In patients with renal impairment, depending on the degree of impairment, prolonged plasma peak will continue to provide good diagnostic contrast for at least 30 minutes. Slow diffusion of the diagnostic contrast that can be achieved.

The initial concentration and volume of the medium, in conjunction with appropriate patient management (see PATIENT MANAGEMENT). Sterile technique must be used with any spinal puncture.

Intrathecal administration of corticosteroids with OMNIPAQUE is contraindicated. Because of the possibility of overdosage, immediate repeat myelography in the event of technical failure is contraindicated (see DOSAGE AND ADMINISTRATION).

### WARNINGS—General

#### SEVERE ADVERSE EVENTS - INADVERTENT INTRATHecal ADMINISTRATION

Serious adverse reactions have been reported due to the inadvertent intrathecal administration of iodinated contrast media that are not indicated for intrathecal use. These serious adverse reactions include: death, convulsions, cerebral hemorrhage, coma, paralyisis, arachnoiditis, acute renal failure, cardiac arrest, seizures, rhabdomyolysis, hypertensive encephalopathy, and brain edema. Special attention must be given to insure that OMNIPAQUE 350 is not administered intrathecally. (OMNIPAQUE 240 and OMNIPAQUE 300 are approved for intrathecal administration).

If an extremely bloody CSF is encountered, the possible benefits of a myelographic procedure should be considered in terms of the risk to the patient. Caution is advised in patients with a history of epilepsy, severe cardiovascular disease, chronic alcohoism, or multiple sclerosis. Elderly patients may present a greater risk following myelography. The need for the procedure in these patients should be evaluated carefully. Special attention must be paid to dose and concentration of the medium, hydration, and technique used. Patients who are receiving anticonvulsant medications should be maintained on this therapy. Should a seizure occur, intravenous diazepam or phenobarbital sodium is recommended. In patients with a history of seizure activity who are not on anticonvulsant therapy, premedication with anticonvulsant medication or steroids should be considered. Prophylactic anticonvulsant treatment with barbiturates should be considered in patients with evidence of inadvertent intracranial entry of a large or concentrated bolus of the contrast medium, in conjunction with appropriate patient management (see PATIENT MANAGEMENT). Direct intrathecal or ventricular administration for standard radiography (not CT) is not recommended.

In most reported cases of major motor seizures with nonionic myelographic media, one or more of the following factors were present. Therefore avoid:

- Deviations from recommended procedure or in myelographic management.

- Use in patients with a history of epilepsy.

- Overdose.

- Intracranial entry of a bolus or premature diffusion of a high concentration of the medium.

- Medication with neuroleptic drugs or phenothiazine antipsychotics.

- Failure to maintain elevation of the head during the procedure, on the stretcher, or in bed.

- Excessive and particularly rapid movement or stride.

#### 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.)

Preparatory dehydration is dangerous and may contribute to acute renal failure in patients with advanced or severe disease, diabetic patients, and in susceptible nondiabetic patients (often elderly with preexisting renal disease). Dehydration in these patients seems to be enhanced by the osmotic diuretic action of contrast agents. Patients should be well hydrated prior to and following administration of any high osmolar medium. Dehydration may be considered in advance for the immediate treatment of severe reactions, and that adequate and appropriate facilities and 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). 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 some pretreating 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 the usual pretreating in predicting potential adverse reactions. (See 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). Premedication with antihistamines or corticosteroids to avoid or minimize possible allergic reactions in such patients should be considered. Recent reports indicate that such pretreatment does not prevent serious life-threatening reactions, but may reduce both their incidence and severity.

In patients with severe renal insufficiency or failure, compensatory biliary excretion of the drug is anticipated to occur, with a slow clearance into the bile. Patients with hepatic insufficiency should not be examined unless the possibility of benefit clearly outweighs the additional risk.

Administration of contrast media should be performed by qualified personnel familiar with the procedure and appropriate patient management (see PATIENT MANAGEMENT). Sterile technique must be used with any spinal puncture.

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

Parenteral products should be inspected visually for particulate matter and discoloration prior to administration. If particulate matter or discoloration is present, do not use.

#### Preparatory Procedures:

In the clinical judgment of the physician sequential or repeat examinations are required, a suitable interval of time between administrations should be observed to allow for normal clearance of the drug from the body (see DOSAGE AND ADMINISTRATION and CLINICAL PHARMACOLOGY).
**Information for Patients or (if applicable), children:**

Patients receiving injectable radiopaque diagnostic agents should be instructed to:

1. Inform your physician if you are pregnant (see CLINICAL PHARMACOLOGY).
2. Inform your physician if you are diabetic or if you have multiple myeloma, pemphigus foliaceus, homocystic 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 or pharmacist if you are currently taking, including non-prescription drugs, before you are administered this drug.

**Drug Interactions**

Drugs which lower seizure threshold, especially phenothiazine derivatives including those used for their antipsychotic and antianxiety properties, are not recommended for use with OMNIPAQUE. Others include monoamine oxidase (MAO) inhibitors, tricyclic antidepressants, CNS stimulants, sedatives, hypnotics, or antidepressants. Such medications should be discontinued at least 48 hours before myelography, should not be used for the control of nausea or vomiting during or after myelography, and should not be used during pregnancy. OMNIPAQUE should not be used in association with multiple ionizing radiation procedures. Nonselective procedures in patients on these drugs, consider prophylactic use of anticonvulsants.

**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 4.0 g/kg (2.1 times the maximum recommended dose for a 50 kg human, or approximately 0.4 times the maximum recommended dose for 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 4.0 g/kg and 2.5 g/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 isohexal 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 intravenous or intrathecal contrast agents 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 with asthma, a sensitivity to medication and/or allergies, congestive heart failure, a serum creatinine greater than 1.5 mg/dL or those less than 12 months of age.

