ULTRAVIST- iopromide injection
Bayer HealthCare Pharmaceuticals Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ULTRAVIST Injection safely and effectively. See full prescribing information for ULTRAVIST Injection.
ULTRAVIST (iopromide) Injection, for intravenous or intra-arterial use
Initial U.S. Approval: 1995

WARNING: NOT FOR INTRATHECAL USE

See full prescribing information for complete boxed warning.

Intrathecal administration, even if inadvertent, may cause death, convulsions, cerebral hemorrhage, coma, paralysis, arachnoiditis, acute renal failure, cardiac arrest, seizures, rhabdomyolysis, hyperthermia, and brain edema. ULTRAVIST is not approved for intrathecal use. (5.1)

RECENT MAJOR CHANGES

Indications and Usage (1.2) 5/2023
Dosage and Administration (2.3, 2.5) 5/2023
Warning and Precautions (5.8) 4/2023

INDICATIONS AND USAGE

ULTRAVIST is a radiographic contrast agent indicated for:
Intra-Arterial Procedures†

- Cerebral arteriography and peripheral arteriography in adults (1.1)
- Coronary arteriography and left ventriculography, visceral angiography, and aortography in adults (1.1)
- Radiographic evaluation of cardiac chambers and related arteries in pediatric patients aged 2 years and older (1.1)

Intravenous Procedures†

- Excretory urography in adults and pediatric patients aged 2 years and older (1.2)
- Contrast computed tomography (CT) of head and body in adults and pediatric patients aged 2 years and older (1.2)
- Contrast mammography in adults as an adjunct following mammography and/or ultrasound (1.2)

†Specific concentrations and presentations are recommended for each type of imaging procedure. (2.2, 2.3, 2.4)

DOSAGE AND ADMINISTRATION

- Individualize the volume and concentration according to the specific dosing tables accounting for factors such as age, body weight, size of the vessel, and the rate of blood flow within the vessel. (2.2, 2.3, 2.4)
- For contrast mammography, use ULTRAVIST with a device that is cleared for dual-energy full field digital mammography. (2.5)
- See full prescribing information for important dosage and administration instructions and directions for use of pharmacy bulk packages and imaging bulk packages. (2.1, 2.6, 2.7)

DOSAGE FORMS AND STRENGTHS

Injection: 300 mg Iodine per mL and 370 mg Iodine per mL in single-dose vials, pharmacy bulk packages, and imaging bulk packages. (3)

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

- Hypersensitivity Reactions: Life-threatening or fatal reactions can occur. Always have emergency equipment and trained personnel available. (5.2)

- Acute Kidney Injury: Acute injury including renal failure can occur. Dose minimization and hydration may decrease risk. (5.3)
- Cardiovascular 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

Common adverse reactions (>1%) are headache, nausea, injection site and infusion site reactions, vasodilatation, vomiting, back pain, urinary urgency, chest pain, pain, dysgeusia, and abnormal vision. (6)
To report SUSPECTED ADVERSE REACTIONS, contact Bayer HealthCare Pharmaceuticals Inc. at 1-888-842-2937 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 5/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: NOT FOR INTRATHECAL USE

1 INDICATIONS AND USAGE

ULTRAVIST® Injection is an iodinated contrast agent indicated for:

1.1 Intra-Arterial Procedures*

ULTRAVIST is indicated for:

- Cerebral arteriography and peripheral arteriography in adults
- Coronary arteriography and left ventriculography, visceral angiography, and aortography in adults
- Radiographic evaluation of cardiac chambers and related arteries in pediatric patients aged 2 years and older

1.2 Intravenous Procedures*

ULTRAVIST is indicated for:

- Excretory urography in adults and pediatric patients aged 2 years and older
- Contrast Computed Tomography (CT) of the head and body (intrathoracic, intra-abdominal, and retroperitoneal regions) for the evaluation of neoplastic and non-neoplastic lesions in adults and pediatric patients aged 2 years and older
- Contrast mammography to visualize known or suspected lesions of the breast in adults, as an adjunct following mammography and/or ultrasound

†Specific concentrations and presentations of ULTRAVIST are recommended for each type of imaging procedure *[see Dosage and Administration (2.2, 2.3, 2.4)].*

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Information

- ULTRAVIST is for intra-arterial or intravenous use only and must not be administered intrathecally *[see Warnings and Precautions (5.1)]*.
- Specific concentrations and presentations of ULTRAVIST are recommended for each type of imaging procedure *[see Dosage and Administrations (2.2, 2.3, 2.4)]*.
- Hydrate patients, as appropriate, prior to and following the administration of ULTRAVIST *[see Warnings and Precautions (5.3)]*.
- Individualize the volume, concentration, and injection rate of ULTRAVIST according to the specific dosing tables *[see Dosage and Administration (2.2, 2.3, 2.4)]*. Consider factors such as age, body weight, size of the vessel, and the rate of blood flow within the vessel; also consider extent of opacification required, structure(s) or area to be examined, disease processes affecting the patient, and equipment and technique to be employed.
- Visually inspect ULTRAVIST for particulate matter and/or discoloration, whenever solution and container permit. Do not administer ULTRAVIST if particulate matter (including crystals) and/or discoloration is observed or if containers are defective.
- Use aseptic technique for all handling and administration of ULTRAVIST.
- Warm ULTRAVIST to body temperature before administration.
- ULTRAVIST can be used with 0.9% Sodium Chloride Injection in a power injector suitable for simultaneous injection of contrast *[see Dosage and Administration (2.3)]*. However, do not mix or inject ULTRAVIST in intravenous administration lines containing other drugs or total nutritional admixtures.
- Discard any unused portion remaining in the single-dose container following initial use.

2.2 Recommended Dosage for Intra-Arterial Procedures in Adults

- The recommended doses for intra-arterial procedures in adults are shown in Table 1.
- Inject at rates approximately equal to the flow rate in the vessel being injected.

Table 1: Recommended Concentrations and Volume of ULTRAVIST to Administer per Single Injection for Selected Injection Sites of Intra-Arterial Procedures in Adults

Imaging Procedure	Cerebral Arteriography	Peripheral Arteriography	Coronary Arteriography	Visceral Angiography

				and Left Ventriculography	and Aortography
Concentration (mg Iodine per mL)		300*	300*	370*	370*
Intra-Arterial Injection Sites	Carotid Arteries	3 mL to 12 mL	-	-	-
	Vertebral Arteries	4 mL to 12 mL			
	Aortic Arch Injection (four vessel study)	20 mL to 50 mL			
	Subclavian or Femoral Artery	-	5 mL to 40 mL	-	-
	Aortic Bifurcation (distal runoff)		25 mL to 50 mL		
	Right Coronary Artery	-	-	3 mL to 14 mL	-
	Left Coronary Artery			3 mL to 14 mL	
	Left Ventricle			30 mL to 60 mL	
	Aorta and Major Abdominal Branches	-	-	-	Individualize a volume approximately equal to the blood flow and related to the vascular and pathological characteristics of the specific vessels being studied.
Maximum Total Dose		150 mL	250 mL	225 mL	225 mL

*Use single-dose vials or pharmacy bulk package.

2.3 Recommended Dosage for Intravenous Procedures in Adults

Recommended doses for intravenous procedures in adults are shown in Table 2.

Table 2: Recommended Concentrations and Volume of ULTRAVIST for Intravenous Procedures in Adults

Imaging Procedure	Excretory Urography	Contrast Computed Tomography		Contrast Mammography
Concentration (mg Iodine per mL)	300*	300‡	370‡	300‡ or 370‡
Excretory Urography	1 mL/kg body weight	-	-	-
CT of Head	-	50 mL to 200 mL	41 mL to 162 mL	-
CT of Body - Single Phase Contrast Bolus Injection Rapid Infusion	-	50 mL to 200 mL 100 mL to 200 mL	41 mL to 162 mL 81 mL to 162 mL	-
CT of Body – Multiple Phase Contrast	-	50 mL to 200 mL total volume Phase 1: 100% contrast, Phase 2: 20% to 60% contrast, using a power injector suitable for simultaneous injection of contrast and 0.9% Sodium Chloride Injection	41 mL to 162 mL total volume Phase 1: 100% contrast, Phase 2: 20% to 60% contrast, using a power injector suitable for simultaneous injection of contrast and 0.9% Sodium Chloride Injection	-
Contrast Mammography	-	-	-	1.5 mL/kg body weight using a power injector at 2 mL/second to 4 mL/second
Maximum Total Dose	100 mL	200 mL	162 mL	150 mL

*Use single-dose vials or pharmacy bulk package.

‡Use single-dose vials, pharmacy bulk package or imaging bulk package.

2.4 Recommended Dosage in Pediatric Patients Aged 2 Years and Older

The recommended doses in pediatric patients aged 2 years and older are shown in Table 3.

