

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use OPTIRAY safely and effectively. See full prescribing information for OPTIRAY

OPTIRAY® (ioversol) injection, for intra-arterial or intra-venous use Initial U.S. Approval: 1988

WARNING: RISKS WITH INADVERTENT INTRATHECAL ADMINISTRATION

FOR INTRA-ARTERIAL AND INTRAVENOUS USE ONLY

Inadvertent intrathecal administration may cause death, convulsions, cerebral hemorrhage, coma, paralysis, arachnoiditis, acute renal failure, cardiac arrest, seizures, rhabdomyolysis, hyperthermia, and brain edema. (5.1)

RECENT MAJOR CHANGES

Warnings and Precautions, Thyroid Dysfunction in Pediatric Patients 0 to 3 Years of Age (5.8)

INDICATIONS AND USAGE

OPTIRAY is a radiographic contrast agent indicated for the following:

Intra-arterial Procedures (1.1)

Adults:

- Cerebral Arteriography (300, 320 mg iodine/mL)
- Peripheral Arteriography (300, 320, 350 mg iodine/mL)
- Visceral and Renal Arteriography, Aortography (320 mg iodine/mL)
- Coronary Arteriography and Left Ventriculography (320, 350 mg iodine/mL)

Pediatric Patients: Angiocardiology (320, 350 mg iodine/mL)

Intravenous Procedures (1.2)

Adults:

- Computed tomography (CT) Imaging of Head and Body (300, 320, 350 mg iodine/mL)
- Venography (300, 320, 350 mg iodine/mL)
- Intravenous Excretory Urography (300, 320, 350 mg iodine/mL)
- Intravenous Digital Subtraction Angiography (350 mg iodine/mL)

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FULL PRESCRIBING INFORMATION

WARNING: RISKS WITH INADVERTENT INTRATHECAL ADMINISTRATION

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1 INDICATIONS AND USAGE

OPTIRAY is indicated for:

1.1 Intra-arterial

In adults

- **OPTIRAY 300:** cerebral arteriography and peripheral arteriography.
- **OPTIRAY 320:** cerebral arteriography, peripheral arteriography, visceral and renal arteriography, aortography, coronary arteriography, and left ventriculography.

Pediatric Patients: CT Imaging of the Head and Body, and Intravenous Excretory Urography (320 mg iodine/mL)

DOSAGE AND ADMINISTRATION

Adjust the volume and concentration of OPTIRAY. Modify the dose accounting for factors such as age, body weight, vessel size, blood flow rate within the vessel. Please see details in full Prescribing Information. (2)

DOSAGE FORMS AND STRENGTHS

OPTIRAY (ioversol) Injection comes in three strengths: 300 mg iodine/mL (ioversol 64%), 320 mg iodine/mL (ioversol 68%), 350 mg iodine/mL (ioversol 74%) in single-dose vials, bottles, or syringes. (3)

CONTRAINDICATIONS

Symptomatic Hyperthyroidism (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity Reactions: life-threatening or fatal reactions can occur. Always have emergency equipment and trained personnel available. (5.2)
- Contrast Induced Acute Kidney Injury: Acute injury, including renal failure, can occur. Minimize dose and maintain adequate hydration to minimize risk. (5.3)
- Cardiovascular Adverse Reactions: hemodynamic disturbances including shock and cardiac arrest may occur during or after administration. (5.4)
- Thyroid Dysfunction in Pediatric Patients 0 to 3 Years of Age: Individualize thyroid function monitoring based on risk factors such as prematurity. (5.8)

ADVERSE REACTIONS

The most common reaction is nausea, occurring at a rate of 1 percent. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact LIEBEL-FLARSHEIM COMPANY LLC at 855-266-5037 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

- Lactation: A lactating woman may pump and discard breast milk for 8 hours after OPTIRAY administration. (8.2)

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Revised: 2/2023

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- **OPTIRAY 350:** peripheral arteriography coronary arteriography, and left ventriculography.

