Attached, please find the product information kit for Omnipaque™ (iohexol) Injection, a low-osmolar, iodinated contrast agent approved for oral use in adults and children for use in examination of the gastrointestinal tract.

The components of the product information kit for Omnipaque for oral use include:

• Product Overview
• Clinical Studies
• Dosing and Administration Guidelines
• Important Risk and Safety Information
• Ordering and Contact Information
• Coding and Reimbursement Information
• Material Safety Data Sheet
• Full Prescribing Information
• FDA Approval Letters for Use in Adults and Children

Note: The materials in this product information kit do not cover approved intravascular, intrathecal, or body cavity use for Omnipaque.

Please contact your local GE Healthcare Contrast Media Sales Specialist, or visit www.gehealthcare.com/omnipaque if you need additional information.

For any medical inquiries, please contact GE Healthcare Medical Affairs at 1 800 654 0118 and select option 2 followed by option 3.
Product Overview

What is Omnipaque™ (iohexol) Injection?

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:

![Chemical Structure of Iohexol](image)

For Oral Use:

Omnipaque is provided as a sterile, pyrogen-free, colorless to pale-yellow solution, in the following iodine concentrations: 180, 240, 300, and 350 mg I/mL. Omnipaque 180 contains 388 mg of iohexol equivalent to 180 mg of organic iodine per mL; Omnipaque 240 contains 518 mg of iohexol equivalent to 240 mg of organic iodine per mL; 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. Unused portions must be discarded. Iohexol solution is sensitive to light and therefore should be protected from exposure.
The available concentrations have the following physical properties:

<table>
<thead>
<tr>
<th>Concentration (mg I/mL)</th>
<th>Osmolality* (mOsm/kg water)</th>
<th>Osmolarity (mOsm/L)</th>
<th>Absolute Viscosity (cp) 20°C</th>
<th>Absolute Viscosity (cp) 37°C</th>
<th>Specific Gravity 37°C</th>
</tr>
</thead>
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<tr>
<td>180</td>
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<td>2.0</td>
<td>1.209</td>
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<tr>
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<td>520</td>
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<td>3.4</td>
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<td>20.4</td>
<td>10.4</td>
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</tr>
</tbody>
</table>

*By vapor-pressure osmometry.

**Indications and Usage – Oral Use:**

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

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

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

Omnipaque 180 at a concentration of 180 mg I/mL administered orally or rectally is indicated in children for use in examination of the gastrointestinal tract.

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

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

**Important Risk and Safety Information:**

Oral use of Omnipaque is associated with mild transient diarrhea, especially following high concentrations and volumes that may result in hypovolemia. Plasma fluid loss may be sufficient to cause a shock-like state that, if untreated, could be dangerous, especially in the elderly, cachectic patients of any age, and infants and small children.

**Clinical Pharmacology:**

For most body cavities, iohexol is absorbed into the surrounding tissue and eliminated by the kidneys and bowel. Approximately 90% or more of the administered 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 iohexol body clearance is due primarily to renal clearance.

Renal accumulation is sufficiently rapid that the period of maximal opacification of the renal passages may begin as early as 1 minute after the dose is administered. 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 administration. 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.

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 perforation or bowel obstruction. Iohexol is well tolerated and readily absorbed if leakage into the peritoneal cavity occurs.

Orally administered Omnipaque produces good visualization of the gastrointestinal tract.

Omnipaque is particularly useful when barium sulfate is contraindicated as in patients with suspected bowel perforation or those where aspiration of contrast medium is a possibility.
Clinical Studies

The following clinical abstracts are from published studies. They are not NDA clinical studies of Omnipaque™ for oral use. These results apply to the agents studied and reported in these single-center trials.


This study was a nonrandomized, observational, single-center study of radiographic quality and taste acceptance in gastrointestinal examinations, using Omnipaque at full strength (350 mg I/mL, n=4) or diluted with water (175 mg I/mL, n=29). Omnipaque was administered orally (n=14; taste acceptance reported for 11), via feeding tube (n=17), or rectally (n=2) in pediatric patients (0-14 years of age). The strengths and doses were outside those specified in approved US labeling. The concurrent dose of intravenous contrast was not specified.

In 29 examinations (age varied between one day and 14 years; 18 infants were less than one year), Omnipaque (350 mg I/mL) was diluted with equal amounts of water. In four examinations, undiluted contrast medium was used. The contrast medium was given orally in 14 examinations, by feeding tube in 17, and rectally in two examinations. The dose varied between 8 mL and 255 mL, median 40 mL. Taste acceptance was recorded in 11 examinations and described as neutral in seven and less good in four. Radiographic quality was judged as excellent in 31 and less good in two examinations. No adverse reactions and no cases of diarrhea were reported.


A nonrandomized, observational, single-center study of radiographic quality and taste acceptance in 32 consecutive gastrointestinal examinations of infants and children (13 males and 19 females, aged 31 weeks to 13 years). Contrast was administered as iohexol 350 mg I/mL diluted to 7 mg I/mL and administered orally (120 to 500 mL), via gastric tube (60 to 300 mL), or rectally (60 to 120 mL) in pediatric patients. In 25 patients, 3 mL/kg body weight of iohexol 350 mg I/mL was also administered intravenously. Taste was assessed in 20 patients and diagnostic quality, bowel enhancement, and safety in all 32. The undiluted strength and IV doses were greater than those specified in approved US labeling.

Acceptance and tolerability of the contrast medium were good. No serious adverse reactions were recorded. Visualization of the bowel was good in all cases where the amount retained was adequate, except in cases with excessive amounts of air in the bowel.

This study was a randomized, double-blind, prospective, single-center study of diagnostic quality, adverse effects, and taste in consecutive pass-through examinations for gastrointestinal obstruction in adults, using 100 mL of oral (undiluted) Omnipaque 350 mg I/mL (N=25) or sodium diatrizoate 370 mg I/mL (N=25). Patient groups were similar except for overrepresentation of women in the 50-60 and 60-70 age groups in the Omnipaque and sodium diatrizoate groups, respectively. Taste results were not reported for one patient taking Omnipaque and two patients who took sodium diatrizoate.

Fifty patients with clinical symptoms of gastrointestinal obstruction referred for enteric follow-through examination were selected. Of the 50 patients, median age was 61.5 for men and 52 for women using Omnipaque, and for those given sodium diatrizoate, the median age was 64 for men and 69 for women. No statistically significant difference was seen across contrast agent groups in overall radiographic quality of the examination. No complications were noted in this series of 50 patients. However, two patients in the sodium diatrizoate group became worse within one hour of ingestion of the contrast medium and needed laparotomy to release totally obstructing adhesive bands. No significant difference was found between the contrast media regarding taste, nausea, vomiting, or diarrhea.


This study was a double-blind, randomized, prospective, single-center study of diagnostic quality, taste, and adverse experiences for 800 mL of three oral concentrations (diluted with water to concentrations of 4.5, 6.75, and 9 mg I/mL) of Omnipaque, prepared from a 350 mg I/mL formulation in adult patients referred for abdominal computerized tomography (CT). Patient demographics were similar between groups.

The taste and the consistency of the contrast medium were recorded on a visual analogue scale of 0% (poor acceptance) to 100% (good acceptance). The contrast medium was ingested in four 200-mL portions, one every 40 minutes, during two hours prior to the CT examination. The last portion of 200 mL was taken immediately prior to examination. Patient demographics were similar between dose groups. The 4.5-mg I/mL dose is below the minimum in approved US labeling. The labeled concurrent intravenous dose of Omnipaque used was not identified.

