

GE Healthcare

**OMNIPAQUE™**  
(iohexol) Injection



**300 350**

**IMAGING BULK PACKAGE**

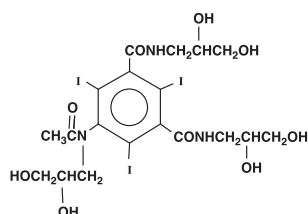
**NOT FOR INTRATHECAL USE**

**For use only with an ulrich Transfer Set iodinated contrast media transfer set or other iodinated contrast media transfer set cleared for use with this contrast agent in this Imaging Bulk Package**

**R<sub>x</sub> ONLY**

### DESCRIPTION

Iohexol, *N,N* - Bis(2,3-dihydroxypropyl)-5-[*N*-(2,3-dihydroxypropyl)-acetamido]-2,4,6- triiodoisophthalamide, is a nonionic, water-soluble radiographic contrast medium with a molecular weight of 821.14 (iodine content 46.36%). In aqueous solution each triiodinated molecule remains undissociated. The chemical structure is:



OMNIPAQUE is provided as a sterile, pyrogen-free, colorless to pale-yellow solution, in an Imaging Bulk Package, in the following iodine concentrations: 300 and 350 mg iodine/mL. An Imaging Bulk Package is used to dispense multiple single doses, utilizing a transfer set cleared for use with this contrast agent in this Imaging Bulk Package. OMNIPAQUE 300 contains 647 mg of iohexol equivalent to 300 mg of organic iodine per mL; and OMNIPAQUE 350 contains 755 mg of iohexol equivalent to 350 mg of organic iodine per mL. Each milliliter of iohexol solution contains 1.21 mg tromethamine and 0.1 mg edetate calcium disodium with the pH adjusted between 6.8 and 7.7 with hydrochloric acid or sodium hydroxide. All solutions are sterilized by autoclaving and contain no preservatives. Iohexol solution is sensitive to light and therefore should be protected from exposure. The available concentrations have the following physical properties:

Concentration (mg iodine/mL)	Osmolality* (mOsm/kg water)	Osmolarity (mOsm/L)	Absolute Viscosity (cp)			Specific Gravity
			20°C	37°C	37°C	
300	672	465	11.8	6.3	1.349	
350	844	541	20.4	10.4	1.406	

\* By vapor-pressure osmometry.

OMNIPAQUE 300 and OMNIPAQUE 350 have osmolalities from approximately 2.2 to 3 times that of plasma (285 mOsm/kg water) or cerebrospinal fluid (301 mOsm/kg water) as shown in the above table and are hypertonic under conditions of use.

### CLINICAL PHARMACOLOGY—Intravascular

Following intravascular injection, iohexol is distributed in the extracellular fluid compartment and is excreted unchanged by glomerular filtration. It will opacify those vessels in the path of flow of the contrast medium permitting radiographic visualization of the internal structures until significant hemodilution occurs. Approximately 90% or more of the injected dose is excreted within the first 24 hours, with the peak urine concentrations occurring in the first hour after administration. Plasma and urine iohexol levels indicate that the iohexol body clearance is due primarily to renal clearance. An increase in the dose from 500 mg iodine/kg to 1500 mg iodine/kg does not significantly alter the clearance of the drug. The following pharmacokinetic values were observed following the intravenous administration of iohexol (between 500 mg iodine/kg to 1500 mg iodine/kg) to 16 adult human subjects: renal clearance—120 (86-162) mL/min; total body clearance—131 (98-165) mL/min; and volume of distribution—165 (108-219) mL/kg.

Renal accumulation is sufficiently rapid that the period of maximal opacification of the renal passages may begin as early as 1 minute after intravenous injection. Urograms become apparent in about 1 to 3 minutes with optimal contrast occurring between 5 to 15 minutes.

In nephropathic conditions, particularly when excretory capacity has been altered, the rate of excretion may vary unpredictably, and opacification may be delayed

after injection.

Severe renal impairment may result in a lack of diagnostic opacification of the collecting system and, depending on the degree of renal impairment, prolonged plasma iohexol levels may be anticipated. In these patients, as well as in infants with immature kidneys, the route of excretion through the gallbladder and into the small intestine may increase.

Iohexol displays a low affinity for serum or plasma proteins and is poorly bound to serum albumin. No significant metabolism, deiodination or biotransformation occurs.

