LIPIODOL ULTRA-FLUIDE (480 mg l/ml), solution for injection.

Composition
Ethyl esters of iodized fatty acids of poppy seed oil* qs ad for one ampoule
* Iodine content: 48 %, i.e. 480 mg per ml.
Solution for injection in 5 ml or 10 ml ampoules.

Pharmaco-therapeutic class
Contrast agent.

Guerbet
BP 57400
95943 ROISSY CdG Cedex - FRANCE

When to use this medicinal product (therapeutic indications)
This medicinal product is an iodinated contrast agent. It has been prescribed to you for a radiological examination which is to be performed for diagnostic purposes or during a surgical procedure. It can also be used to prevent iodine deficiency disorders when iodization of salt or drinking water cannot be undertaken.

WARNINGS!
When not to use this medicinal product (contraindications)
In radiology
This product MUST NOT BE ADMINISTERED by general intra-arterial, intravenous or intrathecal injection (injection of the product via the same route as for lumbar puncture).
To the treatment of iodine deficiency
This medicinal product MUST NOT BE USED in the following situations:
- if you suffer from hyperthyroidism,
- if you have a large, multinodular goiter and are aged over 45 years, due to the high risk of hyperthyroidism,
- if you are breastfeeding,

Special warnings
In diagnostic or interventional radiology
You should inform the doctor who is to perform the injection if you have or have had any problems of an allergic nature:
• allergic reactions to iodinated products, particularly during previous radiological examinations with contrast agents,
• food or drug-related allergies,
• urticaria,
• eczema,
• asthma,
• hay fever.
- Or if you suffer from cardiac or respiratory insufficiency.
- Or if you have a liver (cirrhosis) or thyroid disorder.

In iodine deficiency
Do not associate with other methods of iodine supplementation (iodization of salt or drinking water) which could increase the risk of hyperthyroidism.
It is advisable to avoid using this medicinal product in persons over the age of 45 years.

Pregnancy - Lactation
In iodine deficiency
If you are pregnant, your doctor may prescribe you iodine supplementation. Due to the risk of hypothyroidism in neonates, Lipiodol is contraindicated during breastfeeding.

IF IN DOUBT, ASK YOUR DOCTOR OR PHARMACIST FOR ADVICE
AS A GENERAL RULE, IF YOU ARE PREGNANT OR BREASTFEEDING, YOU SHOULD ALWAYS ASK THE ADVICE OF YOUR DOCTOR OR PHARMACIST BEFORE TAKING ANY MEDICINAL PRODUCT.

HOW TO USE THIS MEDICINAL PRODUCT
Dosage
Dosage varies according to the indication and is determined by the doctor performing the injection.

Method and route of administration
This product must be administered using a glass syringe.

In diagnostic radiology
Lymphography: intralymphatic injection only
Diagnosis of liver lesions: selective intra-arterial injection only

In interventional radiology
Embolization with surgical glues: selective intra-arterial injection only

In iodine deficiency
Intramuscular injection only

Duration of treatment
This medicinal product will be administered to you in a single dose.

UNDESIRABLE EFFECTS
AS WITH ALL ACTIVE PRODUCTS, THIS MEDICINAL PRODUCT MAY CAUSE SOME UNDESIRABLE EFFECTS OF VARIABLE INTENSITY IN CERTAIN PERSONS:
possible onset of allergic reactions.

In diagnostic radiology
You may experience transient fever during the first few hours following the examination.
You may experience gastrointestinal disorders (nausea, vomiting or diarrhoea)

In iodine deficiency
You may present signs of hyperthyroidism (weight loss, accelerated heart rate, increased intestinal transit rate, anxiety, insomnia, etc.).

PLEASE REPORT ANY UNDESIRABLE EFFECT WHICH IS NOT MENTIONED IN THIS LEAFLET TO YOUR DOCTOR OR PHARMACIST.