All patients were able to drink the entire volume of contrast medium and said they would accept drinking it again. No side effects of clinical importance were reported during or after the investigation.

This study was a nonrandomized, prospective, single-center study of contrast enhancement, taste, and microbiological quality in abdominal CT with Omnipaque (7 mg I/mL, n=32; or 6 mg I/mL, n=128) diluted with water, juice, lemonade, or milk administered orally (N=142), via feeding tube (n=5), or rectally (n=19) in pediatric patients (ages 0 to 16 years). Six patients received drug both orally and rectally. Taste acceptance was recorded only for 7-mg I/mL strength. Both strengths were less than the range specified in approved labeling, and the 6-mg I/mL doses were prepared from vials of contrast left over from angiocardiography studies (stored for five days to two months). Oral dose volumes (0-1500 mL) were outside the range in approved US labeling. The concurrent dose of IV contrast was not specified.

A total of 160 consecutive pediatric patients scheduled for body CT were included in the study. Patient ages ranged from 8 days to 16 years; 79 patients were less than 5 years of age. The Omnipaque 350 mg I/mL used was diluted with a beverage of the child’s choice; milk formula was used for neonates. In the first 32 patients, the formula of Omnipaque used deviated from the formula normally used for intravenous use in not being autoclaved before use and in containing small amounts of preserving agents but not taste additives. The remaining 128 patients received 6 mg I/mL prepared from leftovers of Omnipaque 300 mg I/mL from the angiocardiographic studies conducted at the facility. Of the 142 patients given diluted contrast medium either by cup or bottle, only three patients (2.1%) refused to take the intended amount. Two patients did not take any contrast medium at all due to nausea and vomiting, and one 10-year-old refused after taking 20 mL. Among the children in the first group who received a 7-mg I/mL solution of Omnipaque, taste acceptance was registered in 20 patients, and was recorded as good in six patients, neutral in 13 patients, and less good in one patient. In the second part of the study, no attempts to register taste acceptance were made. Vomiting occurred in four (2.8%) of the patients who were given contrast medium orally. Sixty-one patients retained more than 400 mL of diluted contrast medium, and in this group there were no refusals and no noticeable side effects.
Dosing and Administration Guidelines

**Adults:** The recommended dosage of undiluted Omnipaque 350 at a concentration of 350 mg I/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 I/mL to 9 mg I/mL for contrast enhanced computed tomography of the abdomen in adults is 500 mL to 1000 mL. Smaller administered volumes are needed as the concentration of the final solution is increased. In conjunction with dilute oral administration, the recommended dosage of Omnipaque 300 administered intravenously is 100 mL to 150 mL. The oral dose is administered about 20 to 40 minutes prior to the intravenous dose and image acquisition.

**Children:** The dosage of undiluted Omnipaque 300 at a concentration of 300 mg I/mL, OMNIPAQUE 240 at a concentration of 240 mg I/mL or Omnipaque 180 at a concentration of 180 mg I/mL for oral pass-thru examination of the gastrointestinal tract in children is dependent on the nature of the examination and the size of the patient. Based on clinical experience, it is recommended that Omnipaque 180 be used in children less than 3 months of age. Omnipaque 180, Omnipaque 240 or Omnipaque 300 may be used in children 3 months of age and older. The following dosage guidelines are recommended:

<table>
<thead>
<tr>
<th>Age</th>
<th>Volume of Omnipaque</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 3 months</td>
<td>5 - 30 mL</td>
</tr>
<tr>
<td>Three months to 3 years</td>
<td>Up to 60 mL</td>
</tr>
<tr>
<td>Four years to 10 years</td>
<td>Up to 80 mL</td>
</tr>
<tr>
<td>Greater than 10 years</td>
<td>Up to 100 mL</td>
</tr>
</tbody>
</table>

When given rectally, larger volumes may be used. The recommended oral dosage of Omnipaque diluted to concentrations of 9 mg I/mL to 21 mg I/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. The total oral dose in grams of iodine should generally not exceed 5 gI for children under 3 years of age and 10 gI 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:

<table>
<thead>
<tr>
<th>To Achieve One Liter of Contrast Medium at A Final Concentration (mg/L/mL) of</th>
<th>Add</th>
<th>Stock Concentration of OMNIPAQUE (mg/L/mL)</th>
<th>Volume (mL)</th>
<th>To Water, Carbonated Beverage, Milk, or Juice (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>240</td>
<td>25</td>
<td>975</td>
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<tr>
<td>300</td>
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<tr>
<td>350</td>
<td>60</td>
<td>940</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

Please see Important Risk and Safety Information on the following page.
Important Risk and Safety Information About Omnipaque™ (iohexol) Injection

**INDICATIONS: Oral/Body Cavity Use — Adults:** Omnipaque 350 is indicated for arthrography and oral pass-through examination of the gastrointestinal (GI) tract. Omnipaque 300 is indicated for arthrography and hysterosalpingography. Omnipaque 240 is indicated for arthrography, endoscopic retrograde pancreatography and cholangiopancreatography, herniography, and hysterosalpingography. **Children:** Omnipaque 300 is indicated for examination of the gastrointestinal (GI) tract. Omnipaque 240 is indicated for examination of the GI tract. Omnipaque 180 is indicated for examination of the GI tract. Omnipaque diluted to concentrations from 50 mg/mL to 100 mg/mL is indicated for voiding cystourethrography.

**Oral/IV Use:** Oral Omnipaque diluted to concentrations from 9 mg/mL to 21 mg/mL (pediatric) or 6 mg/mL to 9 mg/mL (adult), administered orally in conjunction with Omnipaque 240 (pediatric) or 300 (pediatric and adult) administered intravenously, is indicated for use in contrast-enhanced computed tomography of the abdomen.

**CONTRAINDICATIONS:** Omnipaque should not be administered to patients with a known hypersensitivity to iohexol.

**WARNINGS — Oral/Intravascular Use:** Serious, rarely fatal, thromboembolic events causing myocardial infarction and stroke have been reported during angiographic procedures with both ionic and nonionic contrast media. Omnipaque should be used with extreme care in patients with severe functional disturbances of the liver and kidneys, severe thyrotoxicosis, or myelomatosis. Diabetic patients 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. Contrast media are potentially hazardous in patients with multiple myeloma or other paraproteinemia. Ionic contrast media, when injected intravenously or intra-arterially, may promote sickling in individuals who are homozygous for sickle cell disease. Administration of contrast to patients known or suspected of having pheochromocytoma should be performed with extreme caution, and the dose 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. Incidences of thyroid storm have been reported following the use of iodinated, ionic contrast media in patients with hyperthyroidism or with an autonomously functioning thyroid nodule. Urography should be performed with caution in patients with severely impaired renal function and in patients with combined renal and hepatic disease.