In pediatric patients

- **OPTIRAY 320** and **OPTIRAY 350:** angiocardiology.

1.2 Intra-venous

In adults

- **OPTIRAY 300:** CT imaging of the head and body, venography, and intravenous excretory urography.
- **OPTIRAY 320:** CT imaging of the head and body, venography, and intravenous excretory urography.
- **OPTIRAY 350:** CT imaging of the head and body, venography, intravenous excretory urography, and intravenous digital subtraction angiography (IV-DSA).
- In pediatric patients **OPTIRAY 320:** CT imaging of the head and body, and intravenous excretory urography.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

- OPTIRAY is for intravascular use only [see Boxed Warning, Contraindications (4), and Warnings and Precautions (5.1)].
- Use sterile technique for all handling and administration of OPTIRAY.
- Inspect glass and plastic containers prior to use for breakage or other damage and do not use damaged containers.
- Warm OPTIRAY and administer at body or room temperature.
- Inspect OPTIRAY for particulate matter or discoloration before administration. Do not administer if OPTIRAY contains particulate matter or is discolored.
- Do not mix OPTIRAY with other drugs, solutions or total parenteral nutrition mixtures.
- Use the lowest dose necessary to obtain adequate visualization.
- Adjust the volume and concentration of OPTIRAY. Modify the dose accounting for factors such as age, body weight, vessel size, blood flow rate within the vessel, anticipated pathology, degree and extent of opacification required, structure(s) or area to be examined, disease processes affecting the patient, and equipment and technique to be employed.
- Avoid extravasation when injecting OPTIRAY; especially in patients with severe arterial or venous disease [see Warnings and Precautions (5.6)].
- Hydrate patients before and after OPTIRAY administration [see Warnings and Precautions (5.3)].
- Discard unused portion of OPTIRAY from single-dose container after use.

2.2 Radio Frequency Identification (RFID)-Tagged Syringe Directions for Use

- The RFID-tagged syringe must be used with an Optivantage Injector with RFID technology [see How Supplied/Storage and Handling (16.2)]. The RFID tag allows for the exchange of product information such as lot number, expiration, concentration, and identification of the syringe as being “unused” prior to use and “used” after product administration.
- Do not operate any part of the Optivantage Injector System and RFID-tagged syringes within 6 inches (15 cm) of a pacemaker and/or defibrillator.
- If the RFID tag is damaged or otherwise non-functional, the OPTIRAY syringe with the non-functional RFID tag may still be used; however, no data will be transferred to the injector.

2.3 Intra-arterial Procedures in Adults

- **Cerebral Arteriography**

Use OPTIRAY 300 or OPTIRAY 320. The recommended dose for visualization of cerebral arteries is shown below (may repeat as necessary):

Diagnostic area	Dose	Maximum Cumulative Dose
carotid or vertebral arteries	2 mL to 12 mL	200 mL
aortic arch injection (four vessel study)	20 mL to 50 mL	200 mL

- **Peripheral Arteriography**

Use OPTIRAY 300, OPTIRAY 320 or OPTIRAY 350. The recommended dose for visualization of peripheral arteries is shown below (may repeat as necessary):

Diagnostic area	Dose	Maximum Cumulative Dose
aorta-iliac runoff	60 mL (range 20 mL to 90 mL)	250 mL
common iliac, femoral	40 mL (range 10 mL to 50 mL)	250 mL
subclavian, brachial	20 mL (range 15 mL to 30 mL)	250 mL

- **Visceral and Renal Arteriography and Aortography**

Use OPTIRAY 320. The recommended dose for visualization for the aorta and visceral arteries is shown below (may repeat as necessary):

Diagnostic area	Dose	Maximum Cumulative Dose
Aorta	45 mL (range 10 mL to 80 mL)	250 mL
Celiac	45 mL (range 12 mL to 60 mL)	250 mL
superior mesenteric	45 mL (range 15 mL to 60 mL)	250 mL
renal or inferior mesenteric	9 mL (range 6 mL to 15 mL)	250 mL