STORAGE
Do not use the product after the expiry date indicated on the outer packaging.
Special precautions for storage
Store protected from light.

DATE LEAFLET LAST REVISED
03/11/2005.
DESCRIPTION: Ethiodol, brand of ethiodol oil, is a single injectable radiopaque diagnostic agent for use in hysterosalpingography and lymphography. It contains 37% iodine (45 mg/ml) ingeniously combined with waxy esters of the fatty acids (mainly as alpha-monostearate and alpha-monopalmitate) that have been chemically esterified with iodine. Because of its iodine content, Ethiodol is opaque at the time of injection. Ethiodol is sterile to 1 million units per ml, because of the preservative gentamicin sulfate in the 1% stabilized solution. It is a yellow liquid of density 1.280 specific gravity at 15°C (yielding viscosity of 5.1-10.5）。The high fluidity provides a new feasibility for radiographic exploration.

CLINICAL PHARMACOLOGY: There has been little detailed investigation of the metabolic fate of Ethiodol in either man or animals. However, the fact that Ethiodol follows lymphangiography in lymphatics, and that radiographic visualization of the lymphatics is sustained for a long time after injection, suggests that Ethiodol is not absorbed into the general circulation. Its iodine content is not excreted; it is metabolized by the body as a whole, and is not excreted, but is retained. After injection of the contrast medium into the lymphatics of the body, it is excreted with the lymphatics, which is a definite risk of adverse reactions. While most reactions are minor, life threatening and fatal reactions have been reported, and lym phography.

Ethiodol in either man or animals. Howe ve, the fate of Ethiodol following lymphangiography in lymphatics. These conditions include uterine bleeding, in the immediate pre-or postmenstrual phase, or within 30 days of curettage or conization.

Women: When a pregnancy may exist. Salpingography should not be performed if the blood is exuding from the uterus.

The precise structure of Ethiodol is: ethyl diiodostearate) of poppy seed oil. Stabilized with poppy seed oil, 1%. The simplified molecular structure, possesses a greatly reduced viscosity (1.280 specific gravity at 15°C)

Lower radiographic visualization. For this reason, and to prevent inadvertent venous administration, radiographic monitoring of patients is recommended during the injection of Ethiodol.

The timing and choice of anesthesia following Ethiodol injection may be influenced by consideration of the above noted increase in pulmonary and capillary blood flow and density. It should be noted that although an average of 0.0-1 days was required for complete reabsorption of the contrast material in the skin, an occasional patient required up to 12 days to return to baseline values.

FIBRIN formation of hybrid anode tubes should be carried out per the lymphangiographic procedures because interference with these tests may be anticipated for as long as one year. In the presence of elevated liver function tests, Ethiodol lymphography should be carried out with greatest prudence.

Pathology: The use of instilled ethiodol presents a significant hazard in patients with pre-existing pulmonary disease characterized by a decrease in pulmonary diffusing capacity and/or pulmonary blood flow. A few fatalities have been noted in such patients. With reference to the potential complications, recent studies indicate a significant decrease in both pulmonary diffusing capacity and pulmonary blood flow following Ethiodol lymphography without appreciable concurrent clinical manifestations. Also, care should be exercised in patients with other types of pulmonary disease in view of the more frequent occurrence of overt pulmonary complications such as acute radiation pneumonitis, fever, cough, dyspnea and chest pain.

PROCEDURES: Pregnancy: The iodine content of Ethiodol is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Ethiodol, a decision should be made whether to discontinue nursing or to discontinue the drug.

The presence of elevated liver function tests, the choice of anesthesia following Ethiodol injection may be influenced by consideration of the above noted increase in pulmonary and capillary blood flow and density. It should be noted that although an average of 0.0-1 days was required for complete reabsorption of the contrast material in the skin, an occasional patient required up to 12 days to return to baseline values.