Table 3: Recommended Concentrations and Volume per Body Weight of ULTRAVIST for Cardiac Chambers and Related Arteries, Excretory Urography, and Contrast Computed Tomography in Pediatric Patients Aged 2 Years and Older

Imaging Procedure	Intra-arterial	Intravenous	
	Cardiac Chambers and Related Arteries	Excretory Urography	Contrast Computerized Tomography
Concentration (mg Iodine/mL)	370*	300*	300‡
Volume (mL/kg body weight)	1 to 2	1 to 2	1 to 2
Maximum Total Dose (mL/kg)	4	3	3

*Use single-dose vials or pharmacy bulk package.
‡Use single-dose vials, pharmacy bulk package or imaging bulk package.

2.5 Imaging Instruction for Contrast Mammography

For contrast mammography, use ULTRAVIST with a device that is cleared for dual-energy full field digital mammography.

2.6 Directions for Use of ULTRAVIST Pharmacy Bulk Package

- ULTRAVIST Pharmacy Bulk Package (PBP) is not for direct infusion.
- Perform the transfer of the PBP in a suitable work area, such as a laminar flow hood, utilizing aseptic technique.
- Penetrate the container closure only one time, utilizing a suitable transfer device.
- After initial puncture, use the contents of the PBP within 10 hours. Discard any unused portion

2.7 Directions for Use of ULTRAVIST Imaging Bulk Package

- ULTRAVIST Imaging Bulk Package (IBP) is for intravenous use only.
- ULTRAVIST IBP is for use only with an automated contrast injection system, contrast management system, or contrast media transfer set approved or cleared for use with this contrast agent in this IBP. Please see drug and device labeling for information on devices indicated for use with this IBP and techniques to help assure safe use.
- The IBP is to be used only in a room designated for radiological procedures that involve intravascular administration of a contrast agent.

- Using aseptic technique, penetrate the container closure of the IBP only one time with a suitable sterile component of the automated contrast injection system, contrast management system, or contrast media transfer set approved or cleared for use with this contrast agent in this IBP.
- Once the IBP is punctured, do not remove it from the work area during the entire period of use. Maintain the bottle in an inverted position such that container contents are in continuous contact with the dispensing set.
- After the container closure is punctured, if the integrity of the IBP and the delivery system cannot be assured through direct continuous supervision, discard the IBP and all associated disposables for the automated contrast injection system, contrast management system, or contrast media transfer set.
- A maximum use time from initial puncture is 10 hours. Discard any unused portion remaining in IBP container.
- Storage temperature of IBP after the closure has been entered should not exceed 25°C (77°F) with excursions permitted to 15°C to 30°C (59°F to 86°F); however, it is desirable that the contents be warmed to body temperature prior to injection.

3 DOSAGE FORMS AND STRENGTHS

ULTRAVIST injection is a clear, colorless to slightly yellow, odorless solution available in two concentrations:

300 mg Iodine per mL available as

- 50 mL, 100 mL, 125 mL, and 150 mL in single-dose vials
- 200 mL and 500 mL in pharmacy bulk packages
- 200 mL and 500 mL in imaging bulk packages

370 mg Iodine per mL available as

- 50 mL, 100 mL, 125 mL, and 150 mL in single-dose vials
- 200 mL and 500 mL in pharmacy bulk packages
- 200 mL and 500 mL in imaging bulk packages

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Risks Associated with Intrathecal Use

Intrathecal administration, even if inadvertent, can cause death, convulsions, cerebral hemorrhage, coma, paralysis, arachnoiditis, acute renal failure, cardiac arrest, seizures, rhabdomyolysis, hyperthermia, and brain edema. ULTRAVIST is for intra-arterial or intravenous use only *[see Dosage and Administration (2.2, 2.3, 2.4)].* ULTRAVIST is not approved for intrathecal use.

5.2 Hypersensitivity Reactions

ULTRAVIST can cause life-threatening or fatal hypersensitivity reactions including anaphylaxis. Manifestations include respiratory arrest, laryngospasm, bronchospasm, angioedema, and shock *[see Adverse Reactions (6.2)]*. Most severe reactions develop shortly after the start of injection (e.g., within 1 to 3 minutes), but delayed reactions can also occur. There is increased risk of hypersensitivity reactions in patients with a history of previous reaction to a contrast agent and known allergic disorders (that is, bronchial asthma, allergic rhinitis, and food allergies), or other hypersensitivities. Premedication with antihistamines or corticosteroids does not prevent serious life-threatening reactions but may reduce both their incidence and severity.

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

5.3 Acute Kidney Injury

Acute kidney injury, including renal failure, may occur after administration of ULTRAVIST. Risk factors include: pre-existing renal insufficiency, dehydration, diabetes mellitus, congestive heart failure, advanced vascular disease, elderly age, concomitant use of nephrotoxic or diuretic medications, multiple myeloma or other paraproteinemia, and repetitive and/or large doses of ULTRAVIST.

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

5.4 Cardiovascular Adverse Reactions

ULTRAVIST 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, or combined renal and cardiac disease, particularly when repetitive and/or large doses are administered. Fatal cardiovascular reactions have occurred mostly within 10 minutes of ULTRAVIST injection; the main feature was cardiac arrest with cardiovascular disease as the main underlying factor. Hypotensive collapse and shock have occurred. Cardiac decompensation, serious arrhythmias, and myocardial ischemia or infarction can occur during coronary arteriography and ventriculography.

The administration of ULTRAVIST may cause pulmonary edema in patients with heart failure. Based upon published 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 ULTRAVIST 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

angiography procedures. During these procedures, increased thrombosis and activation of the complement system can occur. Risk of thromboembolic events can be influenced by: length of procedure, catheter and syringe material, underlying disease state, and concomitant medications.

To decrease thromboembolic events, use meticulous angiographic techniques and minimize the length of the procedure. Avoid blood remaining in contact with syringes containing iodinated contrast agents, which increases the risk of clotting. Avoid angiography in patients with homocystinura because of the risk of inducing thrombosis and embolism.

5.6 Extravasation and Injection Site Reactions

Extravasation can occur with ULTRAVIST, particularly in patients with severe arterial or venous disease. Inflammation, blistering, skin necrosis, and compartment syndrome have been reported following extravasation. In addition, injection site reactions such as pain and swelling at the injection site can also occur *[see Adverse Reactions (6.1)]*. 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

Thyroid storm has occurred after the intravascular use of iodinated contrast agents in patients with hyperthyroidism or with an autonomously functioning thyroid nodule. Evaluate the risk in such patients before use of ULTRAVIST.

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.

The safety and effectiveness of ULTRAVIST in pediatric patients younger than 2 years of age have not been established, and ULTRAVIST is not approved for use in pediatric patients younger than 2 years of age *[see Use in Specific Populations (8.4)].*

5.9 Hypertensive Crisis in Patients with Pheochromocytoma

Hypertensive crisis in patients with pheochromocytoma has occurred with iodinated contrast agents. Closely monitor patients when administering ULTRAVIST if pheochromocytoma or catecholamine-secreting paragangliomas are suspected. Inject the minimum amount of ULTRAVIST necessary and have measures for treatment of a 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 ULTRAVIST administration and use only if the necessary imaging information cannot be obtained with alternative imaging modalities.

5.11 Severe Cutaneous Adverse Reactions

Severe cutaneous adverse reactions (SCAR) may develop from 1 hour to several weeks after intravascular contrast agent administration. These reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN), acute generalized exanthematous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS). Reaction severity may increase and time to onset may decrease with repeat administration of contrast agent; prophylactic medications may not prevent or mitigate severe cutaneous adverse reactions. Avoid administering ULTRAVIST to patients with a history of a severe cutaneous adverse reaction to ULTRAVIST.

5.12 Interference with Laboratory Tests

ULTRAVIST can interfere with protein-bound iodine test *[see Drug Interactions (7.2)]*.

6 ADVERSE REACTIONS

The following adverse reactions are described elsewhere in the labeling:

- Risks Associated with Intrathecal Use *[see Warnings and Precautions (5.1)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.2)]*
- Acute Kidney Injury *[see Warnings and Precautions (5.3)]*
- Cardiovascular Adverse Reactions *[see Warnings and Precautions (5.4)]*
- Thromboembolic Events *[see Warnings and Precautions (5.5)]*
- Extravasation and Injection Site Reactions *[see Warnings and Precautions (5.6)]*
- Thyroid Dysfunction in Pediatric Patients 0 to 3 Years of Age *[see Warnings and Precautions (5.8)]*
- Severe Cutaneous Adverse Reactions *[see Warnings and Precautions (5.11)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect or predict the rates observed in practice.

The common adverse reactions reported in >1% of patients in clinical studies with ULTRAVIST are shown in Table 4.