<table>
<thead>
<tr>
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<tr>
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**Drug** depression, hyperesthesia, visual or auditory or speech disturbances, confusion and disorientation. In addition, malaise, weakness, convulsion, EEG changes, meningismus, hyperreflexia or areflexia, hypertonia or flaccidity, hemiplegia, paralysis, quadriplegia, respiratory, tremor, echococasia, echolalia, asthenia, cerebral hemorrhage, and dysphasia have occurred. Profound mental disturbances have also rarely been reported. They have usually consisted of various degrees of additional mental confusion, disorientation, the onset is usually at 8 to 10 hours and lasts for about 24 hours, without aftereffects. However, occasionally they have been manifest as apprehension, agitation, or progressive withdrawal in several instances to the point of coma. Some of these reported cases have been accompanied by transient hearing loss or other auditory symptoms and visual disturbances (believed subjective or delusional), including unilateral or bilateral loss of vision which may last for hours. In one case, permanent cortical loss of vision has been reported in association with convulsions. Ventricular block has been reported; amnesia of varying degrees may be present for the reaction event. Rarely, persistent transient weight loss in the leg or ocular muscles has been reported. Peripheral neuropathy have been rare and transitory. They include sensory and/or motor, or nerve root disturbances, myelitis, persistent leg muscle pain or weakness, 6th nerve palsy, or cauda equina syndrome. Muscle cramps, fasciulation or myoclonia, spinal convulsion, or spastic paralysis or visual disturbances has been reported to occur in association with intrathecal use of OMNIPAQUE. In general, the reactions which are known to occur upon parenteral administration of iodinated contrast agents are possible with any nonionic agent. Approximately 95 percent of adverse reactions accompanying the use of water-soluble contrast agents are mild to moderate in degree. However, severe, life-threatening, anaphylactoid and fatal reactions, mostly of cardiovascular origin and central nervous system origin, have occurred. Adverse reactions to injectable contrast media fall into two categories: hemotoxic 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 promoted by the contrast medium are included in this category. Iodometric reactions include all other reactions. They occur more frequently in patients 20 to 40 years old. Iodometric 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 based on the situation and patient status. The reported incidence of adverse reactions to contrast media in patients with a history of allergy is twice that of the general population. Patients with a history of previous reactions to a contrast medium are three times at increased risk of adverse reactions. 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.

**OVERDOSAGE**

Clinical consequences of overdosage with OMNIPAQUE have not been reported. However, based on experience with other nonionic myelographic media, physicians should be alert to a potential increase in the frequency and severity of CNS-mediated reactions. Even use of a recommended dose can produce effects tantamount to overdosage, if incorrect management of the patient during or immediately following the procedure permits inadvertent early intracranial entry of a large volume of the medium.

The intrathecal LD50 value of OMNIPAQUE (in grams of iodine per kilogram body weight) is greater than 2.0 in mice.

**DOSAGE AND ADMINISTRATION**

The volume and concentration of OMNIPAQUE 240 or OMNIPAQUE 300 to be administered will depend on the degree and extent of contrast required in the area(s) under examination and on the equipment and technique employed.

OMNIPAQUE 240 at a concentration of 240 mg I/mL or OMNIPAQUE 300 at a concentration of 300 mg I/mL are recommended for intrathecal examination of the lumbar, thoracic, and cervical regions in adults by lumbar or direct cervical injection and is slightly hypertonic to CSF.

A total dose of 3000 mg iodine or a concentration of 300 mg I/mL should not be exceeded in adults in a single intrathecal injection. This is based on clinical trial evaluation in adults. As in all diagnostic procedures, the minimum volume and dose to produce adequate visualization should be used. Most procedures do not require either maximum dose or concentration. Administration is not necessary for patients who have had prior intravascular contrast media exposure and do not exhibit any untoward reaction (see PRECAUTIONS). Patients should be well hydrated prior to and following contrast administration. Severe-prone patients should be maintained on anticonvulsant medication.

Many radioactive contrast agents are incompatible in vivo with some antibiotics and many other drugs; therefore, concurrent drugs should not be administered with contrast agents.

**Rate of Injection:** To avoid excessive mixing with CSF and consequent dilution of contrast, injection should be made slowly over 1 to 2 minutes. Depending on the estimated volume of contrast medium which may be required for the procedure a small amount of CSF may be removed to minimize distention of the subarachnoid spaces.

The lumbar or cervical puncture needle may be removed immediately following injection since the equipment and technique employed.

**Thoracic Myelography**

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**Adverse Reactions to Contrast Media**

Physicians should remain alert for the occurrence of adverse effects in addition to those discussed above, particularly the following reactions which have been reported in the literature for other nonionic, water-soluble myelographic media, and rarely with iohexol. These have included, but are not limited to, convulsion, asceptic and bacterial meningitis, and CNS and other neurological disturbances. An asptic meningitis syndrome has been reported rarely (less than 0.01%). It was usually preceded by pronounced headaches, nausea and vomiting. The usual onset occurred about 12 to 18 hours postprocedure. Prominent features were meningitis, fever, sometimes with oculomotor signs and mental confusion. Lumbar puncture revealed a high white cell count, high protein content often with a low glucose level and with absence of organisms. The condition usually started to clear spontaneously about 10 hours after onset, with complete recovery over 2 to 3 days. Allergy or idiosyncrasy: Chills, fever, profuse diaphoresis, pruritis, urticaria, naso congestion, dyspnea, and a case of Guillain-Barre syndrome.

CNS Irritation: Mild and transitory perceptual alterations such as hallucinations, depersonalization, amnesia, hostility, amblyopia, diplopia, photophobia, psychosis, insomnia, anxiety,
The pharmacokinetics of ioxeol 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 scans within three seconds of the 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. As discussed, occasionally repeating unenhanced or unenhanced images 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 ioxeol provides scanning through 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 radiologic, 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 by normal brain is due to the presence of contrast enhancement in 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 intracellular 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 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 nonmural lesions, such as arteriomegaly, stenoses, and aneurysms, is probably dependent on the iodine content of the circulating blood pool. In instances 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 to 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 intracellular tissue barrier. Since these factors can vary significantly, 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, GENERAL—INTRAVASCULAR

OMNIPAQUE 350 is indicated in adults for angiography (venography, selective arteriography, cerebral arteriography, peripheral venography, and excretory urography). OMNIPAQUE 350 is indicated in children for angiography (venography, pulmonary arteriography, and venography), and arteriography and aortography, including the aortic root, arch, ascending and descending aorta. OMNIPAQUE 300 is indicated in adults for angiography including studies of the aortic arch, abdominal aorta and its branches, contrast enhancement for computed tomographic head and body imaging, cerebral arteriography, peripheral venography (phlebography), and excretory urography.

OMNIPAQUE 300 is indicated in children for angiography (venography, selective arteriography, cerebral arteriography, peripheral venography (phlebography), and excretory urography).

OMNIPAQUE 240 is indicated in adults for contrast enhancement for computed tomographic head imaging and peripheral venography (phlebography).

