormal stool) was observed at 2.5 and 5.0 mL/kg with the greatest effect observed at 2.5 mL/kg. The NOAEL for embryofetal and maternal toxicity was 0.25 mL/kg (approximately 0.5 times the recommended maximum human dose).

Adequate or well-controlled studies were not conducted in pregnant women. OPTISON should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk caution should be exercised when OPTISON is administered to a nursing woman.

Pediatric Use

Safety and efficacy have not been established in pediatric patients, or in patients with congenital heart disease (see WARNINGS).

ADVERSE REACTIONS

Clinical Trials Experience

OPTISON was administered in clinical studies in 279 patients. Of these patients there were 192 (68.8%) men and 87 (31.2%) women. The racial demographics were 199 (71.3%) Caucasian, 52 (18.6%) Black, 24 (8.6%) Hispanic, and 4 (1.4%) other racial or ethnic groups.

In these patients, 47 (16.8%) reported at least one adverse event. Of these one event was serious and required treatment with antihistamines for hypersensitivity manifestations of dizziness, nausea, flushing and temperature elevation. Deaths were not reported during the clinical studies.

Of the reported adverse reactions following the use of OPTISON the most frequently reported were headache (5.4%), nausea and/or vomiting (4.3%), warm sensation or flushing (3.6%), and dizziness (2.5%). The most common adverse events observed in clinical studies of OPTISON are given in Table 4.

No. of Patients Exposed to OPTISON™	279
No. of Patients Reporting on Adverse Event	47 (16.8%)
Body as a Whole	38 (13.6%)
Headache	15 (5.4%)
Warm Sensation/Flushing	10 (3.6%)
Chills/fever	4 (1.4%)
Flu-like Symptoms	3 (1.1%)
Malaise/Weakness/Fatigue	3 (1.1%)
Cardiovascular System	12 (4.3%)
Dizziness	7 (2.5%)
Chest Pain	3 (1.1%)
Digestive System	12 (4.3%)
Nausea and/or Vomiting	12 (4.3%)
Nervous System	3 (1.1%)
Respiratory System	5 (1.8%)
Dyspnea	3 (1.1%)

Skin & Appendages	11 (3.9%)
Injection Site Discomfort	3 (1.1%)
Erythema	2 (0.7%)
Special Senses	9 (3.2%)
Altered Taste	5 (1.8%)
(1) Patients are counted separately within each body system.	
(2) The body system is reported if the aggregate is ≥ 0.5%. Details are not shown if the subsystem is not ≥ 0.5%.	

Adverse events reported in < 0.5% of subjects who received OPTISON included: arthralgia, back pain, body or muscle aches, induration, urticaria, dry mouth, eosinophilia, palpitations, paresthesia, photophobia, premature ventricular contraction, pruritus, rash, irritableness, hypersensitivity, tinnitus, tremor, visual blurring, wheezing, oxygen saturation decline due to coughing, discoloration at the Heplock site, and burning sensation in the eyes.

Overall the reported adverse events with OPTISON were similar in type and frequency to those reported in the 199 patients who received ALBUNEX®.

In the clinical dose ranging studies of 40 normal volunteers, doses higher than those recommended in the DOSAGE AND ADMINISTRATION section tended to be associated with an increased frequency of reported adverse events.

Postmarketing Experience

In a prospective, post-marketing safety surveillance study of OPTISON used in routine clinical practice, a total of 1039 subjects received OPTISON. Of these patients, 648 (62.4%) were male and 391 (37.6%) were female with average age of 59.9 years (min, max: 20, 97). The racial distributions were 864 (83.2%) White, 141 (13.6%) Black, 18 (1.7%) Asian, and 16 (1.5%) other racial or ethnic groups. Overall, 175 patients (16.8%) reported at least one adverse event. No serious adverse reactions, including deaths, were reported in this study, suggesting that these reactions are unlikely to occur at a rate of more than 0.3% when OPTISON is used according to recommendations. The following adverse reactions have been identified during the postmarketing use of OPTISON. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiac arrests and other serious but non-fatal 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 (see WARNINGS).