OMNIPAQUE probably crosses the placental barrier in humans by simple diffusion. It is not known to what extent iohexol is excreted in human milk. Animal studies indicate that iohexol does not cross an intact blood-brain barrier to any significant extent following intravascular administration.

OMNIPAQUE enhances computed tomographic imaging through augmentation of radiographic efficiency. The degree of density enhancement is directly related to the iodine content in an administered dose; peak iodine blood levels occur immediately following rapid intravenous injection. Blood levels fall rapidly within 5 to 10 minutes and the vascular compartment half-life is approximately 20 minutes. This can be accounted for by the dilution in the vascular and extravascular fluid compartments which causes an initial sharp fall in plasma concentration. Equilibration with the extracellular compartments is reached in about ten minutes; thereafter, the fall becomes exponential.

The pharmacokinetics of iohexol in both normal and abnormal tissue have been shown to be variable. Contrast enhancement appears to be greatest immediately after bolus administration (15 seconds to 120 seconds). Thus, greatest enhancement may be detected by a series of consecutive two-to-three second scans performed within 30 to 90 seconds after injection (ie, dynamic computed tomographic imaging). Utilization of a continuous scanning technique (ie, dynamic CT scanning) may improve enhancement and diagnostic assessment of tumor and other lesions such as abscess, occasionally revealing unsuspected or more extensive disease. For example, a cyst may be distinguished from a vascularized solid lesion when precontrast and enhanced scans are compared; the nonperfused mass shows unchanged x-ray absorption (CT number). A vascularized lesion is characterized by an increase in CT number in the few minutes after a bolus of intravascular contrast agent; it may be malignant, benign, or normal tissue, but would probably not be a cyst, hematoma, or other nonvascular lesion.

Because unenhanced scanning may provide adequate diagnostic information in the individual patient, the decision to employ contrast enhancement, which may be associated with risk and increased radiation exposure, should be based upon a careful evaluation of clinical, other radiological, and unenhanced CT findings.

### CT SCANNING OF THE HEAD

In contrast enhanced computed tomographic head imaging, OMNIPAQUE does not accumulate in normal brain tissue due to the presence of the normal blood-brain barrier. The increase in x-ray absorption in normal brain is due to the presence of contrast agent within the blood pool. A break in the blood-brain barrier such as occurs in malignant tumors of the brain allows for the accumulation of contrast medium within the interstitial tissue of the tumor. Adjacent normal brain tissue does not contain the contrast medium.

Maximum contrast enhancement in tissue frequently occurs after peak blood iodine levels are reached. A delay in maximum contrast enhancement can occur. Diagnostic contrast enhanced images of the brain have been obtained up to 1 hour after intravenous bolus administration. This delay suggests that radiographic contrast enhancement is at least in part dependent on the accumulation of iodine containing medium within the lesion and outside the blood pool, although the mechanism by which this occurs is not clear. The radiographic enhancement of nontumoral lesions, such as arteriovenous malformations and aneurysms, is probably dependent on the iodine content of the circulating blood pool.

In patients where the blood-brain barrier is known or suspected to be disrupted, the use of any radiographic contrast medium must be assessed on an individual risk to benefit basis. However, compared to ionic media, nonionic media are less toxic to the central nervous system.

### CT SCANNING OF THE BODY

In contrast enhanced computed tomographic body imaging (nonneural tissue), OMNIPAQUE diffuses rapidly from the vascular into the extravascular space. Increase in x-ray absorption is related to blood flow, concentration of the contrast medium, and extraction of the contrast medium by interstitial tissue of tumors since no barrier exists. Contrast enhancement is thus due to the relative differences in extravascular diffusion between normal and abnormal tissue, quite different from that in the brain.

### INDICATIONS AND USAGE

OMNIPAQUE (iohexol) Injection is indicated for intravenous contrast enhancement of computed tomographic (CECT) imaging of the head and body in adult and pediatric patients.

### CT SCANNING OF THE HEAD

OMNIPAQUE may be used to redefine diagnostic precision in areas of the brain which may not otherwise have been satisfactorily visualized.