**PRECAUTIONS — General:** Patients should be well hydrated prior to and following administration of any contrast medium. The possibility of a reaction, including serious, life-threatening, fatal, anaphylactoid, cardiovascular (CV), or central nervous system reactions, should always be considered. The possibility of an idiosyncratic reaction in susceptible patients should always be considered. 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, and patients with a known clinical hypersensitivity such as bronchial asthma, hay fever, and food allergies. After parenteral administration of a contrast agent, competent personnel and emergency facilities should be available for at least 30 to 60 minutes, since severe, delayed reactions have
Renal Impairment: Use in patients with hepatorenal insufficiency only if the possibility of benefit clearly outweighs the additional risk. Diabetic Patients: Acute renal failure has been reported in diabetic patients with diabetic nephropathy and in susceptible nondiabetic patients (often elderly with preexisting renal disease) following excretory urography. Congestive Heart Failure (CHF): The potential transitory increase in the circulatory osmotic load in patients with CHF 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. Angiography should be avoided whenever possible in patients with homocystinuria, because of the risk of inducing thrombosis and embolism. Selective coronary arteriography should be performed only in those patients in whom the expected benefits outweigh the potential risk. Repeat Procedures: If 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. 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 breastfeedings 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, sensitivity to medication and/or allergens, CHF, a serum creatinine greater than 1.5 mg/dL, or those younger than 12 months of age.

ADVERSE REACTIONS — Oral Use: Is associated with mild, transient diarrhea, especially following high concentrations and volumes, which may result in hypovolemia. Plasma fluid loss may be sufficient to cause a shock-like state that, if untreated, could be dangerous, especially in the elderly, cachectic patients of any age, and infants and small children. General Reactions to Contrast Media: Serious, life-threatening, and fatal reactions, mostly of CV origin, have been associated with the administration of all iodine-containing contrast media. Aseptic meningitis syndrome has been reported rarely. Profound mental disturbances have been reported rarely, usually consisting of various forms and degrees of aphasia, mental confusion, or disorientation. The onset is usually at eight to 10 hours and lasts for about 24 hours, without aftereffects. Rarely, persistent though transitory weakness in the leg or ocular muscles has been reported. Peripheral neuropathies have been rare and transitory. In general, the reactions, which are known to occur upon parenteral administration of iodinated contrast agents, are possible with any nonionic agent. 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 more susceptible than other patients. Most adverse reactions to injectable contrast media appear within one to three minutes after the start of injection, but delayed reactions may occur. The injection of contrast media is frequently associated with the sensation of warmth and pain, especially in peripheral angiography.

Prior to Omnipaque administration, please read the Full Prescribing Information.
Ordering and Contact Information

Omnipaque is available in glass and our innovative +PLUSPAK™ (polymer) bottle packaging.

### Glass

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### +PLUSPAK™

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<tr>
<td>350 mg/mL +PLUSPAK of 200 mL</td>
<td>Y546</td>
<td>0407-1414-94</td>
</tr>
<tr>
<td>350 mg/mL +PLUSPAK of 500 mL (Pharmacy Bulk Package)</td>
<td>Y548B</td>
<td>0407-1414-98</td>
</tr>
</tbody>
</table>

To learn more about Omnipaque, please use the following resources:

- Contact your local GE Healthcare Contrast Media Sales Specialist
- Contact GE Healthcare Customer Service at 800 292 8514
- Visit www.gehealthcare.com/omnipaque
- For any medical inquiries, please contact GE Healthcare Medical Affairs at 800 654 0118 and select option 2 followed by option 3
Coding and Reimbursement Information

Medicare Coding and Payment for Contrast Agents Used in Computerized Tomography and X-ray Procedures

<table>
<thead>
<tr>
<th>Medicare Codes and Payment Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CPT®/HCPCS Code</strong></td>
</tr>
<tr>
<td>Q9965</td>
</tr>
<tr>
<td>Q9966</td>
</tr>
<tr>
<td>Q9967</td>
</tr>
</tbody>
</table>

Private insurer and Medicaid payment rates may vary and different codes may be required.

Coding and Payment Information

Under the Hospital Outpatient Prospective Payment System (HOPPS), Medicare will continue “packaging” payment for contrast imaging agents into the payment for the associated procedure.

Physicians performing diagnostic imaging procedures using contrast media should report the appropriate Healthcare Common Procedure Coding System (HCPCS) code for the product along with the appropriate Common Procedural Terminology (CPT) code(s) for the procedure(s). Physicians should select codes based on the iodine concentration used in the procedure. Volume of contrast in mL reported should be consistent with the volume of contrast in mL administered to the patient to complete the imaging study. Listed above are the applicable codes for Omnipaque.

Contrast media is separately payable in physician offices and freestanding imaging centers. Payment is based on the average sales price (ASP) + 6%. ASP rates are adjusted quarterly and are based on the prior quarter’s ASP data. The rates can be viewed on the Centers for Medicare & Medicaid Services website at: http://www.cms.gov/McrPartBDrugAvgSalesPrice/

The information referenced and provided is based on coding experience and research of current general coding practices. The existence of codes does not guarantee coverage or payment for any procedure or contrast agent by any payer. The final decision for the coding of any procedure must be made by the provider of care after considering the medical necessity of the services and supplies provided as well as the regulations and local, state, or federal laws that may apply. The coding and payment data are furnished for general informational purposes only and should not be relied upon for the purposes of determining payer coverage and coding for a specific case or claim for payment. Providers should refer to authoritative coding sources such as the CPT and HCPCS codes.

For any specific reimbursement-related inquiries, please call the GE Healthcare Reimbursement Hotline at 800 767 6664.
Omnipaque™ (iohexol) Injection

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Product Name: Omnipaque (140, 180, 240, 300 & 350 mg I/ml)

Synonyms: None

Manufacturer/Distributor: GE Healthcare, Inc.
101 Carnegie Center
Princeton, NJ 08540-9998

Technical Information No.: 800 654-0118

CHEMTREC Emergency No.: 800 424-9300 for US / 708 527-3887 outside US

2. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS No.</th>
<th>% V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iohexol</td>
<td>66108-95-0</td>
<td>&gt;25</td>
</tr>
<tr>
<td>Water</td>
<td>7732-18-5</td>
<td>&gt;25</td>
</tr>
</tbody>
</table>

3. HAZARD IDENTIFICATION

Omnipaque is a nonionic, water-soluble, radiographic contrast medium that is administered by intravascular injection in humans.

Physical & Chemical Hazard Ratings [0 = no hazard]

<table>
<thead>
<tr>
<th>NFPA: Health</th>
<th>Flammability</th>
<th>Stability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HMIS: Health</th>
<th>Flammability</th>
<th>Stability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Transportation Symbol: None

Emergency Overview: Read package insert prior to use. As part of good laboratory practice, personal hygiene and safety procedure, avoid unnecessary exposure to this substance. If exposure occurs, flush the affected area with soap and water.

Potential Health Effects: Not expected to be a health hazard via routes of entry into the body (inhalation, Ingestion, absorption or injection). No adverse effects expected upon skin or eye contact. No adverse effects expected as a result of chronic exposure.

Eyes: In case of eye contact, immediately flush eyes with water for at least 15 minutes. Call a physician if irritation develops.

Skin: Wash exposed area with soap and water. Call a physician if irritation develops.

Ingestion: No adverse effects expected. Call a physician if cramping or nausea develops.

Inhalation: No adverse effects expected, which would require first aid or other medical assistance.

Note to Physician: Treat symptomatically
Flammable Properties: Not flammable

Extinguishing Media: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Hazardous Combustion products: Carbon oxides

Explosion Data: None

Protective Equipment and Precautions for Firefighters: As in any fire, wear self-contained breathing apparatus pressure-demand. MSHA/NIOSH (approved or equivalent) and full protective gear.

SPILLS:

Since the quantity per vial is small (ml), spills can be absorbed with an inert material and discarded.

Wash the affected area with soap and water.