- **Coronary Arteriography and Left Ventriculography**

Use OPTIRAY 320 or OPTIRAY 350. The recommended dose for visualization of the coronary arteries and left ventricle is shown below (may repeat as necessary):

Diagnostic area	Dose	Maximum Cumulative Dose
left coronary	8 mL (range 2 mL to 10 mL)	250 mL
right coronary	6 mL (range 1 mL to 10 mL)	250 mL
left ventricle	40 mL (range 30 mL to 50 mL)	250 mL

2.4 Intravenous Procedures in Adults

- **Computed Tomography**

Use OPTIRAY 300, OPTIRAY 320 or OPTIRAY 350 for head and body imaging.

Head Imaging

The recommended dosing is shown below:

- Scan immediately after completion of the intravenous administration.

	Infusion
OPTIRAY 300	50 mL to 150 mL
OPTIRAY 320	50 mL to 150 mL
OPTIRAY 350	50 mL to 150 mL

Body Imaging

OPTIRAY may be administered by bolus injection, by rapid infusion, or by a combination of both. The recommended dosing is shown below:

- Scanning interval will vary with indication and target organ.

	Bolus Injection	Infusion
OPTIRAY 300	25 mL to 75 mL	50 mL to 150 mL
OPTIRAY 320	25 mL to 75 mL	50 mL to 150 mL
OPTIRAY 350	25 mL to 75 mL	50 mL to 150 mL

- **Venography**

Use OPTIRAY 300, OPTIRAY 320 or OPTIRAY 350. The recommended dose is 50 mL to 100 mL per extremity; with a maximum cumulative dose of 250 mL.

- **Intravenous Urography**

Use OPTIRAY 350, OPTIRAY 320, or OPTIRAY 300. The recommended dose is shown below:

	Usual Dose	High Dose Urography	Maximum Dose
OPTIRAY 300	50 mL to 75 mL	1.6 mL/kg	150 mL
OPTIRAY 320	50 mL to 75 mL	1.5 mL/kg to 2 mL/kg	150 mL
OPTIRAY 350	50 mL to 75 mL	1.4 mL/kg	140 mL

- **Intravenous Digital Subtraction Angiography (IV-DSA)**

Use OPTIRAY 350. The recommended dose range per injection is 30 mL to 50 mL; may repeat as necessary with a maximum cumulative dose of 250mL.

Injection rates will vary depending on the site of catheter placement and vessel size.

- Central catheter injections are usually made at a rate of between 10 mL/second and 30 mL/second.
- Peripheral injections are usually made at a rate of between 12 mL/second and 20 mL/second.

2.5 Pediatric Dosing

Intra-arterial Procedures

- **Angiocardiology**

Use OPTIRAY 350 or OPTIRAY 320. The recommended single ventricular dose is 1.25 mL/kg (range 1 mL/kg to 1.5 mL/kg). The maximum cumulative dose is 5 mL/kg up to a maximum total volume of 250 mL.

Intravenous Procedures

- **Computed Tomography**

Use OPTIRAY 320.

Head and Body Imaging

The recommended dose in pediatric patients is 1.5 mL/kg to 2 mL/kg (range 1 mL/kg to 3 mL/kg).

- **Intravenous Urography**

Use OPTIRAY 320. The recommended dose for pediatric patients is 1 mL/kg to 1.5 mL/kg (range 0.5 mL/kg to 3 mL/kg); with a maximum cumulative dose not exceeding 3 mL/kg.

3 DOSAGE FORMS AND STRENGTHS

Injection: clear, colorless to pale yellow solutions containing no undissolved solids, available in the following strengths and single-dose containers:

	mg of ioversol per mL	mg of organically bound iodine per mL	Presentations			
			Vials	Bottles	Hand-held syringes	Power injector syringes
OPTIRAY 300 (ioversol 64%)	636	300	No	Yes	Yes	Yes
OPTIRAY 320 (ioversol 68%)	678	320	Yes	Yes	Yes	Yes
OPTIRAY 350 (ioversol 68%)	741	350	No	Yes	Yes	Yes

4 CONTRAINDICATIONS

Symptomatic hyperthyroidism.