### Tumors

OMNIPAQUE may be useful to investigate the presence and extent of certain malignancies such as; gliomas including malignant gliomas, glioblastomas, astrocytomas, oligodendrogliomas and gangliomas, ependymomas, medulloblastomas, meningiomas, neuromas, pinealomas, pituitary adenomas, carcinopharyngiomas, germinomas, and metastatic lesions. The usefulness of

contrast enhancement for the investigation of the retrobulbar space and in cases of low grade or infiltrative glioma has not been demonstrated. In calcified lesions, there is less likelihood of enhancement. Following therapy, tumors may show decreased or no enhancement. The opacification of the inferior vermis following contrast media administration has resulted in false-positive diagnosis in a number of otherwise normal studies.

#### Nonneoplastic Conditions

OMNIPAQUE may be beneficial in the image enhancement of nonneoplastic lesions. Cerebral infarctions of recent onset may be better visualized with contrast enhancement, while some infarctions are obscured if contrast medium is used. The use of iodinated contrast media results in enhancement in about 60 percent of cerebral infarctions studied from one to four weeks from the onset of symptoms. Sites of active infection may also be enhanced following contrast medium administration. Arteriovenous malformations and aneurysms will show contrast enhancement. For these vascular lesions the enhancement is probably dependent on the iodine content of the circulating blood pool. Hematomas and intraparenchymal bleeders seldom demonstrate contrast enhancement. However, in cases of intraparenchymal clot, for which there is no obvious clinical explanation, contrast media administration may be helpful in ruling out the possibility of associated arteriovenous malformation.

#### CT SCANNING OF THE BODY

OMNIPAQUE may be useful for enhancement of computed tomographic images for detection and evaluation of lesions in the liver, pancreas, kidneys, aorta, mediastinum, pelvis, abdominal cavity, and retroperitoneal space.

Enhancement of computed tomography with OMNIPAQUE may be of benefit in establishing diagnoses of certain lesions in these sites with greater assurance than is possible with CT alone. In other cases, the contrast agent may allow visualization of lesions not seen with CT alone (ie, tumor extension) or may help to define suspicious lesions seen with unenhanced CT (ie, pancreatic cyst).

### CONTRAINDICATIONS

OMNIPAQUE should not be administered to patients with a known hypersensitivity to iohexol.

#### WARNINGS—General

##### INTRAVASCULAR ADMINISTRATION

Nonionic iodinated contrast media inhibit blood coagulation, *in vitro*, less than ionic contrast media. Clotting has been reported when blood remains in contact with syringes containing nonionic contrast media.

Serious, fatal, thromboembolic events causing myocardial infarction and stroke have been reported with both ionic and nonionic contrast media. The use of plastic syringes in place of glass syringes has been reported to decrease but not eliminate the likelihood of *in vitro* clotting.

OMNIPAQUE should be used with extreme care in patients with severe functional disturbances of the liver and kidneys, severe thyrotoxicosis, or myelomatosis.

Diabetics with a serum creatinine level above 3 mg/dL should not be examined unless the possible benefits of the examination clearly outweigh the additional risk. OMNIPAQUE is not recommended for use in patients with anuria. Radiopaque contrast agents are potentially hazardous in patients with multiple myeloma or other paraproteinemia, particularly in those with therapeutically resistant anuria. Although neither the contrast agent nor dehydration has separately proven to be the cause of anuria in myeloma, it has been speculated that the combination of both may be causative factors.

The risk in myelomatous patients is not a contraindication; however, special precautions are necessary. Partial dehydration in the preparation of these patients prior to injection is not recommended since this may predispose the patient to precipitation of the myeloma protein in the renal tubules. No form of therapy, including dialysis, has been successful in reversing the effect. Myeloma, which occurs most commonly in persons over age 40, should be considered before instituting intravascular administration of contrast agents. Ionic contrast media, when injected intravenously or intra-arterially, may promote sickling in individuals who are homozygous for sickle cell disease.

Administration of radiopaque materials to patients known or suspected of having pheochromocytoma should be performed with extreme caution. If, in the opinion of the physician, the possible benefits of such procedures outweigh the considered risks, the procedures may be performed; however, the amount of radiopaque medium injected should be kept to an absolute minimum. The patient's blood pressure should be assessed throughout the procedure and measures for the treatment of hypertensive crisis should be readily available. Reports of thyroid storm following the use of iodinated contrast media in patients with hyperthyroidism or with an autonomously functioning thyroid nodule suggest that this additional risk be evaluated in such patients before use of any contrast medium.

**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 Omnipaque to patients with a history of a severe cutaneous adverse reaction to Omnipaque.

Urography should be performed with caution in patients with severely impaired renal function and patients with combined renal and hepatic disease.