Table 4: Adverse Reactions Reported in >1% of Patients Receiving ULTRAVIST in Clinical Trials

System Organ Class	**Adverse Reaction**	**ULTRAVIST N=1,142 (%)**
Nervous system disorders	Headache	46 (4)
	Dysgeusia	15 (1.3)

Eye disorders	Abnormal Vision	12 (1.1)
Cardiac disorders	Chest pain	18 (1.6)
Vascular disorders	Vasodilatation	30 (2.6)
Gastrointestinal disorders	Nausea	42 (3.7)
	Vomiting	22 (1.9)
Musculoskeletal and connective tissue disorders	Back pain	22 (1.9)
Renal and urinary disorders	Urinary urgency	21 (1.8)
General disorders and administration site conditions	Injection site and infusion site reactions (hemorrhage, hematoma, pain, edema, erythema, rash)	41 (3.7)
	Pain	13 (1.4)

One or more adverse reactions were recorded in 273 of 1,142 (24%) patients during the clinical trials, coincident with the administration of ULTRAVIST or within the defined duration of the study follow-up period (24–72 hours). ULTRAVIST is often associated with sensations of warmth and/or pain.

Serious, life-threatening, and fatal reactions have been associated with the administration of iodine-containing contrast media, including ULTRAVIST. In clinical trials 7 of 1,142 patients given ULTRAVIST died 5 days or later after drug administration. Also, 10 of 1,142 patients given ULTRAVIST had serious adverse events.

The following adverse reactions were observed in ≤1% of the patients receiving ULTRAVIST:

Cardiac disorders:

atrioventricular block (complete), bradycardia, ventricular extrasystole

Gastrointestinal disorders:

abdominal discomfort, abdominal pain, abdominal pain upper, constipation, diarrhea, dry mouth, dyspepsia, gastrointestinal disorder, gastrointestinal pain, salivation increased, stomach discomfort, rectal tenesmus

General disorders and administration site conditions:

asthenia, chest discomfort, chills, excessive thirst, extravasation, feeling hot, hyperhidrosis, malaise, edema peripheral, pyrexia

Immune system disorders:

asthma, face edema

Investigations:

blood lactate dehydrogenase increased, blood urea increased, hemoglobin increased, white blood cell count increased

Musculoskeletal and connective tissue disorders:

arthralgia, musculoskeletal pain, myasthenia, neck pain, pain in extremity

Nervous system disorders:

agitation, confusion, convulsion, dizziness, hypertonia, hypesthesia, incoordination, neuropathy, somnolence, speech disorder, tremor, paresthesia, visual field defect

Psychiatric disorders:

anxiety

Renal and urinary disorders:

dysuria, renal pain, urinary retention

Respiratory, thoracic and mediastinal disorders:

apnea, cough increased, dyspnea, hypoxia, pharyngeal edema, pharyngitis, pleural effusion, pulmonary hypertension, respiratory disorder, sore throat

Skin and subcutaneous tissue disorders:

erythema, pruritus, rash, urticaria

Vascular disorders:

coronary artery thrombosis, flushing, hypertension, hypotension, peripheral vascular disorder, syncope, vascular anomaly

Pediatric Patients

A total of 274 pediatric patients were evaluated with intra-arterial coronary angiography (n=60), intravenous contrast computerized tomography (CT) (n=87), excretory urography (n=99), and 28 other procedures. These patients received 1 mL/kg to 2 mL/kg body weight of a concentration of 300 mg Iodine per mL for intravenous contrast CT or excretory urography and 370 mg Iodine per mL for intra-arterial and intracardiac administration in the radiographic evaluation of the heart cavities and major arteries *[see Dosage and Administration (2.4)].* Among these, 131 were 2 to 12 years old, 57 were adolescents, and 86 were unreported or other ages. There were 148 females, 94 males, and 32 in whom gender was not reported. The racial distribution was: White 33.9%, Black 0.4%, Asian 2.2%, and unknown 63.5%. The overall character, quality, and severity of adverse reactions in pediatric patients are generally similar to those reported in adult patients.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of ULTRAVIST. 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. Adverse reactions reported in foreign postmarketing surveillance and other trials with the use of ULTRAVIST include:

Cardiac disorders:

cardiac arrest, ventricular fibrillation, atrial fibrillation, tachycardia, palpitations, congestive heart failure, myocardial infarction, angina pectoris

Ear and labyrinth disorders:

vertigo, tinnitus

Endocrine disorders:

hyperthyroidism, thyrotoxic crisis, hypothyroidism

Eye disorders:

mydriasis, lacrimation disorder

Gastrointestinal disorders:

dysphagia, swelling of salivary glands

Immune system disorders:

anaphylactoid reaction (including fatal cases), respiratory arrest, anaphylactoid shock, angioedema, laryngeal edema, laryngospasm, bronchospasm, hypersensitivity

Musculoskeletal and connective tissue disorders:

compartment syndrome in case of extravasation

Nervous system disorders:

cerebral ischemia/infarction, paralysis, paresis, transient cortical blindness, aphasia, coma, unconsciousness, amnesia, hypotonia, aggravation of myasthenia gravis symptoms

Renal and urinary disorders:

renal failure, hematuria

Respiratory, thoracic and mediastinal disorders:

pulmonary edema, acute respiratory distress syndrome, asthma

Skin and subcutaneous tissue disorders:

Reactions range from mild (e.g., rash, erythema, pruritus, urticaria and skin discoloration) to severe [e.g., Stevens-Johnson Syndrome and toxic epidermal necrolysis (SJS/TEN), acute generalized exanthematous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS)].

Vascular disorders:

vasospasm

Pediatric Patients

Additional adverse reactions reported in pediatric patients from foreign marketing surveillance or other information include: epistaxis, migraine, joint disorder (effusion), muscle cramps, mucous membrane disorder (mucosal swelling), conjunctivitis, fixed eruptions, diabetes insipidus, and brain edema.

6.3 Pediatrics

The overall character, quality, and severity of adverse reactions in pediatric patients are generally similar to those reported in adult patients. Additional adverse reactions reported in pediatric patients from foreign marketing surveillance or other information are: *epistaxis, angioedema, migraine, joint disorder (effusion), muscle cramps, mucous membrane disorder (mucosal swelling), conjunctivitis, hypoxia, fixed eruptions, vertigo, diabetes insipidus, and brain edema [see Use in Specific Populations (8.4)]*.

7 DRUG INTERACTIONS

7.1 Drug-Drug Interactions

Metformin

In patients with renal impairment, biguanides can cause lactic acidosis. Iodinated contrast agents appear to increase the risk of metformin-induced lactic acidosis, possibly as a result of worsening renal function. Stop metformin at the time of, or prior to, ULTRAVIST administration in patients with an eGFR between 30 and 60 mL/min/1.73 m2; in patients with a history of hepatic impairment, alcoholism, or heart failure; or in patients who will be administered intra-arterial iodinated contrast agents. Re-evaluate eGFR 48 hours after the imaging procedure and reinstitute only after renal function is stable.

Radioactive Iodine

ULTRAVIST may interfere with thyroid uptake of radioactive iodine (I-131 and I-123) and decrease therapeutic and diagnostic efficacy. Avoid thyroid therapy or testing for up to 6 weeks post ULTRAVIST.

7.2 Drug-Laboratory Test Interactions

Protein-Bound Iodine Test

Iodinated contrast agents, including ULTRAVIST, will temporarily increase protein-bound iodine in blood. Do not perform protein-bound iodine test for at least 16 days following administration of ULTRAVIST. However, thyroid function tests which do not depend on iodine estimations, for example, T_3 resin uptake and total or free thyroxine (T_4) assays are not affected.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no data on ULTRAVIST use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Iopromide crosses the placenta and reaches fetal tissues in small amounts *(see Data)*. In animal reproduction studies, intravenous administration of iopromide to pregnant rats and rabbits during organogenesis at doses up to0.35 and 0.7 times, respectively, the maximum recommended human dose based on body surface area

resulted in no relevant adverse developmental effects *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Human Data

Limited case reports demonstrate that intravenously administered iodinated contrast agents, including iopromide, cross the placenta and are visualized in the digestive tract of exposed infants after birth.

Animal Data

Reproduction studies were performed with intravenous iopromide in rats (day 6 to 15 of gestation) and rabbits (day 6 to 18 of gestation) at dose levels of 0, 0.37, 1.11, and 3.7 g iodine per kg, corresponding to doses up to 0.35 times (rats) and 0.7 times (rabbits) the maximum human recommended dose based on body surface area. Iopromide was not teratogenic at any dose level in rats and rabbits and embryolethality was observed in rabbits that received 3.7 g iodine per kg, but this was considered to have been secondary to maternal toxicity.