Ensure compliance with local, state and federal regulations.
7. HANDLING AND STORAGE

Handling: Always observe good laboratory and hygiene practices when handling. Avoid direct contact with the material. Wear appropriate protective clothing and impervious gloves.

Storage: Store in a temperature controlled room at 20 - 25º C in a tightly closed container. Do not freeze or expose to heat.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Limits: This product is considered not to be hazardous and has no occupational exposure limits (e.g. PEL, TLV, IDLH, etc.) established for it.

Engineering Measures: Eyewash station and good general room ventilation

Eye/Face Protection: Avoid contact with eyes & face use eye protection

Skin & Body Protection: Avoid contact with skin cover exposed skin

Respiratory Protection: Not required

Hygiene Measures: When using, do not eat, drink or smoke. Remove and wash contaminated clothing before re-use.
9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State: Liquid solution
Autoignition Temperature: None

Appearance: Clear to pale yellow
Flammable Limits: None

Odor: Odorless
Boiling Point: No data available

Solubility: Soluble in water
Melting Point: None

Specific Gravity: 1.1 – 1.4
Vapor Pressure (mm Hg): No data available
available

Viscosity: No data available
Evaporation Rate: No data available

pH: 6.8 – 7.7
Vapor Density: No data available

Flash Point: None

10. STABILITY AND REACTIVITY

Stability: Stable under specified conditions of use and storage.

Conditions to Avoid: Exposure to flame or temperatures <300 °F

Incompatible Products: No data available

Hazardous Decomposition Products: Iodine vapors

Hazardous Polymerization: Will not occur.
11. TOXICOLOGICAL INFORMATION

Acute Toxicity: Product does not present an acute toxicity hazard.

Carcinogenicity: No known carcinogenic effects.

Reproductive Toxicity: No known adverse reproductive effects.

Target Organ Effects: No known adverse effects to the eyes or skin.

Endocrine Disruptor Information: Does not contain known or suspected endocrine disruptors.

12. ECOLOGICAL INFORMATION

Ecotoxicity: Contains no substances known to be hazardous to the environment or that are not degradable in waste water treatment plants.

13. DISPOSAL CONSIDERATIONS

If medical waste is involved, such as blood, blood products and/or sharps (needle/syringes, glass, etc.), the waste must be handled as a biohazard and disposed of accordingly. If not a biohazard, waste OMNIPAQUE™ is considered non-hazardous. Consult local, state and federal regulations for proper disposal.

14. TRANSPORT INFORMATION

DOT: Not regulated

IATA: Not regulated

TDG: Not regulated

IMDG/IMO: Not regulated

MEX: Not regulated

RID: Not regulated

ICAO: Not regulated

ADR: Not regulated
OSHA Hazard Communication: This product is not considered hazardous under the OSHA Hazard Communication Standard (29 CFR 1910.1200) guidelines.

CERCLA Reportable Quantities: Not regulated

SARA Title III: Not regulated

CWA: Not regulated

RCRA Hazardous Waste Status: Non-hazardous (See Section 12 for details)

California Proposition 65: Not regulated

Mexico: Minimum risk, Grade = 0

Canada: WHMIS Hazard Class = Non-controlled

Issue Date: 31-Aug-07

Revision Date: 02-Jul-12

Disclaimer:

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### OMNIPAQUE™ (iohexol) Injection

**CONTRAINDICATIONS—Intrathecal**

OMNIPAQUE should not be administered to patients with a known hypersensitivity to iohexol. Myelography should not be performed in the presence of significant local or systemic infection where bacteremia is likely.

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—AND APPROPRIATE INTRAVASCULAR ADMINISTRATION**

Serious adverse reactions have been reported due to the inadvertent intravascular administration of iodinated contrast media that are not indicated for intrathecal use. These serious adverse reactions include anaphylactoid reactions, cardiovascular failure, respiratory arrest, cardiac arrest, seizures, rhabdomyolysis, hyperthermia, and brain edema. Special attention should be given to ensure that OMNIPAQUE 140 and 350 are not administered intravenously. (All other concentrations of OMNIPAQUE are approved for intravascular administration.)

If grossly 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 alcoholism, or multiple sclerosis.

Elderly patients are also presented a greater risk following myelography. The need for the procedure in these patients should be evaluated carefully. Special attention must be paid to dosage and concentration of the medium, hydration, and technique used.

**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 may occur. (See ADVERSE REACTIONS.)

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 advanced vascular disease). Dehydration in these patients seems to be enhanced by the osmotic diuretic action of contrast agents.

Substitution of the osmotic fluid lost by dehydration should be done when necessary with intravenous fluids. Overhydration in susceptible patients should be avoided. Special attention must be paid to dose and concentration of the medium, hydration, and technique used.

**INDICATIONS AND USAGE—Intrathecal**

OMNIPAQUE 180, OMNIPAQUE 240, and OMNIPAQUE 300 are indicated for intrathecal administration in adults including myelography (lumbar, thoracic, cervical, total columnal) and in contrast enhancement for computed tomography (myelography, cisternography, ventriculography).

OMNIPAQUE 180 is indicated for intrathecal administration in children including myelography (lumbar, thoracic, cervical, total columnal) and in contrast enhancement for computed tomography (myelography, cisternography).

<table>
<thead>
<tr>
<th>Concentration (mg/mL)</th>
<th>Osmolality* (mOsm/kg water)</th>
<th>Absolute Viscosity (cP)</th>
<th>Specific Gravity</th>
</tr>
</thead>
<tbody>
<tr>
<td>140</td>
<td>322</td>
<td>2.3</td>
<td>1.164</td>
</tr>
<tr>
<td>180</td>
<td>408</td>
<td>3.1</td>
<td>1.209</td>
</tr>
<tr>
<td>240</td>
<td>520</td>
<td>5.8</td>
<td>1.340</td>
</tr>
<tr>
<td>300</td>
<td>672</td>
<td>11.8</td>
<td>1.406</td>
</tr>
<tr>
<td>350</td>
<td>864</td>
<td>20.4</td>
<td>1.460</td>
</tr>
</tbody>
</table>

*By vapor-pressure osmometry.

OMNIPAQUE 140, OMNIPAQUE 180, OMNIPAQUE 240, OMNIPAQUE 300, and OMNIPAQUE 350 have osmolarities from approximately 1.1 to 3.0 times that of plasma (285 mOsm/kg water) or intravenous fluid (301 mOsm/kg water) as shown in the above table and are hypertonic under conditions of use.

### SECTION I

**CLINICAL PHARMACOLOGY—Intrathecal**

Iohexol is absorbed from cerebrospinal fluid (CSF) into the bloodstream and is eliminated by renal excretion. No significant metabolic degradation, or bioactivation, occurs.

In five adult patients receiving 16 to 18 milliliters of iohexol (180 mg/mL) by lumbar intrathecal injection, approximately 88 (72-198) percent of the injected dose was excreted in the urine within the first 24 hours after administration. The renal and body clearances were 99 (47-137) milliliters per minute. The volume of distribution was 557 (350-849) milliliters per kilogram. In one patient with a large spinal cord tumor, excretion was delayed 67 percent of the dose appeared in the urine within the first 24 hours with no difference in the total overall recovery in the urine after 48 hours. The delay in excretion appeared to be related to a decrease in the rate of transfer of iohexol from the cerebrospinal fluid to the blood (plasma maximal concentration was approximately 35 micrograms/mL).