### PRECAUTIONS

#### General

Diagnostic procedures which involve the use of radiopaque diagnostic agents should be carried out under the direction of personnel with the prerequisite training and with a thorough knowledge of the particular procedure to be performed. Appropriate facilities should be available for coping with any complication of the procedure, as well as for emergency treatment of severe reactions to the contrast agent itself. After parenteral administration of a radiopaque agent, competent personnel and emergency facilities should be available for at least 30 to 60 minutes since severe delayed reactions have occurred (see ADVERSE REACTIONS: Intravascular—General).

Preparatory dehydration is dangerous and may contribute to acute renal failure in patients with advanced vascular disease, diabetic patients, and in susceptible nondiabetic patients (often elderly with preexisting renal disease), infants and small pediatric patients. Dehydration in these patients seems to be enhanced by the osmotic diuretic action of urographic agents. It is believed that overnight fluid restriction prior to excretory urography generally does not provide better visualization in normal patients. *Patients should be well hydrated prior to and following administration of any contrast medium, including iohexol.*

Acute renal failure has been reported in diabetic patients with diabetic nephropathy and in susceptible non-diabetic patients (often elderly with preexisting renal disease). Therefore, careful consideration of the potential risks should be given before performing radiographic procedure in these patients.

The possibility of a reaction, including serious, life-threatening, fatal, anaphylactoid or cardiovascular reactions should always be considered (see ADVERSE REACTIONS: Intravascular—General). It is of utmost importance that a course of action be carefully planned in advance for immediate treatment of serious reactions, and that adequate and appropriate personnel be readily available in case of any reaction.

The possibility of an idiosyncratic reaction in susceptible patients should always be considered (see ADVERSE REACTIONS: Intravascular—General). The susceptible population includes, but is not limited to, patients with a history of a previous reaction to contrast media, patients with a known sensitivity to iodine *per se*, and patients with a known clinical hypersensitivity: bronchial asthma, hay fever, and food allergies.

The occurrence of severe idiosyncratic reactions has prompted the use of several pretesting methods. However, pretesting cannot be relied upon to predict severe reactions and may itself be hazardous for the patient. It is suggested that a thorough medical history with emphasis on allergy and hypersensitivity, prior to the injection of any contrast media, may be more accurate than pretesting in predicting potential adverse reactions.

A positive history of allergies or hypersensitivity does not arbitrarily contraindicate the use of a contrast agent where a diagnostic procedure is thought essential, but caution should be exercised (see ADVERSE REACTIONS: Intravascular—General). Premedication with antihistamines or corticosteroids in these patients should be considered. Pretreatment does not prevent serious life-threatening reactions, but may reduce both their incidence and severity.

Even though the osmolality of OMNIPAQUE is low compared to diatrizoate or iohalamate-based ionic agents of comparable iodine concentration, the potential transitory increase in the circulatory osmotic load in patients with congestive heart failure requires caution during injection. These patients should be observed for several hours following the procedure to detect delayed hemodynamic disturbances. General anesthesia may be indicated in the performance of some procedures in selected adult patients; however, a higher incidence of adverse reactions has been reported in these patients, and may be attributable to the inability of the patient to identify untoward symptoms, or to the hypotensive effect of anesthesia which can reduce cardiac output and increase the duration of exposure to the contrast agent.

#### Information for Patients

Patients receiving injectable radiopaque diagnostic agents should be instructed to:

1. Inform your physician if you are pregnant (see CLINICAL PHARMACOLOGY—Intravascular).
2. Inform your physician if you are diabetic or if you have multiple myeloma, pheochromocytoma, homozygous sickle cell disease, or known thyroid disorder (see WARNINGS).
3. Inform your physician if you are allergic to any drugs, food, or if you had any reactions to previous injections of dyes used for x-ray procedures (see PRECAUTIONS—General).
4. Inform your physician about any other medications you are currently taking, including non-prescription drugs, before you are administered this drug.
5. Advise patients to Inform their physician if they develop a rash after receiving Omnipaque.

#### Drug/Laboratory Test Interaction

If iodine-containing isotopes are to be administered for the diagnosis of thyroid disease, the iodine-binding capacity of thyroid tissue may be reduced for up to 2 weeks after contrast medium administration. Thyroid function tests which do not depend on iodine estimation, eg, T<sub>3</sub> resin uptake or direct thyroxine assays, are not affected.