OMNIPAQUE 240 is indicated in children for contrast enhancement for computed tomographic head imaging.

CONTRAINDICATIONS

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

WARNINGS—General

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, rarely fatal, thromboembolic events causing myocardial infarction and stroke have been reported during angiographic procedures with both ionic and nonionic contrast media. Therefore, meticulous intravascular administration technique is necessary, particularly during angiography of the extremity or subclavian vessels. Daily hematocrit, platelet, and coagulation studies are recommended in patients undergoing angiography. Patients with renal insufficiency, including length of procedure, catheter and syringe material, underlying disease state, and concomitant medications may contribute to the development of thromboembolic events. For these reasons, meticulous intravascular technique is recommended including use of claw guideline and catheter manipulation, use of manifold systems and/or three-way stopcocks, frequent catheter flushing with heparinized saline solutions and minimization of the length of the procedure. The use of plastic syringes in place of glass syringes has been reported to decrease but not eliminate the likelihood of clotting.

OMNIPAQUE should be used with extreme care in patients with severe functional disturbances of heart, lung, liver, and kidneys, severe anemia, or nephrotic syndrome. Hyperlipidemia, diabetes 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.

Radiocontrast agents are potentially hazardous in patients with multiple myeloma or other paraproteinemia, particularly in those with therapeutically resistant anuria. Although neither a contrast agent nor its metabolites have been shown to be the cause of anuria, OMNIPAQUE, 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. Myelomatous patients with serum creatinine above 4.0 mg/dL, should be cared for before instituting intravenous administration of contrast agents.

Ionic contrast media, when injected intraocularly or intra-arterially, may promote killing in individuals who are homogamous for sickle cell disease.
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 does not impair the fertility of male or female rats. Histopathological examinations of the general autopsies up to 4.0 g/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 4.0 g/kg and 2.5 g/kg, respectively, revealed no evidence of harm to the human pregnant female following exposure to OMNIPAQUE. Adequate and well-controlled studies in pregnant women have not been conducted. Because animal reproduction 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

Adverse reactions following the use of OMNIPAQUE 240, OMNIPAQUE 300, and OMNIPAQUE 350 are usually of mild to moderate severity. However, 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, especially in peripheral angiography, pain and visible extravasation of contrast medium being less frequent and less severe with OMNIPAQUE than with many contrast media. Cardiotoxicity: Arhythmias including PVCs and PACs (2%), angina/cheast pain (1%), and hypotension (0.7%). Other include cardiac failure, asystole, bradycardia, tachycardia, and vasomotor reactions were reported with an individual incidence of 0.3% or less. In controlled clinical trials involving 1485 patients, one fatality occurred. A cause and effect relationship between this death and iohexol has not been established. Nervous System: Vertigo including dizziness and lightheadedness (0.5%), pain (3%), vision abnormalities (including blurred vision and photomotor (2%), headache (12%), and taste perversion (1%). Others include anxiety, fever, motor and speech dysfunction, convulsion, paresthesia, somnolence, stiffness, neck, hemiplegia, speech, aphasia, convulsion, ischemic attack, cerebral infarction, and nyctagony 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%), eczema (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 pediatric angiography, urinography, and cholecystography, the incidence of adverse reactions following the use of OMNIPAQUE 240, OMNIPAQUE 300, and OMNIPAQUE 350 were generally less 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 (0.5%). Respiratory System: Congestion (0.3%), and rhinitis (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 other intravenous iodinated contrast media, and rarely with iohexol. Reactions due to technique: hematomae and ecchymoses. Hemodynamic reactions: vein cramp and thrombophlebitis following intravenous injection. Cardiovascular reactions: rare cases of cardiac arrhythmias, reflex tachycardia, chest pain, cyanosis, hypertension, hypotension, peripheral vasodilation, shock, and cardiac arrest. Respiratory reactions: dyspnea, rhinorrhea, and coughing. Other: Diabetic reactions following the administration of OMNIPAQUE. Adverse reactions following the use of OMNIPAQUE 240, OMNIPAQUE 300, and OMNIPAQUE 350 were generally less 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 (0.5%). Respiratory System: Congestion (0.3%), and rhinitis (0.3%). Gastrointestinal System: Nausea (1%), hypoglycemia (0.3%), and vomiting (2%). Skin and Appendages: Rash (0.3%).
Chromatotoxic 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 at least equal to 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 to radiographic contrast media is less than 1%.

Cardiac decompensation, serious arrhythmias, angina pectoris, or myocardial ischemia or infarction may occur during angiography and left ventriculography. Electrocardiographic and hemodynamic abnormalities occur less frequently with OMNIPAQUE than with diatrizoate meglumine and diatrizoate sodium injection.

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, acido-osis, 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 LD₅₀ values of OMNIPAQUE (in grams of iodine per kilogram body weight) are 24.2 in mice and 15.0 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 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 pathological processes and extent of opacification required, structure or area to be examined, and 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 PHARMACY BULK PACKAGE section for instructions.

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

In children, after injection of all sites, but particularly following ventricular and pulmonary artery injections. The position of the patient and catheter tip should be carefully monitored.

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 administer.

INDIVIDUAL INDICATIONS AND USAGE

ANGIOCARDIOGRAPHY

Pharmacology—Hemodynamic Changes

OMNIPAQUE 350 at a concentration of 350 mg I/mL is indicated in adults for angiography (ventriculography, aortic root injections, and selective coronary arteriography).

OMNIPAQUE 300 at a concentration of 300 mg I/mL is indicated in children for angiocardiography. After both ventricular and coronary injection, decreases in systolic pressure were less pronounced with OMNIPAQUE 350 than with diatrizoate meglumine and diatrizoate sodium injection.

OMNIPAQUE 350 produced less Q-T interval prolongation than seen with diatrizoate meglumine and diatrizoate sodium injection.

In children, after injection of all sites, but particularly following ventricular and pulmonary artery injections, decreases in both systolic and diastolic intravascular pressure were significantly less pronounced with OMNIPAQUE 350 than with diatrizoate meglumine and diatrizoate sodium injection. In children, OMNIPAQUE 350 produced significantly less shortening of the R-R interval than seen with diatrizoate meglumine and diatrizoate sodium injection.

If repeat injections are made at rapid succession, all these changes are likely to be more pronounced. (See DOSAGE AND ADMINISTRATION.)

