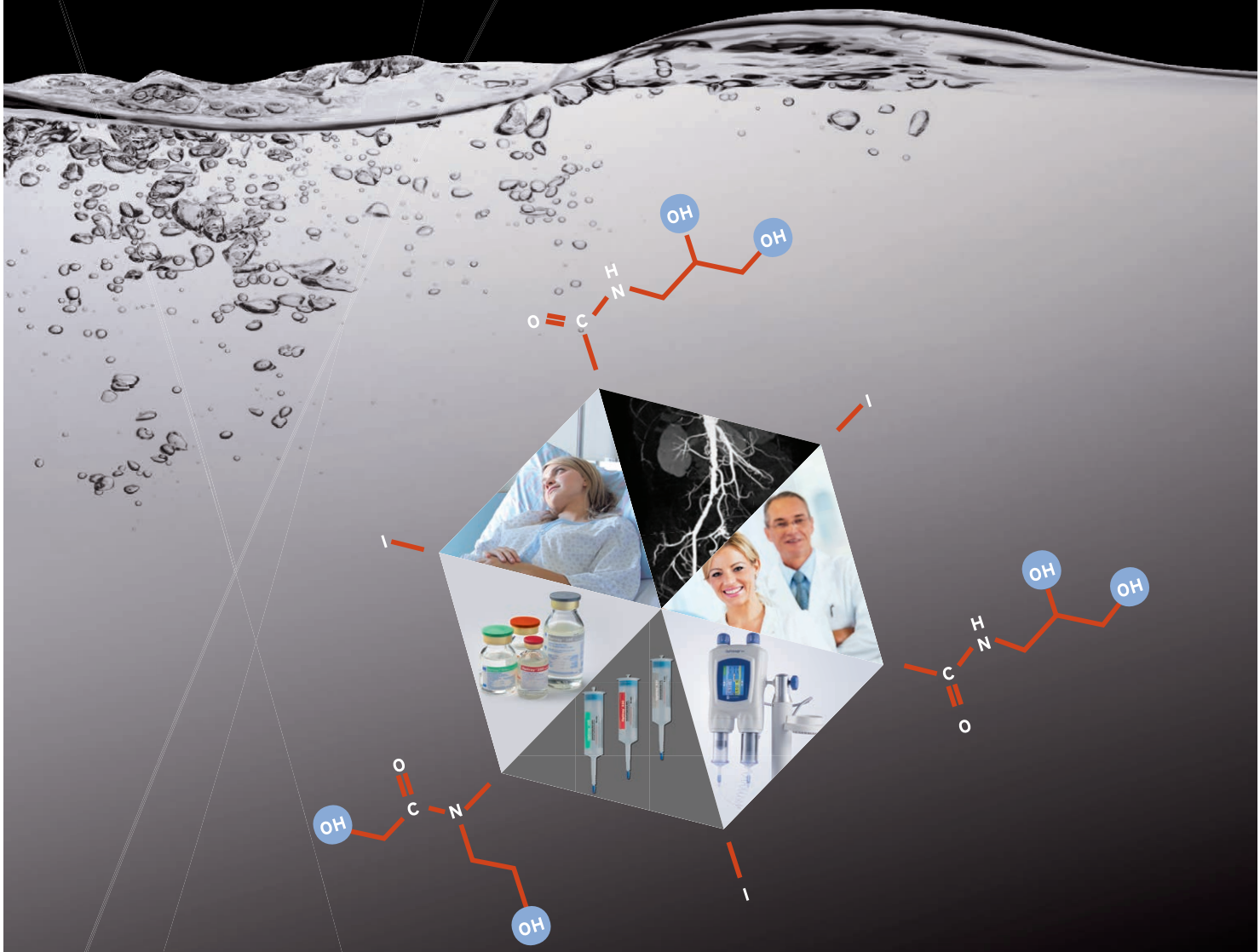
OptiRAY®

ioversol

Optimizes image quality,
patient comfort and clinician confidence

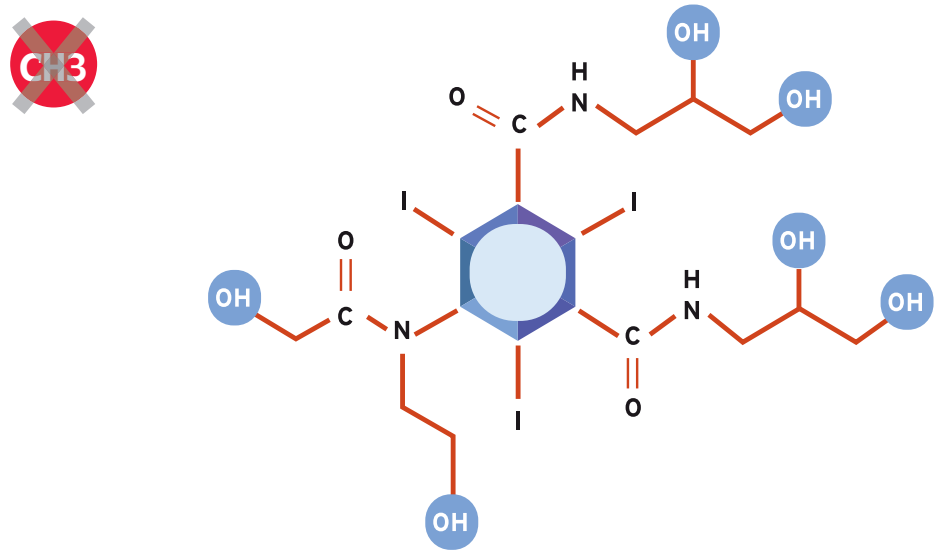


Guerbet

Contrast for Life

The User-friendly X-Ray Contrast Medium

- OptiRAY® (ioversol) is a non-ionic, low osmolar, low viscosity iodine based contrast medium
- OptiRAY® (ioversol) is intended to be therapeutically and biologically inert when injected into the body for use in organ or tissue enhancement in X-ray, computed tomography (CT) and fluoroscopy imaging procedures for which it is approved
- 212.3 million doses of OptiRAY® (all concentrations combined) have been sold since 1989[1]



OptiRAY® (ioversol) molecule

Molecular Structure

- 6 hydroxyl groups (-OH) evenly distributed around the benzene ring
- No methyl group (CH3-)[2,3,4]

Hydrophilicity

- OptiRAY® with 6 hydroxyl groups and no methyl group is a high hydrophilic, low osmolar, non-ionic, monomeric X-ray contrast medium
- Contrast media (CM) should possess high hydrophilic nature for **minimal chemotoxicity**[3], and show low hydrophobic characteristics to **reduce** CM **interactions** with **the lipophilic structures** such as proteins, lipoproteins, enzymes and cell membranes[2]

Good Tolerability

- In 2009, Dr. Tatsuya Gomi from Toho University Ohashi Hospital, published his research comparing differences in acute adverse reactions among five low-osmolar, non-ionic, iodinated contrast media[5]
- The study found that OptiRAY® was one of the contrast media with the lowest incidence of acute adverse reactions[5]

Incidence of Acute Adverse Reactions occurring during or 1 hour after injection of Contrast Media[5]