Many radiopaque contrast agents are incompatible *in vitro* with some antihistamines and many other drugs; therefore, no other pharmaceuticals should

be admixed with contrast agents.

### Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed with OMNIPAQUE to evaluate carcinogenic potential. OMNIPAQUE was not genotoxic in a series of studies, including the Ames test, the mouse lymphoma TK locus forward mutation assay, and a mouse micronucleus assay. OMNIPAQUE did not impair the fertility of male or female rats when administered at dosages up to 4 g iodine/kg (2.3 times the maximum recommended dose for a 50 kg human, or approximately 0.4 times the maximum recommended dose for a 50 kg human following normalization of the data to body surface area estimates.)

### Pregnancy

#### Teratogenic Effects: Pregnancy Category B

Reproduction studies performed in rats and rabbits at dosages up to 4 g iodine/kg and 2.5 g iodine/kg, respectively (2.3 and 1.4 times the maximum recommended dose for a 50 kg human, or approximately 0.4 (rat) and 0.5 (rabbit) times the maximum recommended dose for a 50 kg human following normalization of the data to body surface area estimates) have not revealed evidence of impaired fertility or harm to the fetus due to OMNIPAQUE. Adequate and well-controlled studies in pregnant women have not been conducted. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

### Nursing Mothers

It is not known to what extent iohexol is excreted in human milk. However, many injectable contrast agents are excreted unchanged in human milk. Although it has not been established that serious adverse reactions occur in nursing infants, caution should be exercised when intravascular contrast media are administered to nursing women. Bottle feedings may be substituted for breast feedings for 24 hours following administration of OMNIPAQUE.

### Pediatric Use

Pediatric patients at higher risk of experiencing adverse events during contrast medium administration may include those having asthma, a sensitivity to medication and/or allergens, congestive heart failure, a serum creatinine greater than 1.5 mg/dL or those less than 12 months of age.

## ADVERSE REACTIONS: Intravascular—General

Serious, life-threatening and fatal reactions, mostly of cardiovascular origin, have been associated with the administration of iodine-containing contrast media, including OMNIPAQUE. The injection of contrast media is frequently associated with the sensation of warmth and pain, pain and warmth are less frequent and less severe with OMNIPAQUE than with ionic contrast media.

**Cardiovascular System:** Arrhythmias including PVCs and PACs (2%), angina/chest pain (1%), and hypotension (0.7%). Others including cardiac failure, asystole, bradycardia, tachycardia, and vasovagal reaction were reported with an individual incidence of 0.3% or less.

**Nervous System:** Vertigo (including dizziness and lightheadedness) (0.5%), pain (3%), vision abnormalities (including blurred vision and photomas) (2%), headache (2%), and taste perversion (1%). Others including anxiety, fever, motor and speech dysfunction, convulsion, paresthesia, somnolence, stiff neck, hemiparesis, syncope, shivering, transient ischemic attack, cerebral infarction, and nystagmus were reported, with an individual incidence of 0.3% or less.

**Respiratory System:** Dyspnea, rhinitis, coughing, and laryngitis, with an individual incidence of 0.2% or less.

**Gastrointestinal System:** Nausea (2%) and vomiting (0.7%). Others including diarrhea, dyspepsia, cramp, and dry mouth were reported, with an individual incidence of less than 0.1%.

**Skin and Appendages:** Urticaria (0.3%), purpura (0.1%), abscess (0.1%), and pruritus (0.1%). Individual adverse reactions which occurred to a significantly greater extent for a specific procedure are listed under that indication.

### Pediatrics

In controlled clinical trials involving 391 patients for contrast enhanced computed tomographic head imaging, adverse reactions following the use of OMNIPAQUE 300 and OMNIPAQUE 350 were generally not more frequent than with adults.

**Cardiovascular System:** Ventricular tachycardia (0.5%), 2:1 heart block (0.5%), hypertension (0.3%), and anemia (0.3%).

**Nervous System:** Pain (0.8%), fever (0.5%), taste abnormality (0.5%), and convulsion (0.3%).

**Respiratory System:** Congestion (0.3%) and apnea (0.3%).

**Gastrointestinal System:** Nausea (1%), hypoglycemia (0.3%), and vomiting (2%).

**Skin and Appendages:** Rash (0.3%).

## General Adverse Reactions to Contrast Media

Physicians should remain alert for the occurrence of adverse effects in addition to those discussed above.