8.2 Lactation

Risk Summary

There are no data on the presence of iopromide in human milk, the effects on the breastfed infant, or the effects on milk production. Iodinated contrast agents are poorly excreted into human milk and are poorly absorbed by the gastrointestinal tract of a breastfed infant. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ULTRAVIST and any potential adverse effects on the breastfed infant from ULTRAVIST or from the underlying maternal condition *(see Clinical Considerations)*.

Clinical Considerations

Interruption of breastfeeding after exposure to iodinated contrast agents is not necessary because the potential exposure of the breastfed infant to iodine is small. However, a lactating woman may consider interrupting breastfeeding and pumping and discarding breast milk for 12 to 24 hours (approximately 5 elimination half-lives) after ULTRAVIST administration in order to minimize drug exposure to a breast fed infant.

8.4 Pediatric Use

The safety and efficacy of ULTRAVIST have been established in pediatric patients aged 2 years and older for radiographic evaluation of cardiac chambers and related arteries, excretory urography, and contrast computed tomography of head and body. Use of ULTRAVIST in these age groups for these indications is supported by evidence from adequate and well-controlled studies in adults and additional safety data in pediatric

patients aged 2 years and older, including data from published studies *[see Adverse Reactions (6.1, 6.2) and Clinical Studies (14.1, 14.2)].*

Pediatric patients at higher risk of experiencing an adverse reaction during and after administration of any contrast agent include those with asthma, sensitivity to medication and/or allergens, cyanotic and acyanotic heart disease, congestive heart failure, or serum creatinine greater than 1.5 mg/dL.

Thyroid function tests indicative of thyroid dysfunction, characterized by hypothyroidism or transient thyroid suppression have been reported following iodinated contrast media administration in pediatric patients, including term and preterm neonates; Some patients were treated for hypothyroidism. After exposure to iodinated contrast media, individualize thyroid function monitoring in pediatric patients 0 to 3 years of age based on underlying risk factors, especially in term and preterm neonates *[see Warnings and Precautions (5.8) and Adverse Reactions (6.2)].*

Safety and effectiveness of ULTRAVIST have not been established in pediatric patients younger than 2 years for radiographic evaluation of cardiac chambers and related arteries, excretory urography, and contrast computed tomography of head and body.

Safety and effectiveness of ULTRAVIST for cerebral arteriography, peripheral arteriography, coronary arteriography and left ventriculography, visceral angiography, aortography, and contrast mammography have not been established in pediatric patients.

8.5 Geriatric Use

In a clinical study of ULTRAVIST for CT, 96/434 (22.1%) of patients were 65 and over. No overall differences in safety were observed between these patients and younger patients. Other reported clinical experience has not identified differences in response between the elderly and younger patients. Iopromide is known to be substantially excreted by the kidney, and the risk of adverse reactions to iopromide may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

8.6 Renal Impairment

The clearance of iopromide decreases with increasing degree of renal impairment and results in delayed opacification of the urinary system *[see Clinical Pharmacology (12.3)]*. In addition, preexisting renal impairment increases the risk for acute kidney injury *[see Warnings and Precautions (5.3)]*. Iopromide can be removed by dialysis.

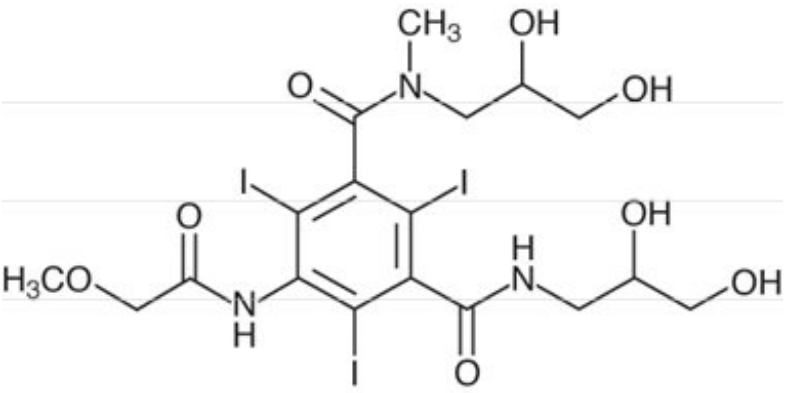
10 OVERDOSAGE

The manifestations of overdosage are life-threatening and affect mainly the pulmonary and cardiovascular systems. Treatment of an overdosage is directed toward the support of all vital functions, and prompt institution of symptomatic therapy. Iopromide can be removed by dialysis.

11 DESCRIPTION

ULTRAVIST(iopromide) injection is a nonionic radiographic contrast agent for intra-arterial or intravenous administration. The chemical name for iopromide is *N,N*'-Bis(2,3-dihydroxypropyl)-2,4,6-triiodo-5-[(methoxyacetyl)amino]-*N*-methyl- 1,3-benzenedicarboxamide. Iopromide has a molecular weight of 791.12 (iodine content 48.12%).

Iopromide has the following structural formula:



Each mL contains 623.4 mg or 768.86 mg iopromide (300 mg or 370 mg iodine, respectively) and the following inactive ingredients: 0.1 mg edetate calcium disodium as a stabilizer and 2.42 mg tromethamine as a buffer. It may also contain sodium hydroxide or hydrochloric acid to adjust pH to 7.4 (6.5–8) at 25± 2°C and contains no preservatives.

ULTRAVIST is a sterile (sterilized by autoclaving), clear, colorless to slightly yellow, odorless, pyrogen-free aqueous solution and has the following physicochemical properties:

Property		**Concentration of ULTRAVIST (mg Iodine/mL)**	
		300	**370**
Osmolality*(mOsmol/kg water)	@ 37°C	607	774
Osmolarity*(mOsmol/L)	@ 37°C	428	496
Viscosity (cP)	@ 20°C @ 37°C	9.2 4.9	22 10
Density (g/mL)	@ 20°C @ 37°C	1.330 1.322	1.409 1.399

*Osmolality was measured by vapor-pressure osmometry. Osmolarity was calculated from the measured osmolal concentrations.

ULTRAVIST 300 mg Iodine per mL and 370 mg Iodine per mL have osmolalities respectively 2.1 and 2.7 times that of plasma (285 mOsmol/kg water).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Intravascular injection of iopromide opacifies those vessels where the contrast agent is present, permitting radiographic visualization of the internal structures through attenuation of photons. In imaging of the body, iodinated contrast agents diffuse from the vessels into the extravascular space. In normal brain with an intact blood-brain barrier, contrast does not diffuse into the extravascular space. In patients with a disrupted blood-brain barrier, contrast agent accumulates in the extravascular space in the region of disruption.

12.2 Pharmacodynamics

Following ULTRAVIST administration, the degree of contrast enhancement is related to the iodine concentration in the tissue of interest.

12.3 Pharmacokinetics

Distribution

After intravenous administration to healthy adult subjects, plasma iopromide concentration time profile shows an initial distribution phase with a half-life of 0.24 hour; a main elimination phase with a half-life of 2 hours; and a terminal elimination phase with a half-life of 6.2 hours. The total volume of distribution at steady state is about 16 L suggesting distribution into extracellular space. Plasma protein binding of iopromide is 1%.

Iodinated contrast agents cross a disrupted blood-brain barrier.

Elimination

Metabolism

Iopromide does not undergo significant metabolism, deiodination, or biotransformation

Excretion

The amounts excreted unchanged in urine represent 97% of the dose in adult healthy subjects. Only 2% of the dose is recovered in the feces. Similar recoveries in urine and feces are observed in middle-aged and elderly patients. This finding suggests that, compared to the renal route, biliary and/or gastrointestinal excretion is not important for iopromide. During the slower terminal phase, only 3% of the dose is eliminated; 97% of the dose is disposed of during the earlier phases, the largest part of which occurs during the main elimination phase. The ratio of the renal clearance of iopromide to the creatinine clearance is 0.82 suggesting that iopromide is mainly excreted by glomerular filtration. Additional tubular reabsorption is possible. Pharmacokinetics of iopromide at intravenous doses up to 80 g iodine are dose proportionate and first order.

The mean total and renal clearances are 107 mL/min and 104 mL/min, respectively.

Specific Populations

Age

Middle-aged (49 to 64 years) and elderly patients (65 to 70 years), without significantly impaired renal function, who received ULTRAVIST in doses corresponding to 9–30 g iodine, had mean steady-state volumes of distribution that ranged between 30–40 L. Mean total and renal clearances were between 81–125 mL/min and 70–115 mL/min, respectively, in these patients, and were similar to the values found in the young subjects. The distribution phase half-life in this patient population was 0.1 hour, the main elimination phase half-life was 2.3 hours, and the terminal elimination phase half-life was 40 hours. The urinary excretion (97% of the dose) and fecal excretion (2%) were comparable to that observed in young healthy subjects, suggesting that, compared to the renal route, biliary and/or gastrointestinal excretion is not significant for iopromide.

