PACKAGE LEAFLET: INFORMATION FOR THE USER

Lipiodol Ultra Fluid 480 mg I/mL solution for injection
Iodised ethyl-esters of fatty acids of poppy seed oil

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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

1. What Lipiodol Ultra Fluid is and what it is used for
2. What you need to know before you use Lipiodol Ultra Fluid
3. How to use Lipiodol Ultra Fluid
4. Possible side effects
5. How to store Lipiodol Ultra Fluid
6. Contents of the pack and other information

1. WHAT LIPIODOL ULTRA FLUID IS AND WHAT IT IS USED FOR

Lipiodol Ultra Fluid is a diagnostic agent. It belongs to the group of contrast agents used for radiological examinations.

Lipiodol Ultra Fluid is used to enhance the contrast of the images obtained during radiological examinations. This contrast enhancement improves the visualisation and outline of certain body parts.

Lipiodol Ultra Fluid is used in radiological examinations of the uterus and Fallopian tubes when searching for causes of infertility.

When mixed with certain medicines used to treat liver cancer, Lipiodol Ultra Fluid carries and delivers the anti-cancer medicine into the area to be treated as part of a TACE procedure.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE LIPIODOL ULTRA FLUID

You should read the information in this section carefully.
You and your doctor should take the information into consideration before you are given Lipiodol Ultra Fluid.

Do not use Lipiodol Ultra Fluid:
- If you are allergic to iodised ethyl-esters of the fatty acids of poppy seed oil (the active substance),
- If you have an overactive thyroid gland (which can cause increased appetite, weight loss or sweating),
- If you have recently had severe injury or bleeding,
- If you are pregnant or think you are pregnant and are due to undergo hysterosalpingography (examination of the uterus and fallopian tubes)
- If you have inflammation in the pelvis affecting your womb (lower abdomen), tubes or ovaries are due to undergo hysterosalpingography (examination of the uterus and fallopian tubes).
- If you need a bronchography, a type of X-ray examination where dye is instilled into the lower lung. Lipiodol Ultra Fluid is not suitable for this X-ray examination.

Warnings and precautions
Talk to your doctor before using Lipiodol Ultra Fluid if:

- you have an history of hypersensitivity to iodine
- you have asthma
- you have a disease affecting your heart or your blood vessels
- you have a disease affecting your lungs
- you have a disease affecting your kidneys
- you have dilated veins in the oesophagus
- you have problems with the ducts which carries the bile
- you have thyroid disorders or a history of thyroid disease
- you are due to undergo a thyroid examination in the near future or treatment with radioactive iodine
- you have swelling of part or all of your arm or leg, including fingers or toes (lymph oedema).

As Lipiodol Ultra Fluid remains in the body for several months, the results of thyroid tests can be affected for up to two years after lymphography.

If you receive Lipiodol Ultra Fluid for hysterosalpingography (investigation of the uterus and fallopian tubes for infertility) and if you are trying to conceive, you should have your thyroid function monitored in the months after the procedure and especially if you have a history of thyroid dysfunction. The dose of Lipiodol Ultra Fluid should be kept as low as possible to minimize the potential risk of thyroid dysfunction. In the event that you become pregnant in the months after hysterosalpingography you will be monitored during your pregnancy for any indication of thyroid dysfunction

In all these cases, your doctor will only give you Lipiodol Ultra Fluid if the benefits outweigh the risks. If you are given Lipiodol Ultra Fluid, your doctor will take the precautions necessary and the administration of Lipiodol Ultra Fluid will be carefully monitored.

Children and elderly patients
If you are a child or an elderly patient, your doctor will take special care when using Lipiodol Ultra Fluid.

Special patient groups
If you have a renal or a hepatic disease, your doctor will take special care when using Lipiodol Ultra Fluid.

Other medicines and Lipiodol Ultra Fluid
Tell your doctor if you are taking, have recently taken or might take any other medicines.
In particular, please inform your doctor if:

- you are taking or have recently taken medicines:
  - for treating diabetes (metformin)
  - for heart and blood pressure disorders such as beta-blockers (tablets for calming the heart and decreasing the blood pressure) or diuretics (water-pills)
- you have recently received interleukin-2 (a drug used to treat cancer or to reinforce your immune system, i.e. your internal defence system).

Lipiodol Ultra Fluid with food and drink
There are no known interactions between Lipiodol Ultra Fluid and food or drinks.
Lipiodol Ultra Fluid is administered by injection. Therefore, there is no special recommendation regarding intake of food and drink. However, please check with your doctor if it is required or not to eat or drink before the examination.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.
Inform your doctor if:

- you are pregnant or might be pregnant
- your period is late

- you are breast-feeding

The product should not be used during pregnancy unless the benefits outweigh the risks. Your doctor will decide if the examination with Lipiodol Ultra Fluid is necessary. Lipiodol Ultra Fluid must not be given to you if you are pregnant or think you are pregnant and are due to undergo hysterosalpingography (examination of the uterus and fallopian tubes).