The following reactions have been reported after administration of intravascular iodinated contrast media. **Reactions due to technique:** hematomas and ecchymoses. **Hemodynamic reactions:** vein cramp and thrombophlebitis following intravenous injection. **Cardiovascular reactions:** Cardiac arrhythmias, reflex tachycardia, chest pain, cyanosis, hypertension, hypotension, peripheral vasodilatation, shock, and cardiac arrest. **Renal reactions:** Transient proteinuria, oliguria or anuria. **Endocrine reactions:** Thyroid function tests indicative of hypothyroidism or transient thyroid

suppression have been uncommonly reported following iodinated contrast media administration to adult and pediatric patients, including infants. Some patients were treated for hypothyroidism. **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)). **Allergic reactions:** asthmatic attacks, nasal and conjunctival symptoms, dermal reactions such as urticaria with or without pruritus, as well as pleomorphic rashes, sneezing and lacrimation, anaphylactic reactions and anaphylactic shock. Fatalities have occurred, due to this or unknown

causes. **Signs and symptoms related to the respiratory system:** pulmonary or laryngeal edema, bronchospasm, dyspnea; or to the nervous system: restlessness, tremors, convulsions. **Other reactions:** flushing, pain, warmth, metallic taste, nausea, vomiting, anxiety, headache, confusion, pallor, weakness, sweating, localized areas of edema, especially facial cramps, neutropenia, and dizziness. Immediate or delayed rigors can occur, sometimes accompanied by hyperpyrexia. Infrequently, "iodism" (salivary gland swelling) from organic iodinated compounds appears two days after exposure and subsides by the sixth day.

In general, the reactions which are known to occur upon parenteral administration of iodinated contrast agents are possible with any nonionic agent. Severe, life-threatening, fatal anaphylactic shock has been reported. Reported incidences of death range from 6.6 per 1 million (0.00066 percent) to 1 in 10,000 (0.01 percent). Most deaths occur during injection or 5 to 10 minutes later; the main feature being cardiac arrest with cardiovascular disease as the main aggravating factor.

Adverse reactions to injectable contrast media fall into two categories: chemotoxic reactions and idiosyncratic reactions.

Chemotoxic reactions result from the physicochemical properties of the contrast media, the dose, and speed of injection. All hemodynamic disturbances and injuries to organs or vessels perfused by the contrast medium are included in this category.

Idiosyncratic reactions include all other reactions. They occur more frequently in patients 20 to 40 years old. Idiosyncratic reactions may or may not be dependent on the amount of dose injected, the speed of injection, and the radiographic procedure. Idiosyncratic reactions are subdivided into minor, intermediate, and severe. The minor reactions are self-limited and of short duration; the severe reactions are life-threatening and treatment is urgent and mandatory.

The reported incidence of adverse reactions to contrast media in patients with a history of allergy are twice that of the general population. Patients with a history of previous reactions to a contrast medium are three times more susceptible than other patients. However, sensitivity to contrast media does not appear to increase with repeated examinations.

Most adverse reactions to injectable contrast media appear within 1 to 3 minutes after the start of injection, but delayed reactions may occur.

Regardless of the contrast agent employed, the overall estimated incidence of serious adverse reactions is higher with angiocardiology than with other procedures. Cardiac decompensation, serious arrhythmias, angina pectoris, or myocardial ischemia or infarction may occur during angiocardiology and left ventriculography.

Immediately following intravascular injection of contrast medium, a transient sensation of mild warmth is not unusual. Warmth is less frequent with OMNIPAQUE than with ionic media. (see ADVERSE REACTIONS: Intravascular—General)

## OVERDOSAGE

Overdosage may occur. The adverse effects of overdosage are life-threatening and affect mainly the pulmonary and cardiovascular systems. The symptoms included: cyanosis, bradycardia, acidosis, pulmonary hemorrhage, convulsions, coma, and cardiac arrest. Treatment of an overdosage is directed toward the support of all vital functions, and prompt institution of symptomatic therapy.

The intravenous LD<sub>50</sub> values of OMNIPAQUE (in grams of iodine per kilogram body weight) are 24.2 in mice and 15 in rats.