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Proc
inferior vena cava obstruction the contrast medium may be shunted partially to the liver, resulting in hepatic embolization. Also, when accidental intravenous administration of Ethiodol results in a con- siderable amount of this medium entering the circulation, embolization other than pulmonary may occur as reported in the literature. Advantages of using the method of cannulation include: (a) bypassing the wall of the vessel, which is in all probability damaged from the severity of the condition; (b) the radiographic visualization of the lymphatics and; (c) the retrieval of the contrast medium from the extremities for laboratory analysis.

DOSEAGE AND ADMINISTRATION: This method applies for both the upper and lower extremities. A lymphatic vessel is selected for cannulation. The selected vessel should be comfortable as an exophytic position on a visible stethoscope or on a ray-later. When available, a radiopaque guidewire should be placed in the vessel and advanced until the tip is in the lower extremity. In the absence of marked obesity, the extremity is selected for cannulation and the contrast medium is administered. The injection should be started at a slow rate, i.e., 0.1 mL to 0.2 mL per minute. Radiographic monitoring or serial radiographic guidance of patients is recommended during the injection of Ethiodol. If the introduction of the needle into the lymphatic vessel is difficult, the vessel is easier to cannulate with a 27 or 30 gauge 5/8 inch needle, depending upon the size of the lymphatic selected for injection. Average dose in the adult patient for unilateral lymphography of the upper extremities is 2 to 4 mL; for the inferior vena cava obstruction the contrast medium may be shunted partially to the liver, resulting in hepatic embolization. Also, when accidental intravenous administration of Ethiodol results in a considerable amount of this medium entering the circulation, embolization other than pulmonary may occur as reported in the literature. Advantages of using the method of cannulation include: (a) bypassing the wall of the vessel, which is in all probability damaged from the severity of the condition; (b) the radiographic visualization of the lymphatics and; (c) the retrieval of the contrast medium from the extremities for laboratory analysis.

SUBJECTS WITH HYPERSENSITIVITY TO LOCAL ANESTHETICS: The lymphatic vessels must be selected for cannulation. The selected vessel should be comfortable as an exophytic position on a visible stethoscope or on a ray-later. When available, a radiopaque guidewire should be placed in the vessel and advanced until the tip is in the lower extremity. In the absence of marked obesity, the extremity is selected for cannulation and the contrast medium is administered. The injection should be started at a slow rate, i.e., 0.1 mL to 0.2 mL per minute. Radiographic monitoring or serial radiographic guidance of patients is recommended during the injection of Ethiodol. If the introduction of the needle into the lymphatic vessel is difficult, the vessel is easier to cannulate with a 27 or 30 gauge 5/8 inch needle, depending upon the size of the lymphatic selected for injection. Average dose in the adult patient for unilateral lymphography of the upper extremities is 2 to 4 mL; for the inferior vena cava obstruction the contrast medium may be shunted partially to the liver, resulting in hepatic embolization. Also, when accidental intravenous administration of Ethiodol results in a considerable amount of this medium entering the circulation, embolization other than pulmonary may occur as reported in the literature. Advantages of using the method of cannulation include: (a) bypassing the wall of the vessel, which is in all probability damaged from the severity of the condition; (b) the radiographic visualization of the lymphatics and; (c) the retrieval of the contrast medium from the extremities for laboratory analysis.

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Lipiodol is an oil-based radiopaque contrast agent indicated for:

- Pulmonary and cerebral embolism can result from inadvertent intravascular injection or intravasation of Lipiodol. Inject Lipiodol slowly with radiologic monitoring; do not exceed recommended dose (5.1).
- Hypersensitivity reactions: avoid use in patients with a history of sensitivity to other iodinated contrast agents, bronchial asthma or allergic disorders because of an increased risk of a hypersensitivity reaction to Lipiodol (5.2).
- Exacerbation of chronic liver disease (5.3).
- Thyroid dysfunction (5.4).
- Pulmonary and cerebral embolism: avoid use in patients with severely impaired lung function, cardiorespiratory failure or right-sided cardiac overload (5.1).
- Hypersensitivity reactions: avoid use in patients with a history of sensitivity to other iodinated contrast agents, bronchial asthma or allergic disorders because of an increased risk of a hypersensitivity reaction to Lipiodol (5.2).

**Dosage and Administration**

**Hysterosalpingography**

Inject increments of 2 mL of Lipiodol into the endometrial cavity until tubal patency is determined; stop the injection if the patient develops excessive discomfort. Inject with radiologic monitoring.

**Lymphography**

Inject Lipiodol into a lymphatic vessel with radiologic monitoring.

- **Unilateral lymphography of the upper extremities:** 2 to 4 mL
- **Unilateral lymphography of the lower extremities:** 6 to 8 mL
- **Cervical lymphography:** 1 to 2 mL

**Hepatocellular carcinoma (HCC)**

Determine the dose depending on the tumor size, local blood flow in the liver and in the tumor(s).

- Inject a minimum of 1 mL to a maximum of 6 mL according to the anatomical area to be visualized. Do not exceed 0.25 mL/kg.

**Selective Hepatic Intra-arterial Use**

Inject 1.5 to 15 mL of Lipiodol slowly under continuous radiologic monitoring. Do not exceed 20 mL total dosage.

**Dosage Forms and Strengths**

Each milliliter of Lipiodol contains 480 mg iodine organically combined with ethyl esters of fatty acids of poppy seed oil (3).

**Contraindications**

- Pulmonary and cerebral embolism: avoid use in patients with severely impaired lung function, cardiorespiratory failure or right-sided cardiac overload (5.1).
- Hypersensitivity reactions: avoid use in patients with a history of sensitivity to other iodinated contrast agents, bronchial asthma or allergic disorders because of an increased risk of a hypersensitivity reaction to Lipiodol (5.2).

**Adverse Reactions**

Adverse reactions caused by Lipiodol include hypersensitivity reactions, pulmonary embolism, pulmonary dysfunction, exacerbation of liver disease, procedural complications, abdominal pain, fever, nausea, vomiting, and thyroid dysfunction (6.2).

*To report SUSPECTED ADVERSE REACTIONS, contact GUERBET LLC at 1-877-729-6679 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch* Revised: 04/2014

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**Recent Major Changes**

**Dosage and Administration**

- **Hysterosalpingography:** Inject increments of 2 mL of Lipiodol into the endometrial cavity until tubal patency is determined; stop the injection if the patient develops excessive discomfort. Inject with radiologic monitoring.

**Lymphography:**

Inject Lipiodol into a lymphatic vessel with radiologic monitoring.

- **Unilateral lymphography of the upper extremities:** 2 to 4 mL
- **Unilateral lymphography of the lower extremities:** 6 to 8 mL
- **Cervical lymphography:** 1 to 2 mL

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**Indications and Usage**

-**Hysterosalpingography in adults:**
-**Lymphography in adult and pediatric patients:**
-**Selective hepatic intra-arterial use for imaging tumors in adults with known hepatocellular carcinoma (HCC):**

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**Full Prescribing Information: Contents**

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1 Dosing Guidelines
- 2.2 Drug Handling

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Pulmonary and Cerebral Embolism
- 5.2 Hypersensitivity Reactions
- 5.3 Exacerbation of Chronic Liver Disease
- 5.4 Thyroid Dysfunction

6 ADVERSE REACTIONS

- 6.2 Postmarketing Experience

7 DRUG INTERACTIONS

- 7.1 Interference with Iodine-Based Diagnostic Tests and Iodine-Based Radiotherapy

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**Full Prescribing Information: Contents**

1 INDICATIONS AND USAGE

Lipiodol is an oil-based radiopaque contrast agent indicated for:

- Hysterosalpingography in adults
- Lymphography in adult and pediatric patients
- Selective hepatic intra-arterial use for imaging tumors in adults with known hepatocellular carcinoma (HCC)

2 DOSAGE AND ADMINISTRATION

- 2.1 Dosing Guidelines

Draw Lipiodol into a glass syringe and use promptly. Discard any unused portion of Lipiodol.

Inspect Lipiodol visually for particulate matter and discoloration before administration. Do not use if the color has darkened.

Each milliliter of Lipiodol contains 480 mg iodine organically combined with ethyl esters of fatty acids of poppy seed oil.

Pediatric patients:

- Inject a minimum of 1 mL to a maximum of 6 mL according to the anatomical area to be visualized. Do not exceed 0.25 mL/kg.
- Selective Hepatic Intra-arterial Use

Inject 1.5 to 15 mL of Lipiodol slowly under continuous radiologic monitoring. Do not exceed 20 mL total dosage.

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**Dosage Forms and Strengths**

Each milliliter of Lipiodol contains 480 mg iodine organically combined with ethyl esters of fatty acids of poppy seed oil.

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**Warnings and Precautions**

- Hypersensitivity to Lipiodol, hyperthyroidism, traumatic injuries, recent hemorrhage or bleeding.
- Lipiodol Hysterosalpingography is contraindicated in:
  - Pregnancy, acute pelvic inflammatory disease, marked cervical erosion, endocervicitis and intrauterine bleeding, in the immediate pre- or postmenstrual phase, or within 30 days of curettage or conization.
- Lipiodol Lymphography is contraindicated in:
  - Right to left cardiac shunt, advanced pulmonary disease, tissue trauma or hemorrhage, advanced neoplastic disease with expected lymphatic obstruction, previous surgery interrupting the lymphatic system, or radiation therapy to the examined area.
- Lipiodol Selective Hepatic Intra-arterial Injection is contraindicated in: the presence of dilated bile ducts unless external biliary drainage was performed before injection.

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**Adverse Reactions**

Adverse reactions caused by Lipiodol include hypersensitivity reactions, pulmonary embolism, pulmonary dysfunction, exacerbation of liver disease, procedural complications, abdominal pain, fever, nausea, vomiting, and thyroid dysfunction.

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**8 Use in Specific Populations**

- 8.1 Pregnancy
- 8.2 Nursing Mothers
- 8.3 Pediatric Use
- 8.4 Geriatric Use
- 8.5 Renal Impairment

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**10 Overdosage**

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**11 Description**

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**12 Clinical Pharmacology**

- 12.1 Mechanism of Action
- 12.3 Pharmacokinetics

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**13 Nonclinical Toxicology**

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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**16 How Supplied/Storage and Handling**

*Sections or subsections omitted from the full prescribing information are not listed.*
4 CONTRAINDICATIONS
Lipiodol is contraindicated in patients with hypersensitivity to Lipiodol, hyperthyroidism, traumatic injuries, recent hemorrhage or bleeding.

Hysterosalpingography
Lipiodol hysterosalpingography is contraindicated in pregnancy, acute pelvic inflammatory disease, marked cervical erosion, endocervicitis and intrauterine bleeding, in the immediate pre- or postmenstrual phase, or within 30 days of curettage or conization.

Lymphography
Lipiodol Lymphography is contraindicated in patients with a right to left cardiac shunt, advanced pulmonary disease, tissue trauma or hemorrhage advanced neoplastic disease with expected lymphatic obstruction, previous surgery interrupting the lymphatic system, radiation therapy to the examined area.

Selective Hepatic Intra-arterial Use Patients with HCC
Lipiodol use is contraindicated in areas of the liver where the bile ducts are dilated unless external biliary drainage was performed before injection.

5 WARNINGS AND PRECAUTIONS

5.1 Pulmonary and Cerebral Embolism
Pulmonary embolism may occur immediately or after a few hours to days from inadvertent systemic vascular injection or extravasation of Lipiodol and cause decreased pulmonary diffusing capacity and pulmonary blood flow, pulmonary infarction, acute respiratory distress syndrome and fatalities. Embolization of Lipiodol to bronchial and other major organs may occur. Avoid use of Lipiodol in patients with severely impaired lung function, cardiorespiratory failure, or right-sided cardiac overload. Perform radiological monitoring during the Lipiodol injection. Do not exceed the recommended maximum dose and rate of injection of Lipiodol. During lymphography to minimize the risk of pulmonary embolism obtain radiographic confirmation of intralymphatic (rather than venous) injection, and terminate the procedure when Lipiodol becomes visible in the thoracic duct or lymphatic obstruction is observed.

5.2 Hypersensitivity Reactions
Anaphylactoid and anaphylactic reactions with cardiovascular, respiratory or cutaneous manifestations, ranging from mild to severe, including death, have uncommonly occurred following Lipiodol administration. Avoid use in patients with a history of sensitivity to other iodinated contrast agents, bronchial asthma or allergic disorders because of an increased risk of a hypersensitivity reaction to Lipiodol.

5.3 Exacerbation of Chronic Liver Disease
Lipiodol hepatic intra-arterial administration can exacerbate the following conditions: portal hypertension and cause variceal bleeds due to obstruction of the intraperitoneal hepatic portal channels by opening a pre sinusoidal anastomosis; hepatic ischemia and cause liver enzyme elevations, fever and abdominal pain; hepatic failure and cause ascites and encephalopathy. Hepatic venous thrombosis, irreversible liver insufficiency and fatalities have been reported. Procedural risks include vascular complications and infections.

5.4 Thyroid Dysfunction
Iodinated contrast media can affect thyroid function because of the free iodine content and can cause hyperthyroidism or hypothyroidism in pre-disposed patients. Patients at risk are those with latent hyperthyroidism and those with Hashimoto thyroiditis, or history of thyroid irradiation. As Lipiodol may remain in the body for several months, thyroid diagnostic results can be affected for up to two years after lymphography.

6 ADVERSE REACTIONS

6.2 Postmarketing Experience
The following adverse reactions (Table 1) have been identified during post approval use of Lipiodol. 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.

The following adverse reactions are described in more detail in other sections of the prescribing information:

Pulmonary and central embolism [see Warnings and Precautions (5.1)]

Hypersensitivity reactions [see Warnings and Precautions (5.2)]

Exacerbation of chronic liver disease [see Warnings and Precautions (5.3)]

Table 1: Adverse Reactions in the Postmarketing Experience

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrine disorders</td>
<td>hypothyroidism, hyperthyroidism, thyroiditis</td>
</tr>
<tr>
<td>Eye disorders</td>
<td>retinal vein thrombosis</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>nausea, vomiting, diarrhea</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>fever, pain, granuloma</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td>hepatic vein thrombosis</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>hypersensitivity, anaphylactic reaction, anaphylactoid reaction</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>cerebral embolism</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>pulmonary embolism, dyspnea, cough, acute respiratory distress syndrome</td>
</tr>
<tr>
<td>Urinary system disorders</td>
<td>renal insufficiency</td>
</tr>
</tbody>
</table>

Hysterosalpingography
Abdominal pain, foreign body reactions, exacerbation of pelvic inflammatory disease.

Lymphography
Cardiovascular collapse, lymphangitis, thrombophlebitis, edema or exacerbation of preexisting lymphedema, dyspnea and cough, fever, iodism (headache, soreness of mouth and pharynx, cornea and skin rash), allergic dermatitis, lipogranuloma, delayed healing at the site of incision.

Selective Hepatic Intra-arterial Injection
Fever, abdominal pain, nausea, and vomiting are the most common reactions; other reactions include hepatic ischemia, liver enzymes abnormalities, transitory decrease in liver function, liver decompensation and renal insufficiency. Procedural risks include vascular complications and infections.

7 DRUG INTERACTIONS

7.1 Interference with Iodine-Based Diagnostic Tests and Iodine-Based Radiotherapy
Following Lipiodol administration, ethiodized oil remains in the body for several months, and may interfere with thyroid function testing for up to two years. Ethiodized oil interferes with radioactive iodine uptake by thyroid tissue for several weeks to months and may impair visualization of thyroid scintigraphy and reduce effectiveness of iodine 131 treatment.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Pregnancy Category C
Risk Summary
There are no adequate and well-controlled studies of Lipiodol effects in pregnant women. Use Lipiodol during pregnancy only if clearly needed.

Human Data
It is not known whether Lipiodol can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

The use of Lipiodol during pregnancy causes iodine transfer which may interfere with the thyroid function of the fetus and result in brain damage and permanent hypothyroidism. Institute thyroid function testing and careful medical monitoring of the neonate exposed to Lipiodol in utero.

Animal Data
Animal reproduction studies have not been conducted using the indicated routes of administration of Lipiodol. Lipiodol was not embryotoxic or teratogenic in rats after oral administration of up to 110 mg iodine/kg each day between gestation days 6 to 17, or in rabbits after 4.5 intermenstrual (once every three days) oral administrations of 12.5 mg iodine/kg between gestation days 6 to 18.

8.2 Nursing Mothers
No nonclinical lactation studies of Lipiodol have been reported.

Lipiodol is excreted in human milk. Avoid use of Lipiodol in a nursing woman because of risk of hypothyroidism in nursing infants.

If breastfeeding is continued the neonate’s thyroid function should be monitored.

8.3 Pediatric Use
For lymphography use a dose of minimum of 1 mL to a maximum of 6 mL according to the anatomical area to be visualized. Do not exceed 0.25 mL/kg. Administer the smallest possible amount of Lipiodol according to the anatomical area to be visualized.

8.4 Geriatric Use
There are no studies conducted in geriatric patients.

8.5 Renal Impairment
Prior to an intra-arterial administration of Lipiodol screen all patients for renal dysfunction by obtaining history and/or laboratory tests.

Consider follow-up renal function assessments for patients with a history of renal dysfunction.

10 OVERDOSAGE
Overdose may lead to respiratory, cardiac or cerebral complications, which can potentially be fatal. Microembolisms to multiple organs may occur more frequently after overdose. Promptly initiate symptomatic treatment and support of vital functions.

11 DESCRIPTION
Lipiodol, ethiodized oil injection, is a sterile injectable radio-opaque agent. Each milliliter contains 480 mg of iodine organically combined with ethyl esters of fatty acids of poppy seed oil. The precise structure of Lipiodol is unknown.

Lipiodol is a sterile, clear, pale yellow to amber colored oil. Lipiodol has a viscosity of 34 – 70 mPa-s at 20°C, and a density of 1.28 g/cm3 at 20°C.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Ethiodized oil is an iodinated poppy seed oil based contrast agent.

12.3 Pharmacokinetics
Following intra-arterial administration of Lipiodol, ethiodized oil retained in normal hepatic parenchyma is phagocytosed by the Kupfer cells of the liver and washed out via the hepatic lymphatic system in about 2 to 4 weeks. In HCC, retention in the liver tumor is prolonged, allowing re-imaging of the tumor for four weeks or longer.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals have not been performed to evaluate carcinogenic potential, or whether Lipiodol can affect fertility in males or females. Lipiodol did not demonstrate mutagenic potential in bacterial reverse mutation assays (in vitro), in a chromosomal aberration test in the mouse lymphoma assay (in vivo), and was negative in an in vivo micronucleus test in rats after intravenous injection of 479 mg/kg.

16 HOW SUPPLIED/STORAGE AND HANDLING
Lipiodol is supplied in a box of one 10 mL ampoule, NDC 67684-1901-1.

Store at controlled room temperature 15°-30°C (59°-86°F) [see USP, Controlled Room Temperature (CRT)]. Protect from light. Remove from carton only upon use.

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