ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

OPTISON 0.19 mg/ml dispersion for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

OPTISON consists of perflutren-containing microspheres of heat treated human albumin, suspended in human albumin solution, 1%.

Concentration: Perflutren-containing microspheres, 5-8 x 10^8/ml with a mean diameter range of 2.5 - 4.5 µm.
The approximate amount of perflutren gas in each ml of OPTISON is 0.19 mg.

Excipient with known effect:
Each ml contains 0.15 mmol (3.45 mg) of sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersion for injection.

Clear solution with white microsphere layer on top.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

OPTISON is a transpulmonary echocardiographic contrast agent for use in patients with suspected or established cardiovascular disease to provide opacification of cardiac chambers, enhance left ventricular endocardial border delineation with resulting improvement in wall motion visualisation. OPTISON should only be used in patients where the study without contrast enhancement is inconclusive.

4.2 Posology and method of administration

OPTISON should only be administered by physicians experienced in the field of diagnostic ultrasound imaging.

Before administering OPTISON, please see section 6.6 for instructions for use/handling.

This medicinal product is intended for left ventricular opacification after intravenous administration. Ultrasound imaging must be performed during injection of OPTISON as optimal contrast effect is obtained immediately after administration.

Posology
The recommended dose is 0.5 ml - 3.0 ml per patient. A dose of 3.0 ml is usually sufficient, but some

patients may need higher doses. The total dose should not exceed 8.7 ml per patient. The duration of the useful imaging time is 2.5 - 4.5 minutes for a dose of 0.5 - 3.0 ml. OPTISON could be repeatedly administered, however, the clinical experience is limited.

Paediatric population

The safety and efficacy of OPTISON in children and adolescents below 18 years has not been established.
Currently available data are described in section 5.1 but no recommendation on a posology can be made.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Pulmonary hypertension with a systolic pulmonary artery pressure > 90 mm Hg.

4.4 Special warnings and precautions for use

Hypersensitivity has been reported. Care should therefore be exercised. A course of action should be planned in advance with necessary drugs and equipment available for immediate treatment, in case a serious reaction should occur.

The experience of OPTISON in severely ill patients is limited. There is limited clinical experience with OPTISON in patients with certain severe states of cardiac, pulmonary, renal and hepatic disease. Such clinical states include adult respiratory distress syndrome, the use of artificial respiration with positive end-expiratory pressure, severe heart failure (NYHA IV), endocarditis, acute myocardial infarction with on-going angina or unstable angina, hearts with prosthetic valves, acute states of systemic inflammation or sepsis, known states of hyperactive coagulation system and/or recurrent thromboembolism, renal or hepatic end-stage disease. OPTISON should be used in these categories of patients only after careful consideration and monitored closely during and after administration. Other routes of administration not specified in section 4.2 above (e.g. intracoronary injection) are not recommended.

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

There are no reports of virus transmissions with albumin manufactured to European Pharmacopoeia specifications by established processes.

It is strongly recommended that every time that OPTISON is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

OPTISON contrast echocardiography should be accompanied by ECG monitoring.

In animal studies, the application of echo-contrast agents revealed biological side effects (e.g. endothelial cell injury, capillary rupture) by interaction with the ultrasound beam. Although these biological side effects have not been reported in humans, the use of a low mechanical index and end-diastolic triggering is recommended.

Paediatric population
Efficacy and safety in patients below 18 years has not been studied.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.
Use during anaesthesia with halothane and oxygen has not been studied.

4.6 Fertility, pregnancy and lactation

Pregnancy
The safety of OPTISON for use during human pregnancy has not been established. In pregnant rabbits exposed to daily doses of 2.5 ml/kg (approximately 15 x the maximum recommended clinical dose) during organogenesis, maternal toxicity and embryo-foetal toxicity including a slight to extreme dilation of ventricles in the brain of developing rabbit embryos was observed. The clinical relevance of this finding is unknown. Therefore, OPTISON should not be used in pregnancy unless benefit outweighs risk and it is considered necessary by the physician.

Breast-feeding
It is not known whether OPTISON is excreted in human milk. Therefore, caution should be exercised when OPTISON is administered to breast-feeding women.

4.7 Effects on the ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Adverse reactions to OPTISON are rare and usually of a non-serious nature. In general, the administration of human albumin has been associated with transient altered taste, nausea, flushing, rash, headache, vomiting, chills and fever. Anaphylactic reactions have been associated with the administration of human albumin products. The reported adverse events following the use of OPTISON in Phase III human clinical studies have been mild to moderate with subsequent full recovery.