Precautions

During administration of large doses of OMNIPAQUE 350, continuous monitoring of vital signs is desirable. Caution is advised in the administration of large volumes to patients with incipient heart failure because of the possibility of aggravating the preexisting condition. Hypotension should be corrected promptly since it may induce serious arrhythmias.

Special care regarding dosage should be observed in patients with right ventricular failure, pulmonary hypertension, or stenotic pulmonary vascular beds because of the hemodynamic changes which may occur after injection into the right heart outflow tract. (See PRECAUTIONS— General.)

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

Cardiovascular system reactions in angiocardiography included anaphylaxis (8.5%), hypotension (12.5%), bradycardia (1.0%), and tachycardia (1.0%). (See ADVERSE REACTIONS: Intravascular—General.)

Dosage and Administration

The individual dose or volume is determined by the size of the structure to be visualized, the anticipated degree of hemodilution, and volar capacity. Weight is a minor consideration in adults, but must be considered in infants and young children. The volume of each injection is a more important consideration than the total dosage used. When large individual volumes are administered, as in ventriculography and arteriography, it has been suggested that several minutes be permitted to elapse between each injection to allow for subsidence of possible hemodynamic disturbances.

The recommended maximum total volume of OMNIPAQUE 350 for angiocardiographic procedures in adults and the recommended single injection volumes of OMNIPAQUE 350 and OMNIPAQUE 300 for angiographic procedures in children are as follows.

Pulmonary Angiography

Adults: The usual adult volume for a single injection is 40 mL with a range of 30 mL to 60 mL. This may be repeated as necessary. When combined with selective coronary arteriography, the total administered volume should not exceed 250 mL (87.5 g). Pediatrics: The usual single injection dose of OMNIPAQUE 350 is 1.25 mL/kg of body weight with a range of 1.0 mL/kg to 1.5 mL/kg. For OMNIPAQUE 300 the usual single injection dose is 1.75 mL/kg with a range of 1.5 mL/kg to 2.0 mL/kg. When multiple injections are given, the total administered dose should not exceed a total volume of 250 mL of OMNIPAQUE 350 or up to a total volume of 291 mL of OMNIPAQUE 300.

Selective Coronary Arteriography

The usual adult volume for right or left coronary arteriography is 5 mL range 3 mL to 14 mL per injection.

Aortic Root and Arch Study When Used Alone

The usual adult single injection volume is 50 mL with a range of 20 mL to 75 mL.

Pediatric Angiography

Pediatrics: The usual single injection dose is 1.0 mL/kg of OMNIPAQUE 350.

Combined Angiocardiographic Procedures

Multiple Procedures

Adults: The visualization of multiple vascular systems and target organs is possible during a single radiographic examination of the patient.

Largest doses of OMNIPAQUE 350 were well tolerated in angiographic procedures requiring multiple injections.

The maximum total volume for multiple procedures should not exceed 250 mL of 350 mg I/mL (87.5 g).

Pediatrics: Visualization of multiple vascular systems and target organs is possible during a single radiographic examination of the patient.

The maximum total dose for multiple injection procedures should not exceed 5.0 mL/kg up to a total volume of 250 mL of OMNIPAQUE 350 or 6.0 mL/kg up to a total volume of 291 mL of OMNIPAQUE 300.

ARTERIOGRAPHY AND SELECTIVE VISCERAL ARTERIOGRAPHY

OMNIPAQUE 350 at a concentration of 350 mg I/mL and OMNIPAQUE 350 at a concentration of 350 mg I/mL are indicated in adults for use in arteriography and selective visceral arteriography including studies of the aortic arch, ascending aorta, and abdominal aorta and its branches and renal, hepatic, mesenteric arteries.

OMNIPAQUE 350 at a concentration of 350 mg I/mL is indicated in children for use in arteriography including studies of the aortic root, aortic arch, and ascending aorta.

Precautions

Under conditions of slowed aortic circulation there is an increased likelihood for arteriography to cause muscle spasm. Occasional serious neurologic complications, including paraplegia, have also been reported in patients with aortoiliac obstruction, femoral artery obstruction, abdominal compression, hypotension, hypertension, spinal anesthetic, and injection of vasopressors to increase contrast. In these patients the concentration, volume and number of repeat injections of the medium should be maintained at a minimum with appropriate intervals between injections. The position of the patient and catheter tip should be carefully monitored. Entry of a large aortic dose into the renal artery may cause, even in the absence of symptoms, albuminuria, hematuria, and an elevated creatinine and urea nitrogen. Rapid and complete return of function usually follows. (See PRECAUTIONS—General.)

Adverse Reactions

See ADVERSE REACTIONS: Intravascular—General, and ADVERSE REACTIONS—ANGIOCARDIOGRAPHY.

Dosage and Administration

Adults: The usual adult volume as a single injection is 50 mL to 80 mL for the aorta, 30 mL to 60 mL for major branches including renal, celiac, mesenteric, and superior mesenteric arteries, and 5 mL to 15 mL for renal arteries. Repeated injections may be performed if indicated, but the total volume should not exceed 291 mL of OMNIPAQUE 300 or 250 mL of OMNIPAQUE 350 (87.5 g).

Pediatrics: The usual single injection dose is 1.0 mL/kg of OMNIPAQUE 350 and should not exceed 5.0 mL/kg up to a total volume of 250 mL of OMNIPAQUE 350.

CEREBRAL ARTERIOGRAPHY

OMNIPAQUE 300 at a concentration of 300 mg I/mL is indicated in adults for use in cerebral arteriography.

The degree of pain and flushing as the result of the use of OMNIPAQUE 300 in cerebral arteriography is less than that seen with comparable injections of many contrast media. In these patients the concentration, volume and number of repeat injections of the medium should be maintained at a minimum with appropriate intervals between injections. The position of the patient and catheter tip should be carefully monitored. Entry of a large aortic dose into the renal artery may cause, even in the absence of symptoms, albuminuria, hematuria, and an elevated creatinine and urea nitrogen. Rapid and complete return of function usually follows. (See PRECAUTIONS—General.)

Adverse Reactions

Cerebral arteriography should be undertaken with extreme care with special caution in elderly patients, patients in poor clinical condition, advanced arteriosclerosis, severe arterial hypertension, recent cerebral embolism or thrombosis, and cardiac decompensation.