DOSAGE AND ADMINISTRATION

The recommended dose of OPTISON is 0.5 mL injected into a peripheral vein. This may be repeated for further contrast enhancement as needed. See individualization of dose below.

1. The injection rate should not exceed 1 mL per second.
2. Follow the OPTISON injection with a flush of 0.9% Sodium Chloride Injection, USP, or 5% Dextrose Injection, USP.
3. The maximum total dose should not exceed 5.0 mL in any 10 minute period.
4. The maximum total dose should not exceed 8.7 mL in any one patient study.

Individualization of Dose

Image quality in cardiac ultrasound is a function of the acoustic window which is influenced by many variables including body habitus, intervening lung tissue, adequacy of transducer skin interface and other acoustic factors. These variables may influence the ultrasound contrast effect.

If the contrast enhancement is inadequate after the dose of 0.5 mL, additional doses in increments of 0.5 mL up to 5.0 mL cumulatively in a 10 minute period may be injected intravenously up to a maximum total dose of 8.7 mL in any one patient study.

DRUG HANDLING DIRECTIONS

FOR SINGLE USE ONLY.

OPTISON does not contain preservatives. Bacterial contamination with the risk of post-infusion septicemia can occur if the container has been damaged or following puncture of the rubber cap. A single vial must not be used for more than one patient. Discard unused product properly.

DO NOT USE if the container has been damaged or the protective seal and/or rubber cap have been entered.

DO NOT USE if the upper white layer is absent. This indicates that the microspheres may have been damaged and may result in poor or no echo contrast.

DO NOT INJECT air into the vial.

1. Invert the OPTISON vial and gently rotate to resuspend the microspheres. This process will allow the product to come to room temperature before use.
2. Inspect the vial for complete resuspension. Failure to adequately resuspend OPTISON may cause an under delivery of the microspheres, and may result in inadequate contrast.
3. Do not use OPTISON if, after resuspension, the solution appears to be clear rather than opaque milky-white.
4. Vent the OPTISON vial with a sterile vent spike or with a sterile 18 gauge needle before withdrawing the OPTISON suspension into the injection syringe.

DO NOT USE if after resuspending the OPTISON, the product remains clear rather than appearing opaque and milky-white.

INJECTION PROCEDURE:

The time from resuspension of the OPTISON to injection must not exceed one minute. If one minute is exceeded, resuspend the microspheres in the syringe by gently rotating and inverting the syringe.

Before injection, provide intravenous access in a peripheral vein with a 20-gauge or larger angiocatheter. Suggested methods of administration include: a short extension tubing, heparin lock, or intravenous line, all with a 3-way stopcock.

For short extension tubing or heparin lock: fill one syringe with 0.9% Sodium Chloride Injection, USP, and flush the line for patency before and after the injection of OPTISON.

For a continuous intravenous line: open an intravenous line with 0.9% Sodium Chloride Injection, USP (or 5% Dextrose Injection, USP) at a slow infusion rate to maintain vascular patency. The line should be flushed immediately after injection of OPTISON.

DO NOT ASPIRATE blood back into the OPTISON containing syringe before administration; this may promote the formation of a blood clot within the syringe.

HOW SUPPLIED

OPTISON (Perflutren Protein-Type A Microspheres Injectable Suspension, USP) is available in a carton of five 3 mL fills in single use 3 mL vials.

NDC 0407-2707-03

STORAGE

Store OPTISON refrigerated between 2°-8°C (36°-46°F).

Caution: Do not freeze.

Rx ONLY

Distributed by GE Healthcare Inc., Princeton, NJ 08540
Manufactured by Mallinckrodt Inc., St. Louis, MO 63042

OPTISON™ is a trademark of GE Healthcare.
GE and the GE Monogram are trademarks of General Electric Company.
ALBUNEX® is a trademark of Mallinckrodt Inc.

© 2012 General Electric Company - All rights reserved.