In clinical trials with OPTISON, undesirable effects were reported as adverse events with the following frequencies given in the table below: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Class	**Undesirable Effects**	**Frequency**
Blood and lymphatic system disorders	Eosinophilia	Uncommon
Nervous system disorders	Dysgeusia (altered taste), headache Tinnitus, dizziness, paraesthesia	Common Rare
Eye disorders	Visual disturbances	Not known*
Cardiac disorders	Ventricular tachycardia	Rare
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Uncommon
Vascular disorders	Flushing	Common

Gastrointestinal disorders	Nausea	Common
General disorders and administration site conditions	Warm sensation Chest pain	Common Uncommon
Immune system disorders	Allergic type symptoms (e.g. anaphylactoid reaction or -shock, face oedema, urticaria)	Not known*

* Reactions for which no frequency rate can be provided due to lack of clinical trial data have been classified as “Not known”.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

No case of overdose has been reported.
In the Phase I trial, healthy volunteers have received up to 44.0 ml of OPTISON and experienced no significant adverse events.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ultrasound contrast medium, ATC Code: V08D A01

When used in conjunction with diagnostic ultrasound, OPTISON provides opacification of cardiac chambers, improvement in delineation of endocardial borders, enhancement of the Doppler signal, and visualisation of wall motion and blood flow within the heart.

The ultrasound echoes from blood and biological soft tissues such as fat and muscles are generated at interfaces due to small differences in the ultrasonic properties of the tissues. The ultrasonic properties of microspheres containing perflutren are very different from that of soft tissue and will generate strong echoes.

OPTISON consists of perflutren -containing microspheres. The microspheres have a mean diameter of 2.5 - 4.5 microns and concentrations of 5-8 x 10^8 microspheres/ml. Microspheres in this size range contribute to the contrast effect by generating strongly enhanced echoes.

As OPTISON consists of microspheres that are stable and small enough for transpulmonary passage, it will also give enhanced echo signals in the left heart cavities.

As a consequence of the complex relationship between the concentration of the microspheres and the ultrasound signal, data processing within the ultrasound equipment and the fact that each individual responds differently due to variability in cardiac and pulmonary function, a strict dose/response relationship cannot be defined. The dose of OPTISON will therefore have to be adjusted individually, although clinical studies have shown that an initial dose of 0.5 - 3.0 ml per patient can be recommended for left heart opacification. Higher doses produce greater contrast effect of longer duration. Duration of useful contrast effect at the recommended dose is adequate to perform a complete echocardiographic examination including Doppler assessment.

Use the smallest dose for adequate opacification of cavities since larger doses produce image blocking effects with the possibility of obscuring important information.

In two uncontrolled studies including a total of 42 children and adolescents, aged 8 months to 19 years, the safety profile appeared to be similar to that seen in adults. Doses administered in one study were 0.2 ml above 25 kg body weight and 0.1ml under 25 kg, and in a second study 0.5ml above 20 kg body weight and 0.3 ml under 20 kg, by bolus peripheral intravenous injection followed by a saline flush. Low mechanical index was used for ultrasound imaging.

The effect of OPTISON on pulmonary haemodynamics was studied in a prospective, open-label study of 30 patients scheduled for pulmonary artery catheterisation, including 19 with an elevated baseline pulmonary arterial systolic pressure (PASP) (>35 mmHg; mean 70.1±33.0 mmHg; range 36.0-176.0 mmHg) and 11 with a normal PASP (≤35 mmHg; mean 29.3±4.6 mmHg; range 22.0-35.0 mmHg). Systemic haemodynamic parameters and ECGs were also evaluated. No clinically important pulmonary haemodynamic, systemic haemodynamic, or ECG changes were observed. This study did not assess the effect of OPTISON on visualisation of cardiac or pulmonary structures.

5.2 Pharmacokinetic properties

Following intravenous injection of 0.21 to 0.33 ml/kg of OPTISON to healthy volunteers, the perflutren component of OPTISON was rapidly and nearly completely eliminated in less than 10 minutes with a dominating pulmonary elimination half-life of 1.3±0.7 minutes. The perflutren levels detected in blood following this dosage were too low and transient to accurately determine pharmacokinetic parameters.

The disposition and elimination of the albumin microspheres have not been studied in humans. Information obtained from a preclinical study in rats with ^{125}I-labelled albumin microspheres indicated that microspheres were rapidly cleared from the circulation, and radio-labelled microspheres, albumin shells and ^{125}I were taken up primarily in the liver. The primary route of elimination of radioactivity was the urine. High levels of radioactivity were also retained in lungs for a considerable time, approx. 10% of the total dose 40 minutes after dose administration (cf. 35% in liver).