Since the contrast medium is given by rapid injection, the patient should be monitored for possible untoward reactions. (See PRECAUTIONS—General.)
CONTRAST ENHANCED COMPUTED TOMOGRAPHY
OMNIPAQUE 240 at a concentration of 240 mg/mL and OMNIPAQUE 300 at a concentration of 300 mg/mL are indicated in adults for use in intravenous contrast enhanced computed tomographic head and body imaging by rapid injection or infusion technique.
OMNIPAQUE 260 at a concentration of 240 mg/mL and OMNIPAQUE 300 at a concentration of 300 mg/mL are indicated in children for use in intravenous contrast enhanced computed tomographic head imaging by bolus injection.

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 in the investigation and extent of certain malignancies such as gliomas including malignant gliomas, glioblastomas, astrocytomas, oligodendrogliomas and gangliogliomas, ependymomas, medulloblastomas, meningiomas, neuromas, pinealomas, pituitary adenomas, mesenchymal malignancies, teratomas, and metastatic lesions. The usefulness of contrast enhancement for the investigation of the retroorbital 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 diagnoses 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 iohexol 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 size, content of the circulating blood pool. Hematomas and intraparenchymal bleeders seldom demonstrate contrast enhancement. However, in cases of intraparenchymal clots, for which there is no obvious clinical explanation, contrast media administration may be helpful in ruling out the possibility of associated arteriogenous malformation.

CT SCANNING OF THE BODY
OMNIPAQUE may be used in the enhancement of computed tomographic images for detection and evaluation of lesions in the liver, pancreas, kidneys, medulloblastomas, kidneys, aorta, medullary cystic disease, cystic disease, and 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, and tumor extension or other may help to define suspicious lesions seen with unenhanced CT (ie, pancreatic cysts). For information regarding the use of dilute oral plus intravenous OMNIPAQUE in CT of the abdomen, see individual indications and usage—oral use.

Precautions
See precautions—oral, general.

Adverse Reactions
Immediately following intravenous injection of contrast medium, a transient sensation of mild warmth is usual, immediately following injection. This has not interfered with the procedure. In phlebography the incidence of leg pain was 21%. This usually was mild and lasted a short time after injection. See adverse reactions—oral, general.

Dosage and Administration
The volume required will depend on the size, flow rate, and disease state of the injected vessel and on the size and condition of the patient, as well as the imaging technique used. The dosage recommended for use in peripheral angiography is as follows:

Arteriovenous shunts: 10 mL to 30 mL of OMNIPAQUE 350 (350 mg/mL)
30 mL to 60 mL of OMNIPAQUE 300 (300 mg/mL)
Selective arteriograms: 10 mL to 30 mL of OMNIPAQUE 350 (350 mg/mL)
10 mL to 60 mL of OMNIPAQUE 300 (300 mg/mL)
Venography (per leg): 20 mL to 150 mL of OMNIPAQUE 240 (240 mg/mL)
40 mL to 100 mL of OMNIPAQUE 300 (300 mg/mL)

EXCRETORY UROGRAPHY
OMNIPAQUE 300 at a concentration of 300 mg/mL or OMNIPAQUE 350 at a concentration of 350 mg/mL is indicated for use in adults for excretory urography to provide diagnostic contrast of the urinary tract.

OMNIPAQUE 300 at a concentration of 300 mg/mL is indicated in children for excretory urography. See section III for information on voiding cystourethrography.

For pharmacokinetics of excretion in adults, see clinical pharmacology—intravenous.

Precautions
Preparatory dehydration is not recommended in the elderly, infants, young children, diabetic or acyanotic patients, or in patients with suspected myelomatisos.

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

Since there is a possibility of temporary suppression of urine formation, it is recommended that a sterile interval elapse before excretory urography is repeated, especially in patients with unilateral or bilateral reduction in renal function. See precautions—oral, general.

Adverse Reactions
See adverse reactions—oral, general.

Dosage and Administration
Adults: OMNIPAQUE 300 and OMNIPAQUE 350 at doses from 200 mg/kg body weight to 350 mg/kg body weight have produced diagnostic opacification of the excretory system in patients with normal renal function.

Pediatrics
Excretory Urography
OMNIPAQUE 300 at doses of 0.5 mg/kg to 3.0 mg/kg of body weight has produced diagnostic opacification of the excretory tract. The usual dose for children is 1.0 mg/kg to 1.5 mg/kg. Dosage for infants and children should be administered in proportion to age and body weight. The total administered dose should not exceed 3 mg/kg.

SECTION III
CLINICAL PHARMACOLOGY—Oral/Body Cavity Use

For most body cavities, the injected iohexol is absorbed into the surrounding tissue and eliminated by the kidneys and bowel as previously described in section II, clinical pharmacology—intravenous.

Orally administered iohexol is very poorly absorbed from the normal gastrointestinal tract. Only 0.1 to 0.5 percent of the oral dose was excreted by the kidneys. This amount may increase in the presence of bowel perfusion or bowel obstruction. Iohexol is well tolerated and readily absorbed if leakage into the peritoneal cavity occurs.

Visualization of the joint spaces, uterus, fallopian tubes, peritoneal herniations, pancreatic and bile ducts, and bladder can be accomplished by direct injection of contrast medium into the region being studied. The use of OMNIPAQUE in the intravenous indentation for contrast medium is a possible.

Precautions
Since the contrast medium is usually administered mechanically under high pressure, rupture of smaller peripheral veins can occur. It has been suggested that this can be avoided by using an intravenous catheter threaded proximally beyond larger tributaries or, in the case of the external jugular, into the superior vena cava. Sometimes the femoral vein is used. See precautions—oral, general.

Adverse Reactions
Cardiovascular system reactions in digital arteriography included transient PVCs (16%) and PACs (6.5%). See adverse reactions—intravenous, general.

Dosage and Administration
The usual injection volume of OMNIPAQUE 350 for the intravenous digital technique is 30 mL to 50 mL as a 350 mg/mL solution, which is injected as a bolus of 5 to 30 mL/second using a high pressure injector. The volume and rate of injection will depend primarily on the type of equipment and technique used.

Frequently three or more injections may be required, up to a total volume not to exceed 250 mL (87.5 g).

PERIPHERAL ANGIOGRAPHY
OMNIPAQUE 300 at a concentration of 300 mg/mL or OMNIPAQUE 350 at a concentration of 350 mg/mL is indicated in adults for use in peripheral angiography. OMNIPAQUE 240 at a concentration of 240 mg/mL or OMNIPAQUE 300 at a concentration of 300 mg/mL is indicated in adults for use in peripheral venography.