Patients with Renal Impairment

A pharmacokinetic study in patients with mild (n=2), moderate (n=6), and severe (n=3) renal impairment was conducted. Mild and moderate patients had a CL_{CR} between 30 to 80 mL/min/1.73 m^2. Severe patients had a CL_{CR} between 10 to 30 mL/min/1.73 m^2. ULTRAVIST 300 mg Iodine per mL was administered intravenously using a single-dose bolus injection. The total clearance of iopromide was decreased proportionately to the baseline decrease in creatinine clearance. The plasma AUC increased about 2-fold in patients with moderate renal impairment and 6-fold in patients with severe renal impairment compared to subjects with normal renal function. The terminal half-life increased from 2.2 hours for subjects with normal renal function to 11.6 hours in patients with severe renal impairment. The peak plasma concentration of iopromide was not influenced by the extent of renal impairment *[see Use in Specific Populations (8.6)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed with iopromide to evaluate carcinogenic potential or effects on fertility. Iopromide was not genotoxic in a series of studies including the Ames test, an *in vitro* human lymphocytes analysis of chromosomal aberrations, an *in vivo* mouse micro-nucleus assay, and in an *in vivo* mouse dominant lethal assay.

14 CLINICAL STUDIES

14.1 Overview of Clinical Studies

The following intra-arterial and intravenous procedures were studied with one of two concentrations of ULTRAVIST (300 mg Iodine per mL and 370 mg Iodine per mL): aortography/visceral angiography, coronary arteriography and left ventriculography, cerebral arteriography, peripheral arteriography, contrast computed tomography (CT) of head and body, excretory urography, and contrast mammography.

Efficacy assessment for most indications was based on the global evaluation of the quality of the images by rating visualization as either excellent, good, poor, or no image, and on the ability to make a diagnosis. For contrast mammography, efficacy assessment was based on rating visualized contrast uptake as negative, none, moderate, or intense.

14.2 Intra-Arterial Studies

Cerebral arteriography was evaluated in two randomized, double-blind clinical trials of ULTRAVIST 300 mg Iodine per mL in 80 patients with conditions such as altered cerebrovascular perfusion and/or permeability occurring in central nervous system diseases due to various CNS disorders. Visualization ratings were good or excellent in 99% of the patients with ULTRAVIST; a radiologic diagnosis was made in the majority of the patients. Confirmation of the radiologic findings by other diagnostic methods was not obtained.

Coronary arteriography/left ventriculography was evaluated in two randomized, double-blind clinical trials and one unblinded, unrandomized clinical trial of ULTRAVIST 370 mg Iodine per mL in 106 patients with conditions such as altered coronary artery perfusion due to metabolic causes and in patients with conditions such as altered ventricular function. Visualization ratings were good or excellent in 99% or more of the patients with ULTRAVIST; a radiologic diagnosis was made in the majority of the patients. Confirmation of the radiologic findings by other diagnostic methods was not obtained.

Aortography/visceral angiography was evaluated in two randomized, double-blind clinical trials of ULTRAVIST 370 mg Iodine per mL in 78 patients with conditions such as altered aortic blood flow and/or visceral vascular disorders. Visualization ratings were good or excellent in the majority of the patients with ULTRAVIST; a radiologic diagnosis was made in 99% of the patients. Confirmation of radiologic findings by other diagnostic methods was not obtained. The risks of renal arteriography could not be analyzed.

Similar studies were completed with comparable findings noted in peripheral arteriography.

14.3 Intravenous Studies

Contrast CT of head and body was evaluated in three randomized, double-blind clinical trials of ULTRAVIST 300 mg Iodine per mL in 95 patients with vascular disorders. Visualization ratings were good or excellent in 99% of the patients with ULTRAVIST; a radiologic diagnosis was made in the majority of the patients. Confirmation of contrast CT findings by other diagnostic methods was not obtained.

ULTRAVIST was evaluated in a blinded reader trial for CT of the head and body. Among the 382 patients who were evaluated with ULTRAVIST 370 mg Iodine per mL, visualization ratings were good or excellent in approximately 97% of patients.

Similar studies were completed with comparable findings noted in excretory urography.

Contrast mammography was evaluated in a published prospective study of 216 women (age range 26–85 years; mean age 54.6 years) who had BI-RADS 3, 4, or 5 findings on mammography and were evaluated using ULTRAVIST 300 mg Iodine per mL. Patients with breast implants, pregnancy or possible pregnancy, history of hypersensitivity reaction to iodinated contrast agents, and renal insufficiency were excluded from study. All breast lesions were evaluated in a blinded manner. A total of 226 lesions was

evaluated, including 98 (43%) malignant lesions. Visualization of lesion contrast was scored on a 4-point scale, with 4 (2%) lesions rated as below background (negative), 93 (41%) as none, 46 (20%) as moderate, and 83 (37%) as intense.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

ULTRAVIST injection is a sterile, clear, colorless to slightly yellow, odorless, pyrogen-free aqueous solution available in the following presentations:

ULTRAVIST 300 mg Iodine per mL			
Package Type	**Volume**	**Sale Unit**	**NDC**
Single-Dose Vials	50 mL	Carton of 10	50419-344-05
	100 mL	Carton of 10	50419-344-10
	125 mL	Carton of 10	50419-344-12
	150 mL	Carton of 10	50419-344-15
Pharmacy Bulk Package	200 mL	Carton of 10	50419-344-21
	500 mL	Carton of 8	50419-344-58
Imaging Bulk Package	200 mL	Carton of 10	50419-344-23
	500 mL	Carton of 8	50419-344-65
ULTRAVIST 370 mg Iodine per mL			
Package Type	**Volume**	**Sale Unit**	**NDC**
Single-Dose Vials	50 mL	Carton of 10	50419-346-05
	100 mL	Carton of 10	50419-346-10
	150 mL	Carton of 10	50419-346-15
	200 mL	Carton of 10	50419-346-20
Pharmacy Bulk Package	200 mL	Carton of 10	50419-346-26
	500 mL	Carton of 8	50419-346-58
Imaging Bulk Package	200 mL	Carton of 10	50419-346-28
	500 mL	Carton of 8	50419-346-65

Storage and Handling

Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) *[see USP Controlled Room Temperature]*. Protect from light.

17 PATIENT COUNSELING INFORMATION

Hypersensitivity Reactions

Advise the patient concerning the risk of hypersensitivity reactions that can occur both during and after ULTRAVIST administration. Advise the patient to report any signs or symptoms of hypersensitivity reactions during the procedure and to seek immediate medical attention for any signs or symptoms experienced after discharge *[see Warnings and Precautions (5.2)]*.

Advise patients to inform their physician if they develop a rash after receiving

ULTRAVIST *[see Warnings and Precautions (5.11)]*

Acute Kidney Injury

Advise the patient concerning appropriate hydration to decrease the risk of contrast induced kidney injury *[see Warnings and Precautions (5.3)].*

Extravasation

If extravasation occurs during injection, advise patients to seek medical care for progression of symptoms *[see Warnings and Precautions (5.6)].*

Thyroid Dysfunction

Advise parents/caregivers about the risk of developing thyroid dysfunction after ULTRAVIST administration. Advise parents/caregivers about when to seek medical care for their child to monitor for thyroid function *[see Warnings and Precautions (5.8)].*

Lactation

Advise lactating women that interruption of breast feeding is not necessary, however, to avoid any exposure a lactating woman may consider pumping and discarding breast milk for 12 to 24 hours after ULTRAVIST administration *[see Use in Specific Populations (8.2)]*.

Manufactured for:

Bayer HealthCare Pharmaceuticals Inc.
Whippany, NJ 07981
Manufactured in Germany

The following are representative examples of ULTRAVIST labeling. See the "How Supplied" section for a complete listing of all components.

Package/Label Display Panel 240mg Iodine per 50mL

NDC 50419-342-05 50 mL

sterile solution

Ultravist®

(brand of iopromide)

240 mgI/mL injection

Rx only

Single-dose container

Discard unused portion.

NOT FOR INTRATHECAL USE

Dose: See package insert. For intravascular use only. Each mL contains 498.72 mg iopromide with 2.42 mg tromethamine as a buffer and 0.1 mg edetate calcium disodium as a stabilizer.