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, acute and repeated dose toxicity and genotoxicity. In the rabbit embryotoxicity study, a significant increase in the number of foetuses with dilated ventricles in the brain was observed (see section 4.6). No such finding was observed in the rat embryotoxicity study.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Human albumin
Sodium chloride
N-acetyltryptophan
Caprylic acid
Sodium hydroxide (pH adjustment)
Water for injections

6.2 Incompatibilities

OPTISON must not be mixed with other medicinal products. A separate syringe should be used.

6.3 Shelf life

Unopened vial in the outer packaging: 2 years.

Finished product after rubber stopper perforation: 30 minutes.

6.4 Special precautions for storage

Store upright in a refrigerator ($2^{o}C$ - $8^{o}C$).
Storage at room temperature (up to $25^{o}C$) for 1 day is acceptable.
Do not freeze.

6.5 Nature and contents of container

3 ml type I glass vial, closed with bromobutyl rubber stopper, and sealed with aluminium cap with coloured plastic flip-off top.

OPTISON is supplied as: 1 vial of 3 ml or 5 vials of 3 ml.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Like all parenteral products, the vials of OPTISON should be inspected visually for integrity of the container.

Vials are intended for single use only. Once the rubber stopper has been penetrated, the contents should be used within 30 minutes and any unused product discarded.

OPTISON in the non-resuspended form has a white layer of microspheres on top of the liquid phase that requires resuspension before use. Homogenous white suspension after resuspension.

The following instructions should be followed:

- Cold solutions taken directly from the refrigerator should not be injected.

- Allow the vial to reach room temperature and inspect the liquid phase for particulate matter or precipitates before resuspension.

- Insert a 20 G plastic cannula in a large antecubital vein, preferably of the right arm. Attach a three-way stopcock to the cannula.

- The OPTISON vial must be inverted and gently rotated for approximately three minutes to completely resuspend the microspheres.

- Complete resuspension is indicated by a uniformly opaque white suspension and absence of any material on stopper and vial surfaces.

- OPTISON should be withdrawn with care into a syringe within 1 minute after resuspension.

- Any pressure instability within the vial should be avoided since it may cause disruption of microspheres and loss of contrast effect. Thus, vent the vial with a sterile spike or with a sterile 18 G needle before withdrawing the suspension into the injection syringe. Do not inject air into the vial as this will damage the product.

- Use the suspension within 30 minutes after withdrawal.

- OPTISON will segregate in an undisturbed syringe and must be resuspended before use.

- Resuspend the microspheres in the syringe immediately before injection by holding the syringe horizontally between the palms of the hands and rolling it quickly back and forth for no less than 10 seconds.

- Inject the suspension through the plastic cannula, no smaller than 20 G at a maximum injection rate of 1.0 ml/s.
  Warning: Never use any other type of route but the open flow connection. If injected otherwise OPTISON bubbles will be destroyed.

- Immediately before injection a careful visual inspection of the syringe is mandatory in order to ensure complete suspension of the microspheres.

Immediately after injection of OPTISON, 10 ml of sodium chloride 9 mg/ml (0.9%) solution for injection or glucose 50 mg/ml (5%) solution for injection should be injected at a rate of 1 ml/s. Alternately, the flushing may be performed by infusion. The infusion set should then be attached to the three-way stopcock and intravenous infusion started at a “to keep open” (TKO) rate. Immediately after OPTISON injection, the intravenous infusion should be wide open until contrast begins to fade from the left ventricle. The infusion should then be returned to a TKO rate.

7. MARKETING AUTHORISATION HOLDER

GE Healthcare AS
Nycoveien 1
NO-0485 Oslo, Norway

8. MARKETING AUTHORISATION NUMBERS

1 x 3 ml presentation: EU/1/98/065/001
5 x 3 ml presentation: EU/1/98/065/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18 May 1998
Date of latest renewal: 12 June 2008

10. DATE OF REVISION OF THE TEXT

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

GE Healthcare AS
Nycoveien 1
NO-0485 Oslo
Norway

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports**

The marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c (7) of Directive 2001/83/EC and published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

OPTISON 0.19 mg/ml dispersion for injection
Perflutren-containing microspheres

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml contains: Perflutren-containing microspheres 5 - 8 x 10^8, with a mean diameter range of 2.5 - 4.5 µm, equivalent to 0.19 mg perflutren gas per ml.