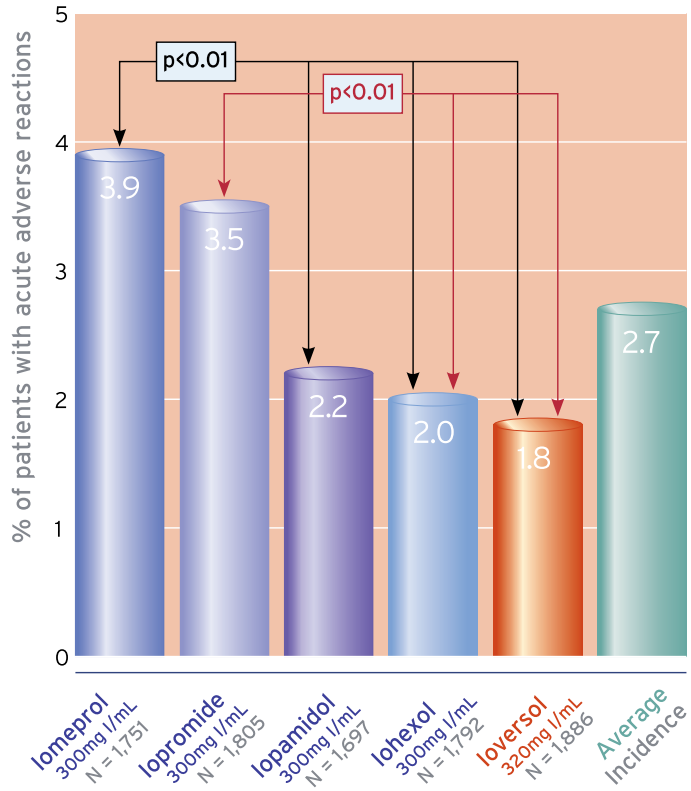


Table 2
Adapted from Gomi et al.

p<0.01 Iomeprol vs iopamidol, iohexol or ioversol

p<0.01 Iopromide vs iohexol or ioversol

- In ventriculography and coronary arteriography procedures, Hirshfeld et al[6] and McGaughey et al[7] have demonstrated in their respective clinical trials that OptiRAY® does not induce any significant ECG nor hemodynamic disturbance

Optimizing Efficacy

OptiRAY®	Indications and usage according to the US SmPC[8]
OptiRAY 350	■ Indicated in adults for peripheral and coronary arteriography and left ventriculography. ■ Indicated for contrast enhanced computed tomographic imaging of the head and body, intravenous excretory urography, intravenous digital subtraction angiography and venography. ■ Indicated in children for angiocardiography.
OptiRAY 320	■ Indicated in adults for angiography throughout the cardiovascular system. The uses include cerebral, coronary, peripheral, visceral and renal arteriography, venography, aortography, and left ventriculography. ■ Indicated for contrast enhanced computed tomographic imaging of the head and body, and intravenous excretory urography. ■ Indicated in children for angiocardiography, contrast enhanced computed tomographic imaging of the head and body, and intravenous excretory urography.
OptiRAY 300	■ Indicated for cerebral angiography and peripheral arteriography. ■ Indicated for contrast enhanced computed tomographic imaging of the head and body, venography, and intravenous excretory urography.
OptiRAY 240	■ Indicated for cerebral angiography and venography. ■ Indicated for contrast enhanced computed tomographic imaging of the head and body and intravenous excretory urography.

Not all the presentations and indications may be available in your country.
Please check with your local Guerbet representative for more information

	Volume
Guerbet current offer in vials[a]	OptiRAY 240: 50 mL, 100 mL
	OptiRAY 300: 10, 20, 50, 75, 100, 150, 500 mL
	OptiRAY 320: 20, 50, 75, 100, 200, 500 mL
	OptiRAY 350: 30, 50, 75, 100, 150, 200, 500 mL
Guerbet current offer in PFS[a]	OptiRAY 240 HH[b]: 50 mL OptiRAY 240 PI[c]: 75, 100, 125 mL
	OptiRAY 300 HH[b]: 30, 50 mL OptiRAY 300 PI[c]: 50, 75, 100, 125 mL
	OptiRAY 320 HH[b]: 50 mL OptiRAY 320 PI[c]: 50, 75, 100, 125 mL
	OptiRAY 350 HH[b]: 50 mL OptiRAY 350 PI[c]: 50, 75, 100, 125 mL

[a] Not all the presentations may be available in your country.
Please check with your local Guerbet representative for more information