The initial concentration and volume of the medium, in conjunction with appropriate patient manipulation, and the volume of CSF into which the medium is placed, will determine the extent of the diagnostic contrast that can be achieved.

Following intrathecal injection in conventional radiography, OMNIPAQUE 180, OMNIPAQUE 240, and OMNIPAQUE 300 will continue to provide good diagnostic contrast for at least 30 minutes. Slow excretion was delayed (67 percent of the dose appeared in the urine within the first 24 hours) with iohexol equivalent to 180 mg of organic iodine per mL. OMNIPAQUE 240 contains 518 mg of equivalent to 240 mg of organic iodine per mL. OMNIPAQUE 300 contains 647 mg of equivalent to 300 mg of organic iodine per mL, and OMNIPAQUE 350 contains 755 mg of organic iodine equivalent to 350 mg of organic iodine per mL. Each milliliter of iohexol solution contains 1.21 milligrams of tromethamine and 0.31 milligram sodium chloride 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. Unused portions must be discarded. Iohexol solution is sensitive to light and therefore should be protected from exposure.

The available concentrations have the following physical properties:

<table>
<thead>
<tr>
<th>Concentration (mg/mL)</th>
<th>Osmolality* (mOsm/kg water)</th>
<th>Absolute Viscosity (cP)</th>
<th>Specific Gravity</th>
</tr>
</thead>
<tbody>
<tr>
<td>140</td>
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</tr>
</tbody>
</table>

*By vapor-pressure osmometry.

OMNIPAQUE 140, OMNIPAQUE 180, OMNIPAQUE 240, OMNIPAQUE 300, and OMNIPAQUE 350 have osmolarities from approximately 1.1 to 3.0 times that of plasma (285 mOsm/kg water) or intravenous fluid (301 mOsm/kg water) as shown in the above table and are hypertonic under conditions of use.
The most frequently occurring adverse reaction following myelography has been headache. Other reactions occurring with an individual incidence of less than 0.7% included:

- Nausea was reported with an incidence of about 6%, and vomiting about 3%.
- Headaches may be severe or persist for days. Headaches occurring on 18% of occasions and vomiting tends to be more frequent and persistent in patients not optimally hydrated.
- Transient alterations in vital signs may occur and their significance must be assessed on an individual basis. Those reactions reported in clinical studies with OMNIPAQUE are listed below, in decreasing order of occurrence, based on clinical studies of 1513 patients.

- Headache: Most frequently occurring adverse reaction following myelography has been headache, with an incidence of approximately 18%. Headache may be caused by either a direct effect of the contrast medium or by CSF leakage at the dural puncture site. However, in managing the patient, it is important to consider whether the headache is of constitutional origin or due to postural management than attempting to control possible CSF leakage (see PATIENT MANAGEMENT).
- Nausea and Vomiting: Nausea was reported with an incidence of about 6%, and vomiting about 3% (see PATIENT MANAGEMENT). Maintaining normal hydration is very important. The use of phenothiazine antinauseants is not recommended. (See WARNINGS—General.) Reassurance to the patient that the nausea will usually cease is often all that is required.
- Dizziness: Transient dizziness was reported in about 2% of the patients.
- Other Reactions: Other reactions occurring with an individual incidence of less than 0.1% included:
  - Feeling of heaviness, hypotension, hypertension, sensation of heat, sweating, vertigo, loss of appetite, drowsiness, palpitation, paresthesia, flushing, lightheadedness, numbness, tingling, neuritis, weakness, dyspnoea, drowsiness, dizziness, and mild with no clinical sequelae.
  - Other Reactions: Other reactions occurring with an individual incidence of less than 0.7% included:
    - Fever, chills, backache, neckache, and stiffness, and neuralgia occurred following injection with an incidence of about 8%.
    - Nausea and Vomiting: Nausea was reported with an incidence of about 6%, and vomiting about 3% (see PATIENT MANAGEMENT). Maintaining normal hydration is very important. The use of phenothiazine antinauseants is not recommended. (See WARNINGS—General.) Reassurance to the patient that the nausea will usually cease is often all that is required.
- Allergy or Idiosyncrasy:
  - An aseptic meningitis syndrome has been reported rarely (less than 0.01%). It was usually preceded by headache, fever, and meningismus. No meningeal irritation or cellular pleocytosis is noted. However, in managing the patient, it is important to consider whether the headache is of constitutional origin or due to postural management than attempting to control possible CSF leakage (see PATIENT MANAGEMENT).
  - Peripheral neuropathies 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, fasciculation or myoclonus, spinal convulsion, or spasticity is unusual and has responded promptly to a small intravenous dose of diazepam.

In general, the reactions which are known to occur upon parenteral administration of iodinated contrast agents are not specific to any normal age group. Approximately, 95 per cent of adverse reactions accompanying the use of water-soluble contrast agents are mild to moderate in degree. However, severe, life-threatening, or fatal reactions, mostly of cardiovascular origin and central nervous system origin, have occurred.

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 medium, 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-limiting and of short duration; the severe reactions are life-threatening and treatable if urgent and mandatory.

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 treated with much more caution. Overdose reactions to injectable contrast media appear within 1 to 5 minutes after the start of injection, but delayed reactions may occur.

DOSE AND ADMINISTRATION — Intrathecal

The volume and concentration of OMNIPAQUE 180, 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 the procedure. The following guidelines are recommended:

**OMNIPAQUE 180 at a concentration of 180 mg/mL**: OMNIPAQUE 240 at a concentration of 240 mg/mL or OMNIPAQUE 300 at a concentration of 300 mg/mL should not be exceeding 1.25 mL for adults and a dose of 0.75 mL for children 2 to < 20 yrs old. For patients over 80 yrs old, and those less than 12 months of age, a dose of 1.0 mL should be administered.

**OMNIPAQUE 180 at a concentration of 180 mg/mL** is recommended for the examination of the lumbar, thoracic, and cervical regions in adults by lumbar or direct cervical injection and is slightly hypertonic to CSF.

**OMNIPAQUE 240 at a concentration of 180 mg/mL** is recommended for the examination of the lumbar, thoracic, and cervical regions in children by lumbar injection and is slightly hypertonic to CSF.

A total dose of 1060 mg iodine or a concentration of 300 mg/mL should not be exceeded in adults and a total dose of 2700 mg iodine or a concentration of 180 mg/mL should not be exceeded in children under 18 yrs old. All intrathecal doses should be based on contrast concentration and volume. All therapeutic procedures, the minimum volume and dose to produce adequate visualization should be used. Most procedures do not require either maximum dose or concentration.

An aseptic meningitis syndrome is rare and treatment is usually not needed (see PRECAUTIONS). Patients should be well hydrated prior to and following contrast administration. Severe, life-threatening reactions to contrast media are rare.

Many radiopaque contrast agents are incompatible in vitro with some antibacterials and many other drugs; therefore, concurrent drugs should not be physically admixed with contrast agents.

**Rate of Injection**: To avoid excessive mixing with CSF and clinical consequences of dilution, 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, the total dose of 3060 mg iodine or a concentration of 300 mg/mL may be administered by slow intrathecal injection.