3. LIST OF EXCIPIENTS

Excipients: Human albumin, sodium chloride, N-acetyltryptophan, caprylic acid, sodium hydroxide and water for injections. See the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

1 x 3 ml
5 x 3 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Ultrasound contrast medium.
Intravenous use.
Resuspend before use.
Do not inject air into the vial.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

For single use only. Discard any unused portion.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store upright in a refrigerator.
Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GE Healthcare AS, Nycoveien 1, 0485 Oslo, Norway

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/98/065/001
EU/1/98/065/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

Not applicable.

PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

OPTISON 0.19 mg/ml dispersion for injection
Perflutren-containing microspheres
Intravenous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml

6. OTHER

GE Healthcare

B. PACKAGE LEAFLET

Package leaflet: Information for the user

OPTISON 0.19 mg/ml dispersion for injection
Perflutren-containing microspheres

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What OPTISON is and what it is used for

OPTISON is an ultrasound contrast agent that helps to obtain clearer pictures (scan) of the heart during an echocardiography (a procedure where an image of the heart is obtained by using ultrasound). OPTISON improves the visualization of the inner cardiac walls in patients where the walls are difficult to see.

OPTISON contains microspheres (tiny gas bubbles) that after injection travel through the veins to the heart and fill the left heart chambers, allowing the doctor to visualise and asses the function of the heart.

This medicine is for diagnostic use only.

2. What you need to know before you use OPTISON

Do not use OPTISON
- if you are allergic (hypersensitive) to perflutren or any of the other ingredients of OPTISON (listed in section 6).
- if you have severe pulmonary hypertension (systolic pulmonary artery pressure > 90 mm Hg).

Warnings and precautions
Talk to your doctor before using OPTISON
- if you have any known allergies
- if you have a severe heart, lung, kidney or liver disease. The experience of OPTISON in severely ill patients is limited
- if you have an artificial valve in your heart
- if you have acute severe inflammation or sepsis
- if you have a known blood clotting problem

Your heart activity and rhythm will be monitored when you get OPTISON.

Children and adolescents
Efficacy and safety in patients below 18 years has not been established.

When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

There are no reports of virus infections with albumin manufactured to European Pharmacopoeia specifications by established processes.

It is strongly recommended that every time you receive a dose of OPTISON the name and batch number of the product are recorded in order to maintain a record of the batches used.

Other medicines and OPTISON
Tell your doctor if you are taking or have recently taken any other medicines.

Pregnancy and breast-feeding
The safety of OPTISON for use during human pregnancy has not been fully established. Therefore, the medicine should not be used in pregnancy unless benefit outweighs risk and it is considered necessary by the doctor. However, because OPTISON is based on human albumin (the main protein in our blood), it is highly unlikely that it will have any harmful effects in pregnancy.

It is not known whether OPTISON passes into human milk. Therefore, caution should be exercised when OPTISON is administered to nursing women.

Driving and using machines
No effects are known.

OPTISON contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially “sodium-free”.

3. How to use OPTISON

OPTISON should only be administered by doctors experienced in the field of diagnostic ultrasound imaging.

OPTISON is administered via an intravenous injection to allow the microspheres to enter the heart chamber and fill the left heart chamber. OPTISON is injected during the ultrasound examination in order to allow the doctor to assess the function of your heart.

The recommended dose is 0.5 ml - 3.0 ml per patient. A dose of 3.0 ml is usually sufficient, but some patients may need higher doses. This dose might be repeated if needed. The duration of the useful imaging time is 2.5 - 4.5 minutes for a dose of 0.5 - 3.0 ml.

Immediately after injection of OPTISON, 10 ml of sodium chloride 9 mg/ml solution for injection or glucose 50 mg/ml solution for injection should be injected at a rate of 1 ml/s to optimise the effect of the contrast agent.

If you are given more OPTISON than you should
Effects suspected to be due to overdose have not been reported.

4. Possible side effects

Like all medicines, OPTISON can cause side effects, although not everybody gets them.

Side effects to OPTISON are rare and usually not serious. In general the administration of human albumin has been associated with transient (non lasting) altered taste, nausea, flushing, rash, headache, vomiting, chills and fever. Rare severe allergic reactions (anaphylaxis) have been associated with the administration of human albumin products. Reported side effects following the use of OPTISON:

Common side effects (affects 1 to 10 users in 100):
- Dysgeusia (altered taste)
- Headache
- Flushing (redness)
- Warm sensation
- Feeling sick (nausea)

Uncommon side effects (affects 1 to 10 users in 1,000):
- Eosinophilia (increased number of a type of white blood cells in the blood)
- Dyspnoea (difficulty in breathing)
- Chest pain

Rare side effects (affects 1 to 10 users in 10,000):
- Tinnitus (noises in the ear)
- Dizziness
- Paraesthesia (tingling sensations)
- Ventricular tachycardia (a series of rapid heartbeats)

Unknown frequency (side effects where frequency cannot be estimated from the available data):
- Allergic type symptoms, for example, a severe allergic reaction or – shock (anaphylaxis), swelling of the face (face oedema), an itchy skin eruption (urticaria).
- Visual disturbances

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store OPTISON

Keep this medicine out of the sight and reach of children.