Contains no antimicrobial preservative.
Protect from light.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Mfd. for:

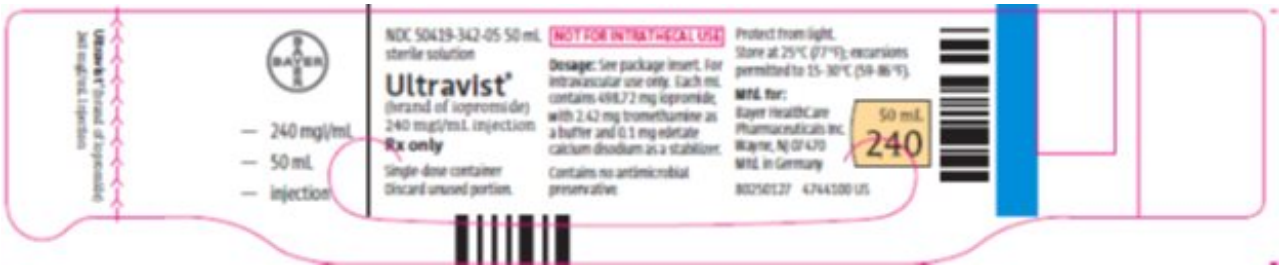
Bayer HealthCare Pharmaceuticals Inc.

Wayne, NJ 07470

Mfd in Germany

50 mL

240



Package/Label Display Panel 300 mg Iodine per 50mL

NDC 50419-344-05 50 mL

sterile solution

Ultravist®

(brand of iopromide)

300 mgI/mL injection

Rx only

Single-dose container

Discard unused portion.

NOT FOR INTRATHECAL USE

Dose: See package insert. For intravascular use only. Each mL contains 623.4 mg iopromide with 2.42 mg tromethamine as a buffer and 0.1 mg edetate calcium disodium as a stabilizer.

Contains no antimicrobial preservative.
Protect from light.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Mfd. for:

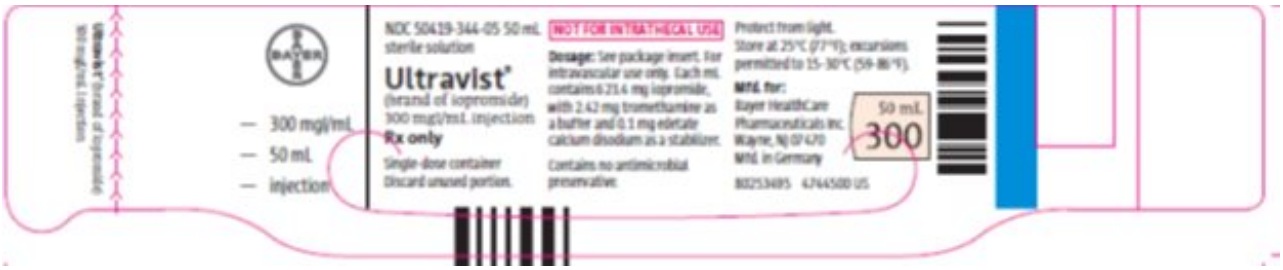
Bayer HealthCare Pharmaceuticals Inc.

Wayne, NJ 07470

Mfd in Germany

50 mL

300



Package/Label Display Panel 370 mg Iodine per 50mL

NDC 50419-346-05 50 mL

sterile solution

Ultravist®

(brand of iopromide)

370 mgI/mL injection

Rx only

Single-dose container

Discard unused portion.

NOT FOR INTRATHECAL USE

Dose: See package insert. For intravascular use only. Each mL contains 768.86 mg iopromide with 2.42 mg tromethamine as a buffer and 0.1 mg edetate calcium disodium as a stabilizer.

Contains no antimicrobial preservative.
Protect from light.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Mfd. for:

Bayer HealthCare Pharmaceuticals Inc.

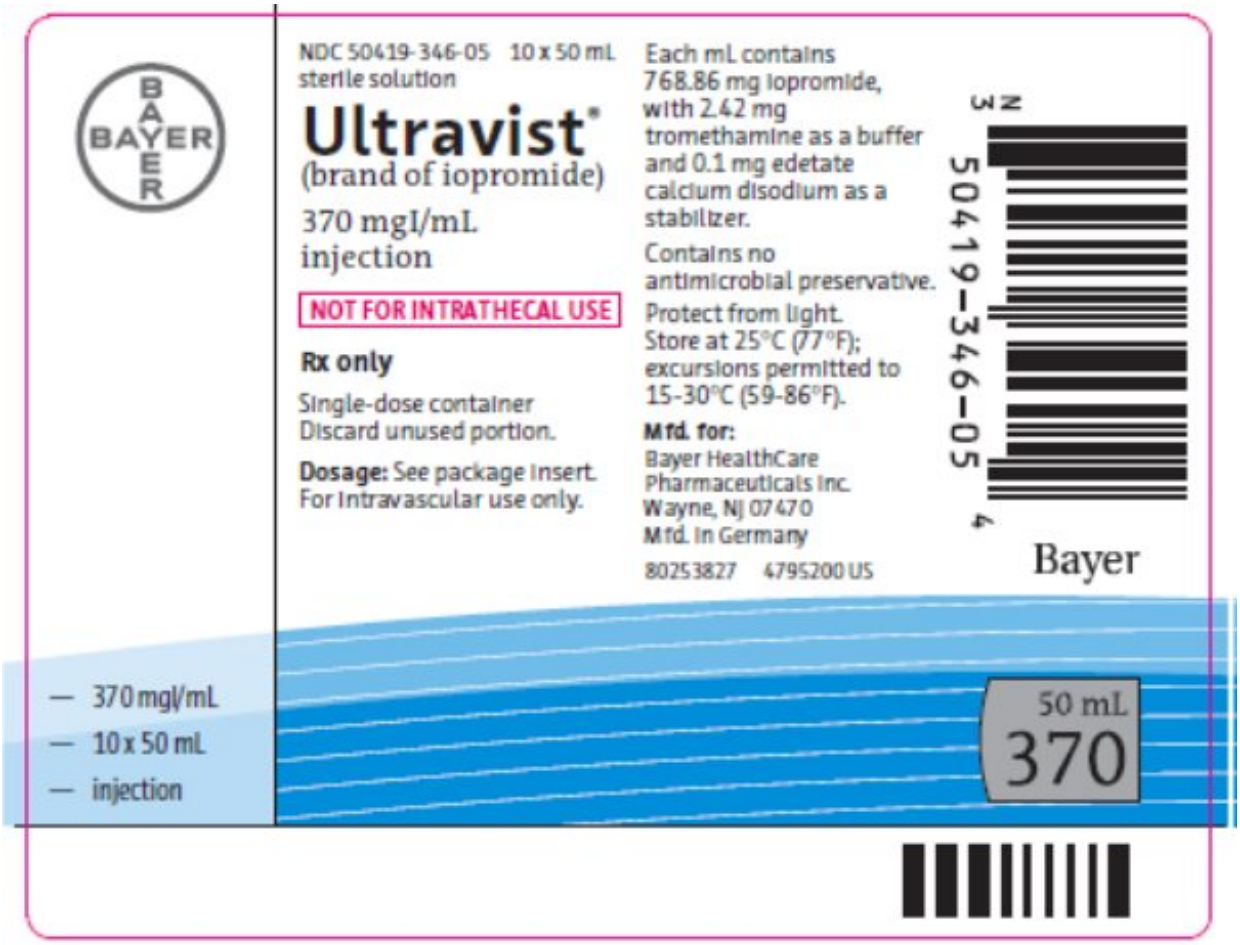
Wayne, NJ 07470

Mfd in Germany

Bayer

50 mL

370



PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

NDC 50419-342-21 200 mL

sterile solution

pharmacy bulk package

not for direct infusion

Ultravist®

(brand of iopromide)s

240 mg Iodine per mL

injection

Rx only

NOT FOR INTRATHECAL USE

Discard unused portion 10 hours after initial puncture of the container.

Dose: See package insert. For intravascular use only.

Each mL contains 498.72 mg iopromide with 2.42 mg tromethamine as a buffer and 0.1 mg edetate calcium disodium as a stabilizer.

Contains no antimicrobial preservative.