**Procedure Formulations (mg/mL)**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Formulations</th>
<th>Concentration (mg/mL)</th>
<th>Volume (mL)</th>
<th>Dose (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar</td>
<td>Myelography</td>
<td>OMNIPAQUE 180</td>
<td>180</td>
<td>10-17</td>
</tr>
<tr>
<td></td>
<td>Iodovol</td>
<td>OMNIPAQUE 240</td>
<td>240</td>
<td>7-12.5</td>
</tr>
<tr>
<td>Thoracic</td>
<td>Iodovol</td>
<td>OMNIPAQUE 240</td>
<td>240</td>
<td>6-12.5</td>
</tr>
<tr>
<td></td>
<td>Iodovol</td>
<td>OMNIPAQUE 300</td>
<td>300</td>
<td>6-10</td>
</tr>
<tr>
<td>Cervical</td>
<td>Iodovol</td>
<td>OMNIPAQUE 180</td>
<td>180</td>
<td>7-10</td>
</tr>
<tr>
<td></td>
<td>Iodovol</td>
<td>OMNIPAQUE 240</td>
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</tr>
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<td></td>
<td>Iodovol</td>
<td>OMNIPAQUE 300</td>
<td>300</td>
<td>6-10</td>
</tr>
</tbody>
</table>

**Pediatrics**: The usual recommended total doses for lumbar, thoracic, cervical, and/or total columnar myelography by lumbar puncture in children are 0.36 to 2.7 g (see table below). Actual volumes administered depend largely on patient size and the following guidelines are recommended.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Formulations</th>
<th>Concentration (mg/mL)</th>
<th>Volume (mL)</th>
<th>Dose (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar</td>
<td>Myelography</td>
<td>OMNIPAQUE 180</td>
<td>180</td>
<td>8-12</td>
</tr>
<tr>
<td></td>
<td>Iodovol</td>
<td>OMNIPAQUE 240</td>
<td>240</td>
<td>5-10</td>
</tr>
<tr>
<td></td>
<td>Iodovol</td>
<td>OMNIPAQUE 300</td>
<td>300</td>
<td>6-10</td>
</tr>
</tbody>
</table>

Withdrawal of contrast agents from their containers should be accomplished under aseptic conditions. Storage at room temperature and expiration date prior to administration. If particulate matter or discoloration is present, do not use.

**Repeat Procedures**: If 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. An interval of at least 48 hours should be allowed before repeat examination; however, whenever possible, 5 to 7 days is recommended.
of contrast medium into the intestinal 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, at which maximum osmotic pressure by the contrast medium would be at a maximum. Maximum osmotic pressure images of the brain have been obtained up to 1 hour after intravenous bolus administration. This delay is necessary for contrast radiographic images. 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 nonvascular lesions is not attributable to the difference in iodine content of the circulating blood pool.

In patients where the blood tumor barrier is known or suspected to be disrupted, the use of any intravascular 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.

**INDICATIONS AND USAGE, GENERAL—Intravascular**

OMNIPAQUE 350 is indicated in adults for angiography (intracranial, selective coronary arteriography, aortography, including studies of the aortic arch, aortic arch, ascending aorta, and its branches, contrast enhancement for computed tomographic head and body imaging, cerebral arteriography, peripheral arteriography, and excretory urography).

OMNIPAQUE 350 is indicated in children for angiography (intracranial, pulmonary arteriography, and venography; studies of the collateral arteries and arterioles, including the aorta, vascular, and its branches, contrast enhancement for computed tomographic head and body imaging). OMNIPAQUE 300 is indicated in adults for angiography involving the use of radiopaque diagnostic agents should be carried out only as necessary.

**CONTRAINDICATIONS**

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

**WARNINGS—General**

Nonionic iohexol contrast media exhibit blood opacification, in vitro, less than iohexol contrast media. Clotting has been reported when blood remains in contact with syringes containing nonionic contrast media. Urinary, 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 angiographic procedures, to minimize thrombomembolic events. For these reasons, meticulous angiographic techniques are recommended including close attention to guidewire and catheter manipulation, use of manifold systems and/or three-way stopcocks, frequent catheter flushing with heparin saline and minimizing 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 in vitro clotting.

OMNIPAQUE should be used with extreme caution in patients with severe functional disturbances of the liver, such as severe protheyrotoxicosis, idiopathic familial hyperlipoproteinemia, severe renal impairment, 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 should be considered. Iohexol displays a low affinity for serum or plasma proteins and is poorly bound to serum albumin. No significant protein binding, distribution, or biotransformation occurs.

**CLINICAL PHARMACOLOGY—Intravascular**

OMNIPAQUE 350 is indicated in adults for angiocardiography (ventriculography, selective coronary arteriography, aortography, including studies of the aortic arch, abdominal aorta and its branches, contrast enhancement for computed tomographic head and body imaging, cerebral arteriography, peripheral arteriography, and excretory urography).

OMNIPAQUE 300 is indicated in children for angiography (intracranial, pulmonary arteriography, and venography; studies of the collateral arteries and arterioles, including the aorta, vascular, and its branches, contrast enhancement for computed tomographic head and body imaging)
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 media are included in this category.

Idiosyncratic reactions include all other reactions to contrast media, and rarely with iohexol.

Adverse reactions to injectable contrast media appear within 1 to 3 minutes after the start of injection. The severity of the reaction is related to the rate of injection, and the radiographic procedure. Idiosyncratic reactions are subdivided into allergic and nonallergic reactions.

Allergic reactions:
- Rash (0.3%), urticaria, vasculitis, angioedema, diffuse urticaria, serum sickness, eczematoid eruption, urticarial vasculitis, erythema multiforme, psoriasis, vasculitis, and, rarely, anaphylactic reactions. Rarely, angioedema followed by urticaria has been reported.
- Hypersensitivity to iodine: symptoms of shock are usually experienced within 1 to 3 minutes after the start of injection. Only occasionally does the onset of shock occur after 6 hours. The shock may be attributable to the inability of the patient to identify untoward symptoms, or to the hypotensive effect of anesthetic that can reduce cardiac output and increase the duration of exposure to the contrast media.

Nonallergic reactions:
- Pain (0.8%), fever (0.5%), taste abnormality (0.5%), and convulsion (0.3%).
- Nausea (1%), hypoglycemia (0.3%), and vomiting (2%).
- Pain (0.8%), fever (0.5%), taste abnormality (0.5%), and convulsion (0.3%).
**CEREBRAL ARTERIOGRAPHY**

OMNIPAQUE 300 at a concentration of 300 mg/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 cerebral arteriography, patients should be appropriately prepared consistent with existing or suspected disease states.

**Precautions**

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.)

**Adverse Reactions**

Cerebral arteriography with water soluble contrast media has been associated with temporary neurologic complications including seizures, drowsiness, transient paresis, and mild disturbances in vision such as photomas of 1-second or less duration.

Central nervous system complications included photomas (15%), headache (5.5%), and pain (4.3%). (See ADVERSE REACTIONS: Intravascular—General.)

**Dosage and Administration**

OMNIPAQUE 300 is recommended for cerebral arteriography at the following volumes: common carotid artery (6 mL to 12 mL), internal carotid artery (8 mL to 10 mL), external carotid artery (6 mL to 9 mL), and vertebral artery (6 mL to 10 mL).

**CONTRAST ENHANCED COMPUTED TOMOGRAPHY**

OMNIPAQUE 240 at a concentration of 240 mg/mL, OMNIPAQUE 300 at a concentration of 300 mg/mL, and OMNIPAQUE 350 at a concentration of 350 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 240 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 rapid bolus injection technique.

**CT SCANNING OF THE HEAD**

OMNIPAQUE may be used to redefine diagnostic precision in the brain which may otherwise have been satisfactorily visualized.