## DOSAGE AND ADMINISTRATION

### General

As with all radiopaque contrast agents, the lowest dose of OMNIPAQUE necessary to obtain adequate visualization should be used. A lower dose may reduce the possibility of an adverse reaction. Most procedures do not require use of either the maximum volume or the highest concentration of OMNIPAQUE. The combination of volume and concentration of OMNIPAQUE to be used should be carefully individualized accounting for factors such as age, body weight, size of the vessel and the rate of blood flow within the vessel. Other factors such as 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 should be considered.

Sterile technique must be used in all vascular injections involving contrast media.

Refer to DIRECTIONS FOR PROPER USE OF OMNIPAQUE IMAGING BULK PACKAGE section for instructions.

If nondisposable equipment is used, scrupulous care should be taken to prevent residual contamination with traces of cleansing agents.

It may be desirable that solutions of radiopaque diagnostic agents be used at body temperature when injected.

Parenteral products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

Solutions of OMNIPAQUE should be used only if clear and within the normal colorless to pale yellow range. If particulate matter or discoloration is present, do not use.



## DOSAGE AND ADMINISTRATION

### General

The concentration and volume required will depend on the equipment and imaging technique used.

#### OMNIPAQUE Injection (Iohexol)

The dosage recommended for use in **adults** for contrast enhanced computed tomography is as follows:

Head Imaging by Injection:	70 mL to 150 mL (21 g Iodine to 45 g Iodine) of OMNIPAQUE 300 (300 mg Iodine/mL) 80 mL (28 g Iodine) of OMNIPAQUE 350 (350 mg Iodine/mL)
Body Imaging by Injection:	50 mL to 200 mL (15 g Iodine to 60 g Iodine) of OMNIPAQUE 300 (300 mg Iodine/mL) 60 mL to 100 mL (21 g Iodine to 35 g Iodine) of OMNIPAQUE 350 (350 mg Iodine/mL)

The dosage recommended for use in **pediatric** for contrast enhanced computed tomography is as follows OMNIPAQUE 300 (300mg Iodine/mL):

Head and body Imaging by Injection:	1mL/kg to 2mL/kg [with maximum = 3mL/kg, maximum single dose = 35g Iodine (116mL)]
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Dosage for infants and children should be administered in proportion to age and body weight.

### DIRECTIONS FOR USE

The OMNIPAQUE Imaging Bulk Package is used for dispensing multiple single doses of Iohexol injection for multiple patients using an Ulrich Transfer Set iodinated contrast media transfer set or other iodinated contrast media transfer set cleared for use with this contrast agent in this imaging bulk package. Please see drug and device labeling for information on devices indicated for use with this Imaging Bulk Package and techniques to help assure safe use.

- The OMNIPAQUE Imaging Bulk Package is to be used only in a room designated for radiological procedures that involve intravascular administration of a contrast agent.
- Transfer OMNIPAQUE from the Imaging Bulk Package utilizing aseptic technique. Prior to penetrating the container closure, swab the face of the container stopper with 70% isopropyl alcohol. The container closure may be penetrated only one time with a suitable sterile component of the iodinated contrast media transfer set cleared for use with this Imaging Bulk Package.
- Once the Imaging Bulk Package is punctured, do not remove it from the work area during the entire period of use, and 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 Imaging Bulk Package and the delivery system cannot be assured through direct continuous supervision, discard the Imaging Bulk Package and all associated disposables for the iodinated contrast media transfer set.
- A maximum time of 8 hours from initial closure entry is permitted to complete fluid transfer. Discard any unused OMNIPAQUE injection **8 hours after initial puncture** of the Imaging Bulk Package.
- Do not heat the container beyond 37°C, after the closure has been entered.

### HOW SUPPLIED

OMNIPAQUE 300

500 mL in +PLUSPAK™ (polymer bottle), boxes of 10 Imaging Bulk Packages (NDC 0407-1413-72)

OMNIPAQUE 350

500 mL in +PLUSPAK™ (polymer bottle), boxes of 10 Imaging Bulk Packages (NDC 0407-1414-72)

Protect polymer bottles of OMNIPAQUE from strong daylight and direct exposure to sunlight. Do not freeze. OMNIPAQUE should be stored at controlled room temperature, 20°-25°C (68°- 77°F); excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature].

OMNIPAQUE Injection in all presentations may be stored in a contrast media warmer for up to one month at 37°C (98.6°F).

**SPECIAL HANDLING AND STORAGE FOR POLYMER BOTTLES ONLY: DO NOT USE IF TAMPER-EVIDENT RING IS BROKEN OR MISSING.**



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