Protect from light.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Mfd. for:

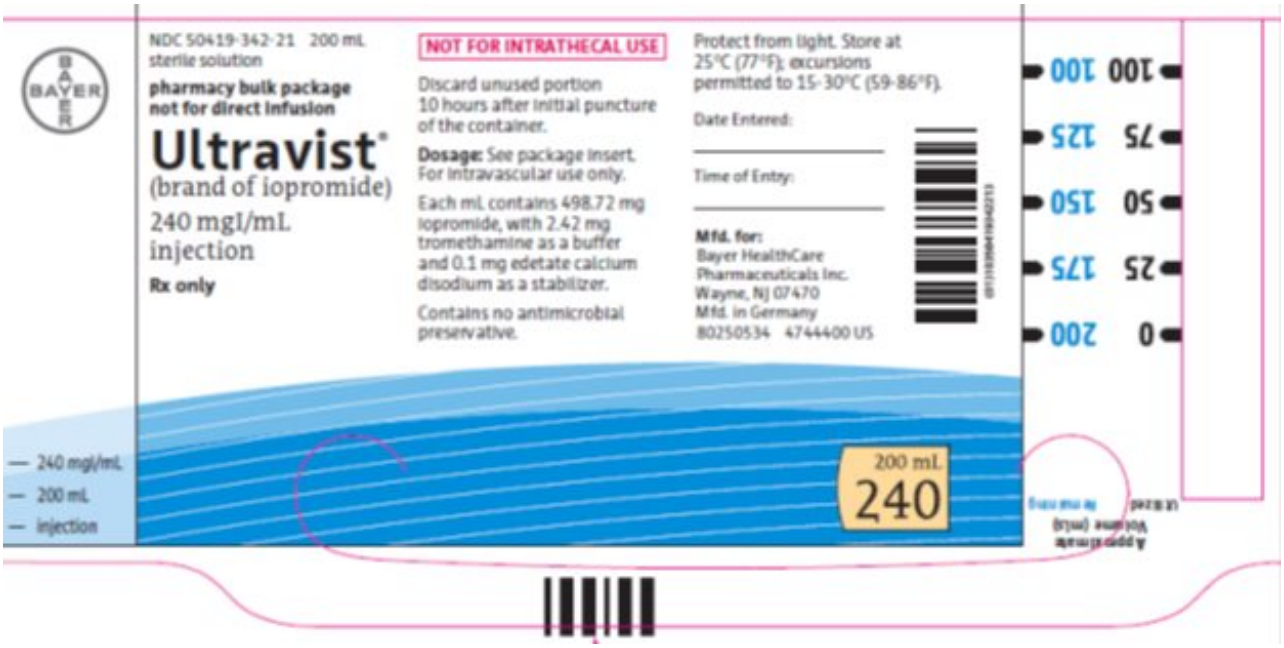
Bayer HealthCare Pharmaceuticals Inc.

Wayne, NJ 07470

Mfd in Germany

200 mL

240



PRINCIPAL DISPLAY PANEL - 500 mL Bottle Package Label

BAYER

- 300 mg Iodine per mL injection
- 8 x 500 mL each
- injection

NDC 50419-344-65
sterile solution

imaging bulk package
not for direct infusion

Ultravist®
(Iopromide)
injection

300 mg Iodine per mL

For Intravenous
Use Only

For use only with an automated contrast injection system, contrast management system, or contrast media transfer set approved or cleared for use with this contrast agent in this Imaging Bulk Package

Discard 10 hours after initial puncture.

Recommended Dosage:
See Prescribing Information.

Not For Intrathecal Use

See drug and device labeling for information on devices indicated for use with this Imaging Bulk Package and techniques to help assure safe use

Each mL contains 623.4 mg iopromide, with 2.42 mg tromethamine as a buffer, 0.1 mg edetate calcium disodium as a stabilizer, and sodium hydroxide and hydrochloric acid for pH adjustment.

Contains no antimicrobial preservative.

Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Protect from light.

Rx only

500 mL
300

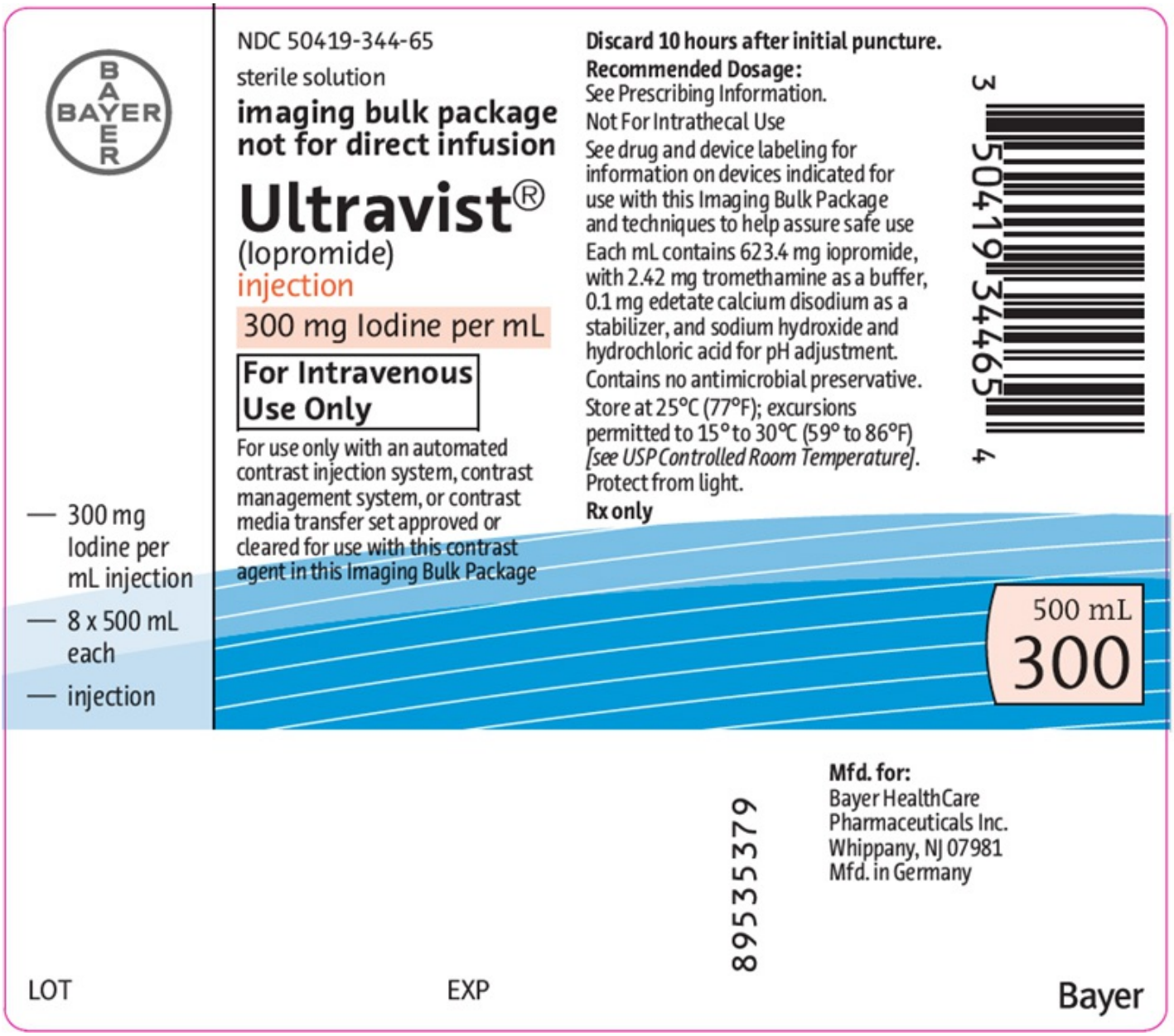
LOT

EXP

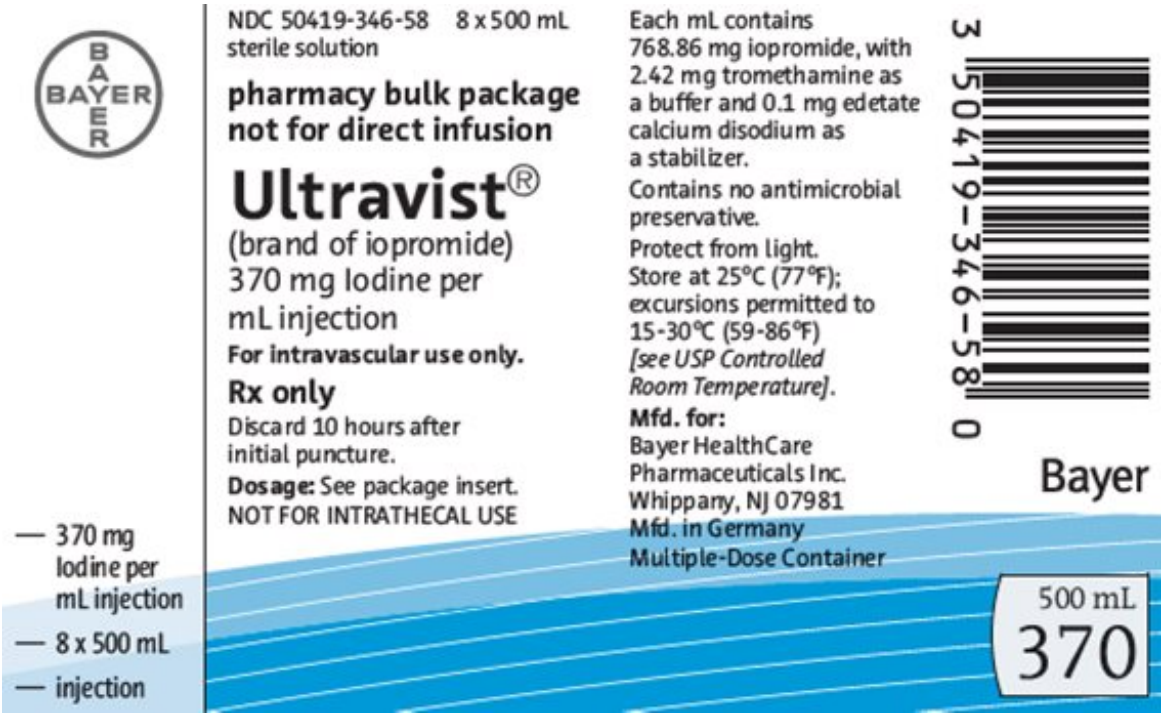
89535379

Mfd. for:
Bayer HealthCare
Pharmaceuticals Inc.
Whippany, NJ 07981
Mfd. in Germany