Do not use OPTISON after the expiry date which is stated on the label, after EXP.
The expiry date refers to the last day of that month.

Store upright in a refrigerator (2°C - 8°C).
Storage at room temperature (up to 25°C) for 1 day is acceptable.
Do not freeze.

The contents of the OPTISON vial should be used within 30 minutes after the rubber stopper has been penetrated.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What OPTISON contains

- The active substance is perflutren-containing microspheres of heat treated human albumin 5-8 x 10^8/ml, suspended in human albumin solution 1%. The approximate amount of perflutren gas in each ml of OPTISON is 0.19 mg
- The other ingredients are human albumin, sodium chloride, N-acetyltryptophan, caprylic acid, sodium hydroxide and water for injections.

What OPTISON looks like and contents of the pack

OPTISON is a dispersion for injection. It is a clear solution with white microsphere layer on top.
The product is supplied as 1 vial of 3 ml and 5 vials of 3 ml.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

GE Healthcare AS
Nycoveien 1,
NO-0485 Oslo, Norway

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Agency website.

The following information is intended for healthcare professionals only:

The recommended dose is 0.5 ml - 3.0 ml per patient. A dose of 3.0 ml is usually sufficient, but some patients may need higher doses. The total dose should not exceed 8.7 ml per patient. The duration of the useful imaging time is 2.5 - 4.5 minutes for a dose of 0.5 - 3.0 ml. OPTISON could be repeatedly administered, however, the clinical experience is limited.

Use the smallest dose for adequate opacification of cavities since larger doses produce image blocking effects with the possibility of obscuring important information.

Like all parenteral products, the vials of OPTISON should be inspected visually for integrity of the container.

Vials are intended for single use only. Once the rubber stopper has been penetrated, the contents should be used within 30 minutes and any unused product discarded.

OPTISON in the non-resuspended form has a white layer of microspheres on top of the liquid phase that requires resuspension before use. Homogenous white suspension after resuspension.

The following instructions should be followed:

- Cold solutions taken directly from the refrigerator should not be injected.

- Allow the vial to reach room temperature and inspect the liquid phase for particulate matter or precipitates before resuspension.

- Insert a 20 G plastic cannula in a large antecubital vein, preferably of the right arm. Attach a three-way stopcock to the cannula.

- The OPTISON vial must be inverted and gently rotated for approximately three minutes to completely resuspend the microspheres.

- Complete resuspension is indicated by a uniformly opaque white suspension and absence of any material on stopper and vial surfaces.

- OPTISON should be withdrawn with care into the syringe within 1 minute after resuspension.

- Any pressure instability within the vial should be avoided since it may cause disruption of microspheres and loss of contrast effect. Thus, vent the vial with a sterile spike or with a sterile 18 G needle before withdrawing the suspension into the injection syringe. Do not inject air into the vial as this will damage the product.

- Use the suspension within 30 minutes after withdrawal.

- OPTISON will segregate in an undisturbed syringe and must be resuspended before use.

- Resuspend the microspheres in the syringe immediately before injection by holding the syringe horizontally between the palms of the hands and rolling it quickly back and forth for no less than 10 seconds.

- Inject the suspension through the plastic cannula, no smaller than 20 G at a maximum injection rate of 1.0 ml/s.
  Warning: Never use any other type of route but the open flow connection. If injected otherwise OPTISON bubbles will be destroyed.

- Immediately before injection a careful visual inspection of the syringe is mandatory in order to ensure complete resuspension of the microspheres.

Immediately after injection of OPTISON, 10 ml of sodium chloride 9 mg/ml (0.9%) solution for injection or glucose 50 mg/ml (5%) solution for injection should be injected at a rate of 1 ml/s.

Alternatively, the flushing may be performed by infusion. The infusion set should then be attached to the three-way stopcock and intravenous infusion started at a ”to keep open” (TKO) rate. Immediately after OPTISON injection the intravenous infusion should be wide open until contrast begins to fade from the left ventricle. The infusion should then be returned to a TKO rate.