In the event that you become pregnant in the months after hysterosalpingography with Lipiodol Ultra Fluid you will be monitored during your pregnancy for any indication of thyroid dysfunction.

You should stop breast-feeding if you are given Lipiodol Ultra Fluid.

Driving and using machines
Lipiodol Ultra Fluid is unlikely to affect your ability to drive or use machines. If you feel unwell after the examination, you should not drive or use machines.

3. HOW TO USE LIPIODOL ULTRA FLUID

Lipiodol Ultra Fluid will be administered to you by injection.

During the examination, you will be under the supervision of a doctor. A needle may be left in your vein; this will allow the doctor to inject you with appropriate emergency medicines if necessary. If you experience an allergic reaction, the administration of Lipiodol Ultra Fluid will be stopped.

The attending staff know what precautions have to be taken for the examination. They are also aware of the possible complications that can occur.

Dosage
Your doctor will determine the dose you will receive. The dose will depend on the particular requirement of the examination that you need and on your body weight.

If you take more Lipiodol Ultra Fluid than you should
You will be given the injection in a medical setting by a trained person. Therefore, it is highly unlikely that you will be given an overdose. An overdose can make you feel ill or unwell. Therefore, you should report any symptom you may have to your doctor. Your doctor will take the appropriate measures if necessary.

4. POSSIBLE SIDE EFFECTS

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

The following terms are used to describe how often side effects have been reported:
• Very common (may affect more than 1 of 10 patients)
• Common (may affect up to 1 of 10 patients)
• Uncommon (may affect up to 1 of 100 patients)
• Rare (may affect up to 1 of 1,000 patients)
• Very rare (may affect up to 1 of 10,000 patients, including isolated reports).
- Not known: frequency cannot be estimated.

When used alone, the following side effects were reported.

There is a small risk that you may have an allergic reaction to Lipiodol Ultra Fluid. Such reactions can be severe and exceptionally result in shock (very rare case of allergic reaction that could put your life in danger). **Any of the symptoms below mentioned may be the first signs of a shock. Inform your doctor or health professional immediately if you feel any of them:**

- swelling of the face, mouth, lips, eyelids or throat which may cause you difficulties in swallowing or

breathing
- hypotension (low blood pressure)
- breathing difficulties
- whistling breathing
- coughing
- itching
- runny nose
- sneezing
- throat irritation or tightening
- eye irritation
- skin redness
- urticaria (skin itching nettlerash)

The above side effects may happen several hours or days after Lipiodol Ultra Fluid is given. If any of these side effects happen after you leave the hospital or clinic, go straight to the emergency department of your nearest hospital.

Other possible side effects:
- nausea (feeling sick), vomiting
- diarrhoea
- fever
- pains and pain in the pelvis (lower abdomen)
- underactive thyroid gland (which can cause tiredness or weight gain)
- increase in size of thyroid gland
- overactive thyroid gland (which can cause increased appetite, weight loss or sweating)
- inflammation of the thyroid gland
- swelling or aggravation of preexisting swelling of the various parts of the body (legs, arms, neck)
- embolism (blockage of blood vessels) in brain, lung, liver and retina. This can occur without clinical signs.
- Granuloma (roughly spherical mass formed in the body by accumulation of oily residue and cells)
- Following hysterosalpingography: a transient fever with pain in the pelvic area is often noted as well as the possibility of salpingitis (inflammation of fallopian tubal) or pelvioperitonitis (inflammation of peritonium) if there is a latent state of infection.

Following sialography (salivary gland examination): mild swelling of salivary ducts is sometimes reported but usually disappears within 48 hours.
Small amounts of Lipiodol Ultra Fluid may leak into the blood supply and end up in other parts of the body such as blood vessels or arteries.

Most side effects are dose-related and dosage should therefore be kept as low as possible.

In exceptional cases, the reaction may be serious. If any of the above signs occur, you should immediately contact your doctor.

If you get any side effects, talk to your doctor. This includes any side effects not listed in this leaflet.