Bayer



PACKAGE/LABEL PRINCIPAL DISPLAY PANEL



NDC 50419-346-58 8 x 500 mL

sterile solution

Pharmacy bulk package

not for direct infusion

Ultravist®

(brand of iopromide)

370 mg Iodine per mL

injection

Rx only

ULTRAVIST

iopromide injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50419-342
Route of Administration	INTRAVENOUS, INTRA-ARTERIAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
IOPROMIDE (UNII: 712BAC33MZ) (IOPROMIDE - UNII:712BAC33MZ)	IODINE	240 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
EDETATE CALCIUM DISODIUM (UNII: 25IH6R4SGF)	
TROMETHAMINE (UNII: 023C2WHX2V)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50419-342-41	10 in 1 CARTON	12/30/2009	07/27/2017
1		50 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
2	NDC:50419-342-10	10 in 1 CARTON	12/30/2009	01/03/2021
2		100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
3	NDC:50419-342-05	10 in 1 CARTON	12/30/2009	01/03/2021
3		50 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
4	NDC:50419-342-43	10 in 1 CARTON	12/30/2009	07/27/2017
4		100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
5	NDC:50419-342-21	10 in 1 PACKAGE	12/30/2009	04/30/2020
5		200 mL in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA020220	12/30/2009	01/03/2021

ULTRAVIST

iopromide injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50419-344
Route of Administration	INTRAVENOUS, INTRA-ARTERIAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
IOPROMIDE (UNII: 712BAC33MZ) (IOPROMIDE - UNII:712BAC33MZ)	IODINE	300 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
EDETATE CALCIUM DISODIUM (UNII: 25IH6R4SGF)	
TROMETHAMINE (UNII: 023C2WHX2V)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50419-344-12	10 in 1 CARTON	12/30/2009	
1		125 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
2	NDC:50419-344-10	10 in 1 CARTON	12/30/2009	
2		100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
3	NDC:50419-344-07	10 in 1 CARTON	12/30/2009	07/27/2017
3		75 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
4	NDC:50419-344-05	10 in 1 CARTON	12/30/2009	
4		50 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
5	NDC:50419-344-41	10 in 1 CARTON	12/30/2009	07/18/2023
5		50 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
6	NDC:50419-344-43	10 in 1 CARTON	12/30/2009	07/18/2023
6		100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
7	NDC:50419-344-91	10 in 1 CARTON	10/11/2016	
7		100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
8	NDC:50419-344-15	10 in 1 CARTON	12/30/2009	
8		150 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
9	NDC:50419-344-21	10 in 1 PACKAGE	12/30/2009	
9		200 mL in 1 BOTTLE; Type 0: Not a Combination Product		
10	NDC:50419-344-48	8 in 1 PACKAGE	12/30/2009	07/18/2023
10		500 mL in 1 BOTTLE; Type 0: Not a Combination Product		
11	NDC:50419-344-97	8 in 1 PACKAGE	10/11/2016	
11		500 mL in 1 BOTTLE; Type 0: Not a Combination Product		
12	NDC:50419-	10 in 1 PACKAGE	05/04/2018	

12	344-23	10 in 1 PACKAGE	05/04/2018	
12		200 mL in 1 BOTTLE; Type 0: Not a Combination Product		
13	NDC:50419-344-65	8 in 1 PACKAGE	05/04/2018	
13		500 mL in 1 BOTTLE; Type 0: Not a Combination Product		
14	NDC:50419-344-32	8 in 1 PACKAGE	10/11/2015	
14		500 mL in 1 BOTTLE; Type 0: Not a Combination Product		
15	NDC:50419-344-58	8 in 1 PACKAGE	12/30/2009	
15		500 mL in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA020220	12/30/2009	

ULTRAVIST

iopromide injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50419-346
Route of Administration	INTRAVENOUS, INTRA-ARTERIAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
IOPROMIDE (UNII: 712BAC33MZ) (IOPROMIDE - UNII:712BAC33MZ)	IODINE	370 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
EDETATE CALCIUM DISODIUM (UNII: 25IH6R4SGF)	
TROMETHAMINE (UNII: 023C2WHX2V)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50419-346-20	10 in 1 CARTON	12/30/2009	
		200 mL in 1 VIAL, GLASS; Type 0: Not a		

1		200 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
2	NDC:50419-346-15	10 in 1 CARTON	12/30/2009	
2		150 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
3	NDC:50419-346-10	10 in 1 CARTON	12/30/2009	
3		100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
4	NDC:50419-346-07	10 in 1 CARTON	12/30/2009	07/18/2023
4		75 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
5	NDC:50419-346-05	10 in 1 CARTON	12/30/2009	
5		50 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
6	NDC:50419-346-12	10 in 1 CARTON	12/30/2009	07/27/2017
6		125 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
7	NDC:50419-346-41	10 in 1 CARTON	12/30/2009	07/18/2023
7		50 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
8	NDC:50419-346-43	10 in 1 CARTON	12/30/2009	07/18/2023
8		100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
9	NDC:50419-346-45	10 in 1 CARTON	12/30/2009	07/27/2017
9		150 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
10	NDC:50419-346-91	10 in 1 CARTON	10/11/2016	
10		100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
11	NDC:50419-346-58	8 in 1 PACKAGE	12/30/2009	
11	NDC:50419-346-33	500 mL in 1 BOTTLE; Type 0: Not a Combination Product		
12	NDC:50419-346-26	10 in 1 PACKAGE	12/30/2009	
12	NDC:50419-346-32	200 mL in 1 BOTTLE; Type 0: Not a Combination Product		
13	NDC:50419-346-97	8 in 1 PACKAGE	12/30/2009	
13		500 mL in 1 BOTTLE; Type 0: Not a Combination Product		
14	NDC:50419-346-65	8 in 1 PACKAGE	05/04/2018	
14		500 mL in 1 BOTTLE; Type 0: Not a Combination Product		
15	NDC:50419-346-28	10 in 1 PACKAGE	05/04/2018	
15		200 mL in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA020220	12/30/2009	

ULTRAVIST

iopromide injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50419-348
Route of Administration	INTRA-ARTERIAL, INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
IOPROMIDE (UNII: 712BAC33MZ) (IOPROMIDE - UNII:712BAC33MZ)	IODINE	370 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
EDETATE CALCIUM DISODIUM (UNII: 25IH6R4SGF)	
TROMETHAMINE (UNII: 023C2WHX2V)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50419-348-10	100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product	06/08/2022	
2	NDC:50419-348-11	100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product	06/08/2022	
3	NDC:50419-348-20	200 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product	06/08/2022	
4	NDC:50419-348-05	10 in 1 CARTON	06/08/2022	
4		50 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
5	NDC:50419-348-12	10 in 1 CARTON	06/08/2022	
5		100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
6	NDC:50419-348-13	10 in 1 CARTON	06/08/2022	
6		100 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		
7	NDC:50419-348-21	10 in 1 CARTON	06/08/2022	

7		200 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA020220	06/08/2022	

ULTRAVIST

iopromide injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50419-347
Route of Administration	INTRAVENOUS, INTRA-ARTERIAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
IOPROMIDE (UNII: 712BAC33MZ) (IOPROMIDE - UNII:712BAC33MZ)	IODINE	300 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
EDETATE CALCIUM DISODIUM (UNII: 25IH6R4SGF)	
TROMETHAMINE (UNII: 023C2WHX2V)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50419-347-05	50 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product	06/08/2022	
2	NDC:50419-347-20	200 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product	06/08/2022	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA020220	06/08/2022	

Labeler - Bayer HealthCare Pharmaceuticals Inc. (005436809)

Registrant - Bayer AG (315097875)

Revised: 3/2026

Bayer HealthCare Pharmaceuticals Inc.