Sedative medication may be employed prior to use. Anesthesia is not considered necessary. Patient discomfort during and immediately following injection is substantially less than that following injection of various other contrast media. Moderate to severe discomfort is very unusual.

Precautions
Pulsation should be present in the artery to be injected. In thromboangiitis obliterans, or ascending infection associated with severe ischemia, angiography should be performed with extreme caution, if at al. See precautions—oral, general.

Adverse Reactions
A transient sensation of mild warmth is usual, immediately following injection. This has not interfered with the procedure.

In phlebography the incidence of leg pain was 21%. This usually was mild and lasted a short time after injection. See side effects—oral, general.

Adverse reactions—oral, general.

Dosage and Administration
The volume required will depend on the size, flow rate, and disease state of the injected vessel and on the size and condition of the patient, as well as the imaging technique used. The dosage recommended for use in peripheral angiography is as follows:

Arterial runoffs: 10 mL to 30 mL of OMNIPAQUE 350 (350 mg/mL)
30 mL to 90 mL of OMNIPAQUE 300 (300 mg/mL)
Selective arteriograms: 10 mL to 30 mL of OMNIPAQUE 350 (350 mg/mL)
10 mL to 60 mL of OMNIPAQUE 300 (300 mg/mL)
Venography (per leg): 20 mL to 150 mL of OMNIPAQUE 240 (240 mg/mL)
40 mL to 100 mL of OMNIPAQUE 300 (300 mg/mL)
INDICATIONS AND USAGE

GENERAL—Oral/Body Cavity Use

OMNIPAQUE 240, OMNIPAQUE 300, and OMNIPAQUE 350 have osmolalities from approximately 1.6 to 3.0 times that of plasma (285 mM-osm/kg water) and are hypertonic under conditions of use. Adults: OMNIPAQUE 350 is indicated in adults for arthrography and oral pass-thru examination of the gastrointestinal tract.

OMNIPAQUE 300 is indicated in adults for arthrography and hysterosalpingography. OMNIPAQUE 240 is indicated in adults for arthrography, endoscopic retrograde pancreatography and cholangiopancreatography, hemorrhage, and hysterosalpingography. OMNIPAQUE diluted to concentrations from 6 mg/mL to 9 mg/mL administered orally in conjunction with OMNIPAQUE 300 at a concentration of 300 mg/mL administered intravenously is indicated in adults for contrast enhanced computed tomography of the abdomen. Children: OMNIPAQUE 300 is indicated in children for examination of the gastrointestinal tract. OMNIPAQUE 240 is indicated in children for examination of the gastrointestinal tract. OMNIPAQUE diluted to concentrations from 50 mg/mL to 100 mg/mL is indicated in children for voiding cystourethrography.

CONTRAINdications

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

WARNINGs—General

See SEECTION II, WARNINGs—General.

PRECAUTIONs—General

SECTION II, PRECAUTIONS—General.

Orally administered hypertonic contrast media draw fluid into the intestines which, if severe enough, could result in hypovolemia. Likewise, in infants and young children, the occurrence of diarrhea may result in hypovolemia. Plasma fluid loss may be sufficient to cause a shock-like state which, if untreated, may be dangerous. This is especially pertinent to the elderly, cachectic patients of any age as well as infants and small children.

ADVERSE REACTIONS: Oral/Body Cavity Use—General

Body Cavities

In controlled clinical trials involving 285 adult patients for various body cavity examinations using OMNIPAQUE 240, 350, and 350, the following adverse reactions were reported.

Cardiovascular System

Incidence > 1%: None

Incidence ≤ 1%: Hypertension

Nervous System

Incidence > 1%: None

Incidence ≤ 1%: Headache, somnolence, fever, muscle weakness, burning, unwell feeling, tremors, lightheadedness, syncope

Recurrent System

None

Gastrointestinal System

Incidence > 1%: None

Incidence ≤ 1%: Flatulence, diarrhea, nausea, vomiting, abdominal pressure

Skin and Appendages

Incidence > 1%: Swelling (2%), heat (7%)

Incidence ≤ 1%: Hematoma at injection site

The most frequent reactions, pain and swelling, were almost exclusively reported after arthrography and were generally related to the procedure rather than the contrast medium. Gastrointestinal reactions were reported most exclusively reported after oral pass-thru examinations. For additional information on adverse reactions that may be expected with specific procedures, see INDIVIDUAL INDICATIONS AND USAGE. For information on general adverse reactions to OMNIPAQUE, see SECTION II, PRECAUTIONS—General. No adverse reactions associated with the use of OMNIPAQUE for VCU procedures were reported in 51 pediatric patients studied.

Oral Use

See INDIVIDUAL INDICATIONS AND USAGE—Oral Use—Adverse Reactions.

OVERDOSE

See also SECTION II, OVERDOSE.

The recommended dose of OMNIPAQUE 350 at a concentration of 350 mg/mL for adult oral pass-thru examination of the gastrointestinal tract is 50 mL. In a Phase I study, 150 mL of OMNIPAQUE 350 was administered orally to 11 healthy male subjects. The incidence of diarrhea was 91% (10 of 11) and abdominal cramping was 27% (3 of 11). Despite all of these events being mild and transient the occurrences were more than double that seen at the recommended doses. It is apparent from this finding that larger volumes of hypertonic contrast media, like OMNIPAQUE, increase the osmotic load in the bowel which may result in greater fluid shifts.

DOSEAGE AND ADMINISTRATION—General

See SECTION II, DOSEAGE AND ADMINISTRATION—General.

INDIVIDUAL INDICATIONS AND USAGE

Oral Use

Adults: OMNIPAQUE 350 at a concentration of 350 mg/mL is indicated in adults for use in oral pass-thru examination of the gastrointestinal tract.

OMNIPAQUE diluted to concentrations from 6 mg/mL to 9 mg/mL administered orally in conjunction with OMNIPAQUE 300 at a concentration of 300 mg/mL administered intravenously is indicated in adults for contrast enhanced computed tomography of the abdomen. Dilute oral plus intravenous OMNIPAQUE may be useful since unenhanced imaging does not provide sufficient delineation between normal loops of the bowel and adjacent organs or areas of suspected pathology.

Children: OMNIPAQUE 350 at a concentration of 300 mg/mL administered orally or rectally is indicated in children for use in examination of the gastrointestinal tract.

OMNIPAQUE 240 at a concentration of 240 mg/mL administered orally or rectally is indicated in children for use in examination of the gastrointestinal tract.