When Lipiodol is mixed with anti-cancer medicines to treat liver cancer as part of TACE procedure, some specific risks and complications can arise:

Very common
- Pain, nausea, fatigue and flu-like symptoms can occur after the procedure (post-embolisation syndrome). These can vary from being very mild to severe. Treatment with painkillers and anti-sickness tablets will be available if you require them. The symptoms may take 1–2 weeks to settle.
- Abnormalities in liver function tests. Decreases in white blood cells, platelets, and anemia which are due to the anti-cancer drugs

Common

- Complications related to the TACE procedure including bleeding or artery injury where the catheter is inserted in your groin
- A buildup of fluid in the lung (called pulmonary edema) or in the pleural cavity, which is the space between the lungs and the walls of the chest (called pleural effusion)
- Liver complications may occur such liver failure (liver damage) which can be fatal with the symptoms of liver inflammation and the additional problems of confusion or coma (encephalopathy) and bruising or bleeding.
- Abnormal accumulation of fluid in abdomen (called ascites)
- Gastrointestinal bleeding due to rupture of gastric or oesophageal varices

Uncommon

- Infection can occur in the area of the liver treated and in the spleen causing abscess and will need treatment with antibiotic injections
- Collection of bile within the abdominal cavity (bilomas)
- Inflammation of gallbladder and risk of damage to your bile duct
- There is a risk of kidney damage in particular in patients with diabetes or other pre-existing kidney disease. This can be due to the contrast, the anti-cancer medicine or dehydration. You will normally have a drip placed before the procedure. This is to give you sufficient fluids to reduce the risk of problems with the kidney function.
- There is a risk of lung complications which include clot in the lung, inflammation of the lungs, sudden respiratory distress syndrome (shortness of breath/ difficulty breathing)

Frequency unknown

- Damage to the liver (liver failure), which can be fatal.
- Risk of hepatitis B or C virus activation
- Inflammation of the pancreas
- Skin damage

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system: HPRA Pharmacovigilance. Website: www.hpra.ie.
By reporting side effects, you can help provide more information on the safety of this medicine.

5. HOW TO STORE LIPIODOL ULTRA FLUID

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

Do not use this medicine after the expiry date which is stated on the ampoule and on the carton, after the abbreviation “Exp”. The expiry date refers to the last day of that month.

Do not store above 25°C.
Keep the ampoule in the outer carton.

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. FURTHER INFORMATION

What Lipiodol Ultra Fluid contains
The active substance is iodised ethyl-esters of the fatty acids of poppy seed oil. Lipiodol Ultra Fluid solution for injection contains approximately 480 mg I/ml organically bound iodine.
There is no other ingredients in Lipiodol Ultra Fluid.

What Lipiodol Ultra Fluid looks like and contents of the pack
Lipiodol Ultra Fluid is a solution for injection. The solution is a pale yellow, clear oily liquid.

The Lipiodol Ultra Fluid pack contains one ampoule. Each ampoule contains 10 ml of solution for injection.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Guerbet
BP 57400
95943 Roissy CdG cedex
France

Manufacturer:
Guerbet
BP 57400
95943 Roissy CDG cedex
France

This medicinal product is authorised in the Member States of the EEA under the following names:
LIPIODOL ULTRA FLUIDE: Belgium, Czech Republic, France, Luxembourg, Netherlands.
LIPIODOL ULTRA FLUID: Austria, Denmark, Germany, Hungary, Ireland, United Kingdom.
LIPIODOL ULTRA FLUIDO: Portugal.

This leaflet was last revised in April 2025.

INFORMATION FOR THE HEALTHCARE PROFESSIONAL

The following information is intended for healthcare professionals only. For full prescribing information please consult the Summary of Product Characteristics.

Dosage and method of administration

<u>In diagnostic radiology</u>
The volume to be administered depends on the particular requirements of the technique and the size of the patient.
<u>Recommended dosages</u>
- Lymphography: 3 to 10 mL (maximum 20 mL)
- Hysterosalpingography: Inject increments of 2 mL of Lipiodol Ultra Fluid into the endometrial cavity under fluoroscopic control until tubal patency is determined.

The total volume to be injected depends on the volume of the uterine cavity, usually not exceeding 15 mL.
The dose of Lipiodol Ultra Fluid for hysterosalpingography should be kept as low as possible to minimize the potential risk of thyroid dysfunction; this is important as women undergoing HSG are likely to be trying to conceive.

- Sialography: Until the gland fills, maximum 5 mL

In interventional radiology - TACE of hepatocellular carcinoma:
The dose used in TACE should be adjusted according to tumour and patient characteristics and should not exceed 15 ml due to risk of pulmonary adverse events when higher volume is used.
Most adverse effects are dose related and dosage should therefore be kept as low as possible.
Lipiodol Ultra Fluid has been used with a number of chemotherapeutic agents in the TACE procedure, and prescribers are advised to consult local guidance or treatment guidelines.
Instructions and precautions for use of the anticancer drugs must be strictly followed.