**Tumors**

OMNIPAQUE may be useful in investigating the presence and extent of certain malignancies such as gliomas including malignant gliomas, glialastomas, astrocytomas, oligodendrogliomas and gangliogliomas, medulloblastomas, meningiomas, neuromas, neurinomas, paragangliomas, adenomas, carcinomas, germinomas, and metastatic lesions. The usefulness of contrast enhancement for the investigation of the retrobulbar space and in cases of low grade or infiltrative gliomas 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 venosafollowing 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 iodinated contrast medium 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 bleeds 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 tomographic imaging 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 be helpful in 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). For information regarding the use of dilute oral plus intravenous OMNIPAQUE in CT of the abdomen, see INDICATIONS AND USAGE—Oral Use.

**Precautions**

See PRECAUTIONS—General.

**Adverse Reactions**

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.)

**Dosage and Administration**

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

**OMNIPAQUE (iomeprol) Injection**

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

**Head Imaging**

- By Injection: 70 mL to 150 mL (121 to 421 g/mL of OMNIPAQUE 300 (100 mg/mL))
- By Infusion: 80 mL to 120 mL (121 to 180 g/mL of OMNIPAQUE 300 (150 mg/mL))

**Head Imaging**

- By Infusion: 120 mL to 250 mL (193 to 600 mL of OMNIPAQUE 240 or 300 mg/mL of OMNIPAQUE 350)

**Body Imaging**

- By Injection: 50 mL to 200 mL (86 to 350 g/mL of OMNIPAQUE 300 (150 mg/mL))
- By Infusion: 60 mL to 100 mL (101 to 180 g/mL of OMNIPAQUE 350 (150 mg/mL))

**Digital Subtraction Angiography**

**Intravenous Administration**

OMNIPAQUE 350 at a concentration of 350 mg/mL is indicated in adults for use in intravenous digital subtraction angiography (IV DSA) of the vessels of the head, neck, and abdominal, renal and peripheral sites. Patients with a history of allergy to nonionic contrast media should be premedicated with an anti-allergenic medication.

Artiograms of diagnostic quality can be obtained following the intravenous administration of contrast media employing digital subtraction and computer imaging enhancement techniques. The intravenous route of administration using these techniques has the advantage of being less invasive than the corresponding selective catheter placement of medium. The dose is administered in a
OMNIPAQUE 300 and OMNIPAQUE 350 at dosages from 200 mg/mL body weight to 350 mg/mL 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 mL/kg to 3.0 mL/kg of body weight has produced diagnostic opacification of the excretory system in children. The usual dose for children under 10 kg body weight is 1.5 mL/kg body weight. Dosage for infants and children should be administered in proportion to age and body weight. The total administered dose should not exceed 3 mL/kg body weight.

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—Intravascular: Excretion of the uterus (hysterosalpingography) and bladder (cystourethrography) involves the almost immediate drainage of contrast medium from the cavity upon conclusion of the radiographic procedure.

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 kidney disease. Leakage into the peritoneal cavity occurs. Visualization of the joint spaces, uterus, fallopian tubes, perineal herniations, pancreatic and bile ducts, and bladder can be accomplished by injection of contrast medium into the region to be studied. The use of appropriate iodine concentrations assures diagnostic density.

Orally administered OMNIPAQUE produces good visualization of the gastrointestinal tract. OMNIPAQUE is particularly useful when barium sulfate is contraindicated as in patients suspected with bowel perforation or those where aspiration of contrast medium is a possibility.

INDICATIONS AND USAGE, GENERAL—Oral/BODY CAVITY USE

OMNIPAQUE 240, OMNIPAQUE 300, and OMNIPAQUE 350 have osmolalities from approximately 1.8 to 2.5 mOsm/kg water and are hypertonatric 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 pancreatoangiography and choledangiopancreatography, hysterosalpingography, and hysterosalpingography.

OMNIPAQUE diluted to concentrations from 9 mg/mL to 9 g/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 180 is indicated in children for 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 340 mg/mL or OMNIPAQUE 300 at a concentration of 300 mg/mL administered intravenously is indicated in children for use in contrast enhanced computed tomography of the abdomen.

CONTRAINdications

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

WARNINGS—General

See SECTION II, WARNINGS—General.

PRECAUTIONS—General

Orally administered hyperosmolar contrast media can cause leakages into the peritoneal cavity which, if severe, 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, could 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, 300, and 350, the following adverse reactions were reported.

Cardiovascular System

Incidence > 1%: None

Incidence ≤ 1%: Hypertension

Nervous System

Incidence > 1%: Paresthesia

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

Respiratory System

None

Gastrointestinal System

Incidence > 1%: None

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

Skin and Appendages

Incidence > 1%: Swelling (22%), 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 almost exclusively observed following oral administration. 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 contrast media, see SECTION II, ADVERSE REACTIONS—Intravascular—General.

No adverse reactions associated with the use of OMNIPAQUE for VCU procedures were reported in 51 pediatric patients studied.

Adverse Reactions

See ADVERSE REACTIONS: Intravascular—General.

Dosage and Administration

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

Pediatrics

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 in 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, information on voiding cystourethrography.) For pharmacokinetics of excretion in adults, see CLINICAL PHARMACOLOGY—Intravascular.

Precautions

Preparatory dehydration is not recommended in the elderly, infants, young children, diabetic or azotemic patients, or in patients with suspected myelomatoses.
See also SECTION II, OVERDOSE.

The recommended dose of OMNIPAQUE 350 at a concentration of 350 mg/mL for adult oral pass-through examination of the gastrointestinal tract is 50 mL to 100 mL. In a Phase 1 study, 150 mL of OMNIPAQUE may be administered orally to 11 healthy male subjects. The incidence of diarrhea was 9/10 (91% of 11) and abdominal cramping was 27% (3 of 11). Despite all of these events being mild and transient, the adverse event rates 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.

**DOSE 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-through 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 use in contrast enhanced computed tomography of the abdomen. Dilute oral plus intravenous OMNIPAQUE may be useful if unenhanced imaging does not provide sufficient delineation between normal loops of the bowel and adjacent organs or areas of suspected pathology.

Children: OMNIPAQUE 300 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 is indicated in children for use in contrast enhanced computed tomography of the abdomen.

**Precautions**

See PRECAUTIONS—General.

**Adverse Reactions**

Oral administration of OMNIPAQUE is most often associated with mild, transient diarrhea especially when high concentrations and large volumes are administered. Nausea, vomiting, and moderate diarreal have also been reported following orally administered OMNIPAQUE, but much less frequently. For CT examinations using dilute oral plus intravenous contrast medium, adverse events are more likely to be associated with the intravenous component of the hypertonic oral solution. It should be noted that serious or anaphylactoid reactions may occur with intravascular iodinated media 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 (2%), 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 (1%).

**Dosage and Administration**

**Adults:** The recommended dosage of undiluted OMNIPAQUE 350 at a concentration of 350 mg/mL for oral pass-through 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 50 mL to 100 mL. Smaller administered volumes are needed as the concentration of the final solution is increased (see Table below). In conjunction with OMNIPAQUE 300 at a concentration of 300 mg/mL administered intravenously, the recommended dosage of OMNIPAQUE 300 administered intravenously is 100 mL to 150 mL. The oral dose is administered about 20 to 40 minutes prior to the intravenous dose and image acquisition.

**Children:** In controlled clinical studies involving 58 pediatric patients for examination of the gastrointestinal tract using OMNIPAQUE 240 and OMNIPAQUE 300, adverse reactions were limited to a single report of vomiting (1%).