OMNIPAQUE diluted to concentrations from 9 mg/mL to 21 mg/mL administered orally in conjunction with OMNIPAQUE 240 at a concentration of 240 mg/mL or OMNIPAQUE 300 at a concentration of 300 mg/mL administered intravenously are indicated in children for use in contrast enhanced computed tomography of the abdomen.

To Achieve Add To

One Liter of Contrast Medium at A Final Concentration (mg/mL) of

Stock Concentration of OMNIPAQUE (mg/mL) Volume (mL) Water, Carbonated Beverage, Milk, or Juice (mL)

6 240 25 975
8 300 20 900
350 17 983
350 17 983
9 240 25 975
300 30 970
350 30 974
12 240 50 950
300 40 960
350 35 965
15 240 63 937
300 50 950
350 43 957
18 240 75 925
300 60 940
350 62 948
21 240 88 912
300 70 930
350 60 940

Dilutions of OMNIPAQUE should be prepared just prior to use and any unused portion discarded after the procedure.

PRECAUTIONs—General.

Adverse Reactions

Oral administration of OMNIPAQUE is associated with mild, transient diarrhea especially when high concentrations and large volumes are administered. Nausea, vomiting, and moderate diarrhea have also been reported following orally administered OMNIPAQUE, but much less frequently. For CT examinations using dilute oral and oral plus intravenous contrast medium, adverse events are more likely to be associated with the intravenous injection than the hypotonic oral solution. It should be noted that serious or anaphylactoid reactions that may occur with a vascularized iodinated solution are possible following administration by other routes.

Adults: In controlled clinical trials involving 54 adult patients for oral pass-thru examination of the gastrointestinal tract using OMNIPAQUE 350, the following adverse reactions were reported: diarrhea (42%), nausea (15%), vomiting (11%), abdominal pain (7%), flatulence (12%), and headache (2%). In controlled clinical studies involving 44 adult patients for dilute oral plus intravenous CT examination of the gastrointestinal tract using OMNIPAQUE 300, adverse reactions were limited to a single report of vomiting (2%).

Children: In controlled clinical studies involving 58 pediatric patients for examination of the gastrointestinal tract at a concentration of 300 mg/mL, the following adverse reactions were reported: diarrhea (16%), vomiting (9%), nausea (5%), fever (5%), hypotension (2%), abdominal pain (2%), and urticaria (12%). In clinical studies an increased frequency and severity of diarrhea was noted with an increase in the administered concentration and dose of the radiocontrast agent.

In controlled clinical studies involving 69 pediatric patients for dilute oral plus intravenous CT examination of the gastrointestinal tract using OMNIPAQUE 240 and OMNIPAQUE 300, adverse reactions were limited to a single report of vomiting (1.4%).

Dosage and Administration

Adults: The recommended dosage of undiluted OMNIPAQUE 350 at a concentration of 350 mg/mL for oral pass-thru examination of the gastrointestinal tract in adults is 50 mL to 100 mL depending on the nature of the examination and the size of the patient. The recommended oral dosage of OMNIPAQUE diluted to concentrations of 6 mg/mL to 9 mg/mL for contrast enhanced computed tomography of the abdomen in adults is 550 mL to 1000 mL. Smaller administered volumes are needed as the concentration of the final solution is increased (see Table below). In conjunction with dilute oral administration, the recommended dosage of OMNIPAQUE 300 intravenously is 100 mL to 150 mL.

Children: The dosage of undiluted OMNIPAQUE 300 at a concentration of 300 mg/mL, OMNIPAQUE 240 at a concentration of 240 mg/mL is dependent on the nature of the examination and the size of the patient. Based on clinical experience, it is recommended that OMNIPAQUE 180 (available in single use vials), be used in children less than 3 months of age. OMNIPAQUE 240 or OMNIPAQUE 300 may be used in children 3 months of age and older. The following dosage guidelines are recommended:

Age Volume of OMNIPAQUE

Less than 3 months 5 to 30 mL

Three months to 3 years Up to 60 mL

Four years to 10 years Up to 80 mL

Greater than 10 years Up to 100 mL

When given rectally, larger volumes may be used. The recommended oral dosage of OMNIPAQUE diluted to concentrations of 9 mg/mL to 21 mg/mL for contrast enhanced computed tomography of the abdomen in children is 180 mL to 750 mL. Smaller administered volumes are needed as the concentration of the final solution is increased (see Table below). The total oral dose in grams of iodine should generally not exceed 5 g for children under 3 years of age and 10 g for children from 3 to 18 years of age. The oral dosage may be given all at once or over a period of 30 to 45 minutes if there is difficulty in consuming the required volume.

In conjunction with dilute oral administration the recommended dosage of OMNIPAQUE 240 and OMNIPAQUE 300 is 2.0 mL/kg when administered intravenously with a range of 1.0 mL/kg to 2.0 mL/kg. Dosage for infants and children should be administered in proportion to age and body weight. The total intravenously administered dose should not exceed 3 mL/kg. The oral dose is administered about 30 to 60 minutes prior to the intravenous dose and image acquisition. OMNIPAQUE may be diluted with water or beverage as follows:
VOIDING CYSTOUROGRAPHY (VCU)
OMNIPAQUE diluted to concentrations from 50 mg/mL to 100 mg/mL is indicated in children for voiding cystourethrography. VCU are often performed in conjunction with excretory urography.

Precautions
See PRECAUTIONS—General.

Since the VCU procedure requires instrumentation, special precautions should be observed in those patients known to have an acute urinary tract infection. Filling of the bladder should be done at a steady rate, exercising caution to avoid excessive pressure. Sterile procedures are essential.

Adverse Reactions
See ADVERSE REACTIONS—General.

Dosage and Administration
OMNIPAQUE may be diluted, utilizing aseptic technique, with Sterile Water for Injection to a concentration of 50 mg/mL to 100 mg/mL for voiding cystourethrography. The concentration may vary depending upon the patient’s size and age and also with the technique and equipment used. Sufficient volume of contrast medium should be administered to adequately fill the bladder. The usual volume ranges from 50 mL to 300 mL of OMNIPAQUE at a concentration of 100 mg/mL and 50 mL to 600 mL of OMNIPAQUE at a concentration of 50 mg/mL. OMNIPAQUE may be diluted with Sterile Water for Injection as indicated in the table below.