Instruction for Use/Handling/Incompatibilities
Lipiodol Ultra Fluid has been shown to dissolve polystyrene; for this reason disposable syringes made from this material must not be used to administer this preparation.

If the product becomes opaque or dark amber in colour it should not be used. For single use only.

Instructions for preparation of the mixture of Lipiodol Ultra Fluid with anticancer medicine(s):

- Prepare two syringes, made from compatible plastic material (i.e: polyamide, polypropylene, polysulfone), large enough to contain the total volume of mixture. The first syringe contains the anticancer drug solution, the second syringe contains Lipiodol Ultra Fluid.
- Connect the two syringes to a 3-way stopcock.
- Perform 15 to 20 back and forth movements between the two syringes to obtain a homogeneous mixture. It is recommended to start by pushing the syringe with the anticancer drug first.
- The mixture is to be prepared at the time of use and must be used promptly after preparation (within 3 hours). In exceptional cases, an early phase separation may be observed during the interventional radiology procedure, in this case the mixture can be re-homogenised as described above.
- When the adequate mixture is obtained, use a 1 to 3 mL syringe to inject in the micro-catheter.

Air embolism, resulting from accidental arterial injections of air bubbles after improper preparation of mixture (Lipiodol Ultra Fluid with chemotherapeutic agent) can potentially be fatal and can lead to respiratory, cardiac or cerebral complications.

Contraindications
- Hypersensitivity to Lipiodol Ultra Fluid (esters of iodised fatty acids of poppy-seed oil)
- Manifest hyperthyroidism
- Patients with traumatic injuries, recent haemorrhage or bleeding (risk of extravasation or embolism).
- Hysterosalpingography during pregnancy, acute pelvic inflammation, marked cervical erosion, endocervicitis and intrauterine bleeding, within 30 days of curettage or conization
- Bronchography (it would rapidly fill the bronchioles and alveoli)

Additional contraindication specific to use in TACE:
- Lipiodol Ultra Fluid mixture for treatment of hepatocellular carcinoma may lead to both ischemic and toxic effects to the bile ducts. Therefore, the treatment is contraindicated in areas of the liver where the bile ducts are dilated, unless post-procedural drainage can be performed.

Special warnings and special precautions for use
Lipiodol Ultra-Fluid must not to be administered by intravenous or intrathecal route.
There is a risk of hypersensitivity, regardless of the dose administered.

Pulmonary embolization occurs in a majority of patients following lymphography with Lipiodol Ultra Fluid. For this reason the doses should be adapted or the examination itself cancelled in subjects with impaired lung function, cardiorespiratory failure, or pre-existing right –sided cardiac overload, in particular elderly patients.

Intravasation of Lipiodol Ultra Fluid may occur in the course of a hysterosalpingography procedure and may result in serious pulmonary or cerebral embolic complications in the next hours following the procedure.

Iodinated contrast media can affect thyroid function because of the free iodine content and can cause hyperthyroidism in predisposed patients.

When injected into certain fistulae, great care should be taken to avoid penetration of vascular channels with the risk of oil embolism. Care should be taken not to inject the product into an area affected by haemorrhage or trauma.

Indications for the use of Lipiodol Ultra-Fluid must be carefully assessed in patients with primary lymph oedema, as the oedema can be exacerbated.

Iodinated contrast agents can induce a transient deterioration of renal function or exacerbate pre-existing renal failure.

Oesophageal varices must be carefully monitored as they can rupture immediately after treatment with TACE.

Interaction with other medicinal products and other forms of Interaction

- Metformin: in diabetic patients, intra-arterial administration of Lipiodol Ultra Fluid may cause lactic acidosis induced by diminished renal function. In patients undergoing TACE, metformin must be discontinued before the examination and resumed no earlier than two days after the procedure.

- Beta blockers, vasoactive substances, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers: these medicines reduce the effectiveness of the cardiovascular mechanisms that compensate for blood-pressure disturbances: the doctor should be informed about these prior to the administration of Lipiodol Ultra Fluid and have resuscitation equipment at hand.

- Diuretics: as diuretics may cause dehydration, the risk of acute renal failure is increased, particularly when high doses of contrast agents are administered. Precautions for use: rehydration before intra-arterial administration of Lipiodol Ultra Fluid for embolization.

- Interleukin II: the risk of developing a reaction to the contrast agents is increased in the event of previous treatment with interleukin II (IV route): skin rash or, more rarely, hypotension, oliguria, or even renal failure.

- Interference with diagnostic tests: As Lipiodol Ultra Fluid remains in the body for several months, thyroid diagnostic results can be affected for up to two years after lymphography.

Storing Lipiodol Ultra Fluid

Do not store above 25C.
Keep in outer carton.
Once opened, use immediately. Discard any unused content.