5 WARNINGS AND PRECAUTIONS

5.1 Risks Associated with Inadvertent Intrathecal Administration

OPTIRAY is indicated for intravascular use only [see Dosage and Administration (2.1)]. Inadvertent intrathecal administration can cause death, convulsions, cerebral hemorrhage, coma, paralysis, arachnoiditis, acute renal failure, cardiac arrest, seizures, rhabdomyolysis, hyperthermia, and brain edema.

5.2 Hypersensitivity Reactions

OPTIRAY can cause life-threatening or fatal hypersensitivity reactions including anaphylaxis and anaphylactic shock. Manifestations include respiratory arrest, laryngospasm, bronchospasm, angioedema, and shock. Most severe reactions develop shortly after the start of the injection (e.g. within 1 to 3 minutes), but delayed reactions may occur. There is an increased risk in patients with a history of a previous reaction to contrast agent, and known allergies (i.e., bronchial asthma, drug, or food allergies), and other hypersensitivities. Premedication with antihistamines or corticosteroids to avoid or minimize possible allergic reactions does not prevent serious life-threatening reactions, but may reduce both their incidence and severity.

Obtain a history of allergy, hypersensitivity, or prior hypersensitivity reactions to iodinated contrast agents. Always have emergency resuscitation equipment and trained personnel available and monitor all patients for hypersensitivity reactions.

5.3 Contrast Induced Acute Kidney Injury

Acute kidney injury, including renal failure, may occur after OPTIRAY administration. Risk factors include: pre-existing renal impairment, dehydration, diabetes mellitus, congestive heart failure, advanced vascular disease, elderly age, concomitant use of nephrotoxic or diuretic medications, multiple myeloma / paraproteinaceous diseases, repetitive and/or large doses of an iodinated contrast agent.

Use the lowest necessary dose of OPTIRAY in patients with renal impairment. Adequately hydrate patients prior to and following OPTIRAY administration. Do not use laxatives, diuretics, or preparatory dehydration prior to OPTIRAY administration.

5.4 Cardiovascular Adverse Reactions

OPTIRAY increases the circulatory osmotic load and may induce acute or delayed hemodynamic disturbances in patients with congestive heart failure, severely impaired renal function, combined renal and hepatic disease, combined renal and cardiac disease, particularly when repetitive or large doses are administered.

Life-threatening or fatal cardiovascular reactions have occurred with the use of OPTIRAY, including cardiac arrest, hypotensive collapse, and shock. Most deaths occur within 10 minutes of injection; with cardiovascular disease as the main underlying factor. Cardiac decompensation, serious arrhythmias, and myocardial ischemia or infarction can occur during coronary arteriography and ventriculography.

Based upon literature reports, deaths from the administration of iodinated contrast agents range from 6.6 per 1 million (0.00066 percent) to 1 in 10,000 patients (0.01 percent). Use the lowest necessary dose of OPTIRAY in patients with congestive heart failure and always have emergency resuscitation equipment and trained personnel available. Monitor all patients for severe cardiovascular reactions.

5.5 Thromboembolic Events

Angiocardiology

Serious, fatal, thromboembolic events causing myocardial infarction and stroke can occur during angiographic procedures with OPTIRAY. During these procedures, increased thrombosis and activation of the complement system occurs. Risk factors for thromboembolic events include: length of procedure, catheter and syringe material, underlying disease state, and concomitant medications.

To minimize thromboembolic events use meticulous angiographic technique. Avoid blood remaining in contact with syringes containing OPTIRAY, which increases the risk of clotting. Avoid angiocardiology in patients with homocystinuria because of the risk of inducing thrombosis and embolism [see Clinical Pharmacology (12.2)].