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Final Vol (mL)</th>
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<tbody>
<tr>
<td>100 mg/mL</td>
<td>200 mL</td>
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<tr>
<td>100 mg/mL</td>
<td>250 mL</td>
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<tr>
<td>150 mg/mL</td>
<td>300 mL</td>
</tr>
<tr>
<td>200 mg/mL</td>
<td>350 mL</td>
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</tbody>
</table>

Injection of OMNIPAQUE into the joint is associated with transient discomfort, ie, pain, swelling. However, delayed, severe or persistent discomfort may occur occasionally. Severe pain may often result from undue use of pressure or the injection of large volumes. Joint swelling after the procedure.

Injection of OMNIPAQUE in hysterosalpingography is associated with immediate but transient pain. The cause of the pain may be due as much to the procedure itself as to the contrast medium injected, therefore attention should be paid to the injection pressure and volume instilled to avoid disruptive distention of the uterus and fallopian tubes. Fluoroscopic monitoring is recommended.

Nervous system: Pain (4%), somnolence and fever each with an individual incidence of 3%. Gastrointestinal system: Nausea (3%).

Adverse Reactions
Injection of OMNIPAQUE in hysterosalpingography is associated with immediate but transient pain. The cause of the pain may be due as much to the procedure itself as to the contrast medium injected, therefore attention should be paid to the injection pressure and volume instilled to avoid disruptive distention of the uterus and fallopian tubes. Fluoroscopic monitoring is recommended.

Sedation: Injection of OMNIPAQUE in ERP/ERCP is associated with transient pain. However, delayed, severe or persistent pain may occur and can persist for 24 hours. The cause of the pain may be due as much to the procedure itself as to the contrast medium injected, therefore, attention should be paid to the injection pressure and total volume injected to minimize disruptive distention of the ducts examined.

Cardiovascular system: Hypertension (1%) and arrhythmia (1%).

Nervous system: Pain (17%), somnolence (1%), and burning (1%).

Gastrointestinal system: Vomiting, diarrhea, and pressure, each with an individual incidence of 1%.

Dosage and Administration
The recommended dose of OMNIPAQUE 240 at a concentration of 240 mg/mL is 10 mL to 50 mL but may vary depending on individual anatomy and/or disease state.

HYSTEROSALPINGOGRAPHY
OMNIPAQUE 240 at a concentration of 240 mg/mL or OMNIPAQUE 300 at a concentration of 300 mg/mL is indicated in radiography of the internal group of adult female reproductive organs; ovaries, fallopian tubes, uterus, and vagina. Hysterosalpingography is utilized as a diagnostic and therapeutic modality in the treatment of infertility and other abnormal gynecological conditions.

Contraindications
The procedure should not be performed during the menstrual period or when menstrual flow is imminent, nor should it be performed when infection is present in any portion of the genital tract, including the external genitalia. The procedure is also contraindicated for pregnant women or for those in whom pregnancy is suspected. Its use is not advised for 6 months after termination of pregnancy or 30 days after conception or curettage.

Precautions
In patients with carcinoma or in those in whom the condition is suspected, caution should be exercised to avoid possible spreading of the lesion by the procedure.

Adverse Reactions
Injection of OMNIPAQUE in hysterosalpingography is associated with immediate but transient pain. The cause of the pain may be due as much to the procedure itself as to the contrast medium injected, therefore attention should be paid to the injection pressure and volume instilled to avoid disruptive distention of the uterus and fallopian tubes. Fluoroscopic monitoring is recommended.

Nervous system: Pain (4%), somnolence and fever each with an individual incidence of 3%. Gastrointestinal system: Nausea (3%).

Dosage and Administration
The recommended dose of OMNIPAQUE 240 is 15 mL to 20 mL and of OMNIPAQUE 300 is 25 mL to 20 mL but will vary depending on individual anatomy and/or disease state.

HERNIOGRAPHY
OMNIPAQUE 240 at a concentration of 240 mg/mL is indicated in adults for use in herniography.

Precautions
See PRECAUTIONS—General.

Adverse Reactions
Nervous system: Pain (7%), headache (3%), and unwell feeling (3%). Gastrointestinal system: Diarrhea (3%) and flatulence (1%).

Gastrointestinal system: Vomiting, diarrhea, and pressure, each with an individual incidence of 1%.

Dosage and Administration
The recommended dose of OMNIPAQUE 240 at a concentration of 240 mg/mL is 10 mL to 50 mL but may vary depending on individual anatomy and/or disease state.

DIRECTIONS FOR THE PROPER USE OF OMNIPAQUE

Pharmacy Bulk Package

a. The transfer of OMNIPAQUE (iohexol injection) from the Pharmacy Bulk Package is restricted to a suitable work area, such as a laminar flow hood.

b. The container closure may be penetrated only once, utilizing a suitable transfer device and aseptic technique.

c. The withdrawal of container contents should be accomplished without delay. However, should this not be possible, a maximum time of 8 hours from initial closure entry is permitted to complete fluid transfer operations. The container should not be removed from the aseptic area during the entire 8 hour period.

d. The temperature of the container should not exceed 37°C, after the closure has been entered.

HOW SUPPLIED

OMNIPAQUE 240
200 mL fill in 200 mL bottle with hanger, 240 mg/mL, boxes of 10 Pharmacy Bulk Packages (NDC 0407-1412-16)

OMNIPAQUE 300
200 mL fill in 200 mL bottle with hanger, 300 mg/mL, boxes of 10 Pharmacy Bulk Packages (NDC 0407-1413-51)

OMNIPAQUE 500 mL in PlusPak™ (polymer bottle), boxes of 10 Pharmacy Bulk Packages (NDC 0407-1413-68)

OMNIPAQUE 350
500 mL in PlusPak™ (polymer bottle), boxes of 10 Pharmacy Bulk Packages (NDC 0407-1414-98)

FEDERAL GOVERNMENT CODES
OMNIPAQUE 300
500 mL in PlusPak™ (polymer bottle), boxes of 10 Pharmacy Bulk Packages (NDC 0407-1414-94)

OMNIPAQUE 350
500 mL in PlusPak™ (polymer bottle), boxes of 10 Pharmacy Bulk Packages (NDC 0407-1414-25)

Protect glass and polymer bottles of OMNIPAQUE from direct sunlight and 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.

OMNIPAQUE (iohexol) Injection

Distributed by GE Healthcare Inc., Princeton, NJ 08540 U.S.A.
Manufactured by GE Healthcare Ireland, Cork, Ireland

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