**Preparations**

**OMNIPAQUE diluted with Sterile Water for Injection as indicated in the table below:**

<table>
<thead>
<tr>
<th>Volume of OMNIPAQUE</th>
<th>OMNIPAQUE 240</th>
<th>OMNIPAQUE 300</th>
<th>OMNIPAQUE 350</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 mL to 10 mL</td>
<td>140</td>
<td>200</td>
<td>250</td>
</tr>
<tr>
<td>10 mL</td>
<td>167</td>
<td>233</td>
<td>289</td>
</tr>
<tr>
<td>20 mL</td>
<td>200</td>
<td>275</td>
<td>338</td>
</tr>
<tr>
<td>40 mL</td>
<td>243</td>
<td>310</td>
<td>400</td>
</tr>
<tr>
<td>80 mL</td>
<td>300</td>
<td>400</td>
<td>500</td>
</tr>
</tbody>
</table>

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

**VOIDING CYSTOURETROGRAPHY (VCU)**

OMNIPAQUE diluted to concentrations from 50 mg/mL to 100 mg/mL is indicated in children for voiding cystourethrography. VCs 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 be increased upon the discretion of the physician and also with the technique and equipment used. Sufficient volume of contrast medium should be administered to adequately fill the bladder. The usual adult volume ranges from 50 mL to 150 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>Volumes of OMNIPAQUE</th>
<th>OMNIPAQUE 240</th>
<th>OMNIPAQUE 300</th>
<th>OMNIPAQUE 350</th>
</tr>
</thead>
<tbody>
<tr>
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<td>400</td>
</tr>
<tr>
<td>80 mL</td>
<td>300</td>
<td>400</td>
<td>500</td>
</tr>
</tbody>
</table>

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

**ARTHROGRAPHY**

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 knee joint in adults, and OMNIPAQUE 240 at a concentration of 240 mg/mL or OMNIPAQUE 300 at a concentration of 300 mg/mL in radiography of the shoulder joint, hip, temporomandibular joint, and other joints in adults and children. Arthrogaphy with OMNIPAQUE may be useful in the diagnosis of posttraumatic or degenerative joint diseases, synovial rupture, visualization of communicating bursae or cysts, and in meniscography.

**Precautions**

See PRECAUTIONS—General.

Strict aseptic technique is required to prevent infection. Fluoroscopic control should be used to ensure proper needle placement, prevent extravascular injection, and prevent dilution of contrast medium. Undue pressure should not be exerted during injection.

**Adverse Reactions**

**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 injection is employed.**

**Dosage and Administration**

Arthography is usually performed under local anesthesia. The amount of OMNIPAQUE injected is dependent on the size of the joint to be examined and the technique employed. Lower volumes of contrast medium are usually injected for knee and shoulder arthography when double-contrast examinations using 15 mL to 100 mL of air are performed.

The following concentrations and volumes are recommended for normal adult knee, shoulder, and temporomandibular joints by sex. These guidelines do not exceed 1 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:

**KNEE**

OMNIPAQUE 240 5 mL to 15 mL
OMNIPAQUE 300 5 mL to 15 mL
OMNIPAQUE 350 5 mL to 10 mL

**SHOULDER**

OMNIPAQUE 300 10 mL
OMNIPAQUE 240 3 mL

**TEMPOROMANDIBULAR**

OMNIPAQUE 300 0.5 mL to 1.0 mL

**Lower volumes recommended for double-contrast examinations.**

**Higher volumes recommended for single-contrast examinations.**
Passive or active manipulation is used to disperse the medium throughout the joint space.

**ENDOSCOPIC RETROGRADE PANCREATOGRAPHY (ERP)/ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)**

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

**Precautions**

See PRECAUTIONS—General.

**Adverse Reactions**

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%)?

Gastrointestinal system: Pain (49%), somnolence and fever each with an individual incidence of 3%.

Pain (17%), somnolence (1%), and burning (1%).

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 disruptive distention of the uterus and fallopian tubes. Fluoroscopic monitoring is recommended.

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 (49%), somnolence and fever each with an individual incidence of 3%.

Gastrointestinal system: Nausea (3%).

**Dosage and Administration**

The recommended dosage of OMNIPAQUE 240 is 15 mL to 20 mL and of OMNIPAQUE 300 is 15 mL to 25 mL fill in 100 mL in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1414-80).

**FEDERAL GOVERNMENT CODES**

**OMNIPAQUE 240**

50 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1412-29)

150 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1412-27)

200 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1412-28)

**OMNIPAQUE 300**

30 ml glass vial, 300 mg/mL, boxes of 10 (NDC 0407-1413-11)

50 ml glass bottle, 300 mg/mL, boxes of 10 (NDC 0407-1413-95)

75 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1413-98)

75 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1413-99)

100 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1413-91)

150 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1413-92)

200 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1413-93)

**OMNIPAQUE 350**

50 ml glass bottle, 350 mg/mL, boxes of 10 (NDC 0407-1414-52)

100 ml glass bottle, 350 mg/mL, boxes of 10 (NDC 0407-1414-53)

50 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1414-21)

75 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1414-29)

100 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1414-22)

150 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1414-23)

200 ml in + PLUS PAK™ (polymer bottle), boxes of 10 (NDC 0407-1414-24)

Protect veins and glass or 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].

**SPECIAL HANDLING AND STORAGE FOR POLYMER BOTTLES ONLY:**

DO NOT USE IF TAMPER-EVIDENT RING IS BROKEN OR MISSING.
Approval Documents
NDA 18-956/S-028

Sterling Winthrop Inc.
1250 Collegeville Road
P.O. Box 5000
Collegeville, Pennsylvania 19426-0900

Attention: Helen Hammes
Associate Director
Project Operations
Drug Regulatory Affairs

Dear Ms. Hammes:

Reference is made to your supplemental new drug application dated January 10, 1990, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Omnipaque (iohexol) Injection.

The supplement provides for a revision in the labeling to include the use of orally or rectally administered Omnipaque 180, 240, and 300 mgI/mL in children for the examination of the gastrointestinal tract.

Reference is also made to your amendments dated February 16, April 17, and June 19, 1990; and August 18, 1992.

We also reference your letter dated June 11, 1993, in which you request that approval of this supplemental application not be contingent upon the approval of S-039, as stated in our approvable letter for this supplement dated June 1, 1993.

We have completed our review of this supplemental application as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the draft labeling dated August 18, 1992. Accordingly the supplemental application is approved the date of this letter.

Please submit twelve copies of the final printed labeling (FPL) identical to the draft labeling dated August 18, 1992, as soon as possible. Seven of the copies should be individually mounted on heavy weight paper or similar material. The submission should be designated for administrative purposes as "FPL for approved NDA 18-956/S-028." Approval of this submission by FDA is not required before the labeling is used. Marketing of the product with FPL that is not identical to the draft labeling may render the product misbranded and an unapproved drug.
The final printed labeling should include only those labeling revisions provided for in the revised draft labeling dated August 18, 1992 for this supplement, and should not contain labeling revisions under consideration for inclusion in S-039.

We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 314.81 for an approved NDA.

Should there be any questions regarding this communication, please contact Mr. Stephen McCort, Consumer Safety Officer at (301) 443-5818.

Sincerely yours,

Patricia Love, M.D., M.B.A.
Acting Director
Division of Medical Imaging,
Surgical and