5.6 Extravasation and Injection Site Reactions

Extravasation can occur with OPTIRAY administration, particularly in patients with severe arterial or venous disease and can be associated with pain, hemorrhage and necrosis. Ensure intravascular placement of catheters prior to injection. Monitor patients for extravasation and advise patients to seek medical care for progression of symptoms.

5.7 Thyroid Storm in Patients with Hyperthyroidism

OPTIRAY is contraindicated in patients with symptomatic hyperthyroidism [see Contraindications (4)]. Thyroid storm has occurred following the intravascular use of iodinated radiopaque agents in patients with hyperthyroidism or with an autonomously functioning thyroid nodule. Evaluate the risk in such patients before use of OPTIRAY.

5.8 Thyroid Dysfunction in Pediatric Patients 0 to 3 Years of Age

Thyroid dysfunction characterized by hypothyroidism or transient thyroid suppression has been reported after both single exposure and multiple exposures to iodinated contrast media (ICM) in pediatric patients 0 to 3 years of age.

Younger age, very low birth weight, prematurity, underlying medical conditions affecting thyroid function, admission to neonatal or pediatric intensive care units, and congenital cardiac conditions are associated with an increased risk of hypothyroidism after ICM exposure. Pediatric patients with congenital cardiac conditions may be at the greatest risk given that they often require high doses of contrast during invasive cardiac procedures.

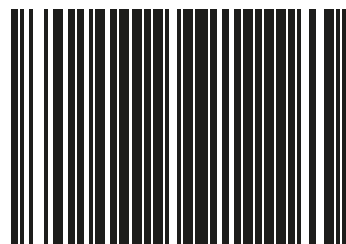
An underactive thyroid during early life may be harmful for cognitive and neurological development and may require thyroid hormone replacement therapy. After exposure to ICM, individualize thyroid function monitoring based on underlying risk factors, especially in term and preterm neonates.

5.9 Hypertensive Crisis in Patients with Pheochromocytoma

Hypertensive crisis has occurred after the use of iodinated radiopaque contrast agents in patient with pheochromocytoma. Closely monitor patients when administering OPTIRAY if pheochromocytoma or catecholamine-secreting paraganglioma is suspected. Inject the minimum amount of OPTIRAY necessary and have measures for treatment of hypertensive crisis readily available.

5.10 Sickle Cell Crisis in Patients with Sickle Cell Disease

Iodinated contrast agents may promote sickling in individuals who are homozygous for sickle cell disease. Hydrate patients prior to and following OPTIRAY administration,



13US0223

OPTIRAY® 350

(Ioversol Injection 74%)

OPTIRAY® 320

(Ioversol Injection 68%)

OPTIRAY® 300

(Ioversol Injection 64%)

Global Labeling Department			
JOB INFORMATION			
Product Brand and Descriptor:	OPTIRAY		
GTIN:	None		
GBU:	Pharmaceuticals		
REV:	02/2023		
ADDITIONAL JOB INFORMATION			
Job #:	230039	Dimensions:	22.75" W x 12.75" H
Artwork/Part #:	GBT 13US0223	Metric Dimensions:	577.85 mm W x 323.85 mm H (approx)
Print Process:	Offset Lithography	Package Type:	Insert
Barcode Format:	Code 128	File Name:	1323ra-in0000-us0223.indd
Notes:			
NUMBER OF COLORS			
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Black			
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
TECHNICAL INFORMATION			
Application:	InDesign		
Linked Images:	Structure outline.eps Insert Grayscale logo.eps		
Fonts Used:	Myriad Pro Family		
Liebel-Flarsheim Company LLC A subsidiary of Guerbet			
<i>Regulatory Affairs</i> 1034 South Brentwood Richmond Heights, MO 63117 USA			
GBU-SPECIFIC INFORMATION			
Manufacturing Site:	Raleigh		
Print Vendor:	CCL - Chicago		
Country:	United States (US)		
Graphic Designer:	jg5		
Date:	August 30, 2023		
OTHER INFORMATION			
Additional Notes:			

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