[b] HH Handheld

[c] PI Power injector

References

1. Data on file, Mallinckrodt, Hazelwood, MO
2. Le Mignon M. M. et al.: Preliminary European intravenous clinical experience with a new, low osmolar, non-ionic contrast medium: ioversol (Optiray®) Eur. J. Radiol., 1991; 13:126-133.
3. Krause W. et al: Physiochemical Parameters of X-Ray Contrast Media. Invest. Radiol., 1994; 29: 72-80.
4. Gallotti A. et al.: The chemistry of iomeprol and physico-chemical properties of its aqueous solutions and pharmaceutical formulations. Eur. J. Radiol., 1994; 18: S1-S12.
5. Gomi T. et al., Are there any differences in acute adverse reactions among five low-osmolar non-ionic contrast media? Eur. Radiol., 2010; 20: 1631-1635
6. Hirshfeld J. et al., Hemodynamic and electrocardiographic effects of Ioversol during cardiac angiography: Comparison with iopamidol and diatrizoate. Invest. Radiol., 1989; 24:138-144.
7. Mc Gaughey M.D. et al., A double-blind study comparing the safety, tolerability, and efficacy of Ioversol-350 in coronary arteriography with left ventriculography. The J Invas Cardiol, 1991; 3: 272-277.
8. US SmPC.

Prescribing **information**

Prescribing information: Please refer to the Summary of Product Characteristics before prescribing. **Composition:** OPTIRAY® 240 Ioversol, 509 mg/ml, which is equivalent to 240 mg/ml of elemental iodine. OPTIRAY® 300 Ioversol, 636 mg/ml, which is equivalent to 300 mg/ml of elemental iodine. OPTIRAY® Ioversol, 678 mg/ml, which is equivalent to 320 mg/ml of elemental iodine. OPTIRAY® Ioversol, 741 mg/ml, which is equivalent to 350 mg/ml of elemental iodine. **Indications:** OPTIRAY® non-ionic X-ray contrast medium for injection or infusion. Depending on the preparation, it is indicated for use in cerebral, coronary, peripheral, visceral and renal angiography, in aortography, left ventriculography, venography, intravenous excretory urography and computed tomography (CT) of the head and body. Except for OPTIRAY® 300, safety and effectiveness of OPTIRAY® in children has not yet been established. **Posology and Method of Administration:** The dosage may vary between 1 ml and 150 ml, maximum total dose 250 ml or less. Please refer to the Summary of Product Characteristics for the recommended dosage schedule. **Contraindications:** Proven hypersensitivity to iodine-containing contrast media. Manifest hyperthyroidism. **Special Warnings and Precautions for Use:** As with all other X-ray contrast media, OPTIRAY® may cause anaphylaxis or other manifestations of pseudo-allergic intolerance reactions, e.g. nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. Pretesting cannot be relied upon to predict severe reactions. The thorough assessment of the medical history of the specific patient may be more accurate in predicting potential adverse reactions. A positive history of allergy is not a contraindication, but does require caution. Diagnostic procedures, which involve the use of iodinated intravascular contrast agents, should be performed under the direction of personnel skilled and experienced in the particular procedure to be performed. Serious or fatal reactions have been associated with the administration of iodinated X-ray contrast media. A fully equipped emergency cart, or equivalent supplies and equipment, and personnel competent in recognising and treating adverse reactions of all types should always be available for at least 30 to 60 minutes after administration. Patients with congestive heart failure should be observed for several hours following the procedure to detect delayed haemodynamic disturbances, which may be associated with a transitory increase in the circulating osmotic load. All other patients should be observed for at least one hour after the application, as it has been reported that most of the adverse events occur in this period. The patient should also be informed that allergic reactions may develop up to several days post administration; in such case, a physician should be consulted immediately. Caution must be exercised in patients with severely impaired renal function, combined renal and hepatic disease, anuria, diabetes mellitus, homozygotic sickle cell disease, or monoclonal gammopathy (multiple myeloma, Waldenströms macro-globulinaemia), particularly when large doses are administered. Serious renal effects, including acute renal failure, may occur in these patients. Preparatory dehydration is dangerous and may contribute to acute renal failure. Iodine-containing contrast media may also be hazardous in patients with hyperthyroidism or with autonomous areas of the thyroid gland. In patients with phaeochromocytoma a premedication with alpha-blockers is advisable when the contrast medium is administered intravascularly due to the risk of a hypertensive crisis. Serious neurologic events have been observed following direct injection into cerebral arteries or vessels supplying the spinal cord, or in angiocardiography due to inadvertent filling of the carotids. General anaesthesia may be indicated in selected patients. However, a higher incidence of adverse reactions has been reported in these patients, probably due to the hypotensive effect of the anaesthetic. In angiographic procedures, the possibility of dislodging plaque or damaging or perforating the vessel wall should be considered during catheter manipulation and contrast medium injection. In patients with advanced atherosclerosis, serious hypertension, cardiac decompensation, senility, preceding cerebral thrombosis or embolism, special caution should be exercised. Cardiovascular reactions as bradycardia, rising or falling of blood pressure may occur more often. Angiography should be avoided whenever possible in patients with homocystinuria due to an increased risk of thrombosis and embolism. OPTIRAY® should be injected with caution to avoid perivascular application. However, significant extravasation of OPTIRAY® may occur especially during the use of power injectors. Generally, it is tolerated without substantial tissue injury applying conservative treatment. However, serious tissue damage (e.g. ulceration) has been reported in isolated cases requiring surgical treatment. **For interactions and specific warnings**, please refer to summary of product characteristics. **Summary of safety profile:** Adverse reactions following the use of OPTIRAY® formulations are generally independent of the dose administered. Usually, they are mild to moderate, of short duration and resolve spontaneously (without treatment). However, even mild adverse reactions may be the first indication of a serious, generalized reaction that can occur rarely after iodinated contrast media. Such serious reactions may be life-threatening and fatal, and usually affect the cardiovascular system. Most adverse drug reactions to OPTIRAY® formulations occur within minutes after administration, however contrast related hypersensitivity reactions may occur with a delay of some hours up to several days. **Adverse reactions may be classified as follows:** Hypersensitivity or anaphylactoid reactions are mostly mild to moderate with symptoms like rash, pruritus, urticaria and rhinitis. However, serious reactions may occur. Serious anaphylactic reactions generally affect the cardiovascular and respiratory system. These may be life-threatening and include anaphylactic shock, cardiac and respiratory arrest, or pulmonary oedema. Fatal cases were reported. Patients with a history of allergic reactions are at increased risk of developing a hypersensitivity reaction. Other type 1 (immediate) reactions include symptoms like nausea and vomiting, skin rashes, dyspnoea, rhinitis, paraesthesia or hypotension. Vasovagal reactions e.g. dizziness or syncope which may be caused either by the contrast medium, or by the procedure. Cardiologic side effects during cardiac catheterisation e.g. angina pectoris, ECG changes, cardiac arrhythmias, conductivity disorders, as well as coronary spasm and thrombosis. Such reactions are very rare and may be caused by the contrast medium or by the procedure. Nephrotoxic reactions in patients with pre-existing renal damage or renal vasopathy, e.g. decrease in renal function with creatinine elevation. These adverse effects are transient in the majority of cases. In single cases, acute renal failure has been observed. Neurotoxic reactions after intra-arterial injection of the contrast medium e.g. visual disorders, disorientation, paralysis, convulsions, or fits. These symptoms are generally transient and abate spontaneously within several hours or days. Patients with pre-existing damage of the blood-brain barrier are at increased risk of developing neurotoxic reactions. Local reactions at the injection site may occur in very rare cases and include rashes, swelling, inflammation and oedema. Such reactions occur probably in most cases due to extravasation of the contrast agent. Extended paravasation may necessitate surgical treatment. Extravasation can cause serious tissue reactions including blistering and skin exfoliation, the extent of which is dependent on the amount and strength of the contrast solution in the tissues.

Marketing Authorization Information: The marketing authorization holder, number and date of approval may be differ from one country to another. Volume, presentation and indication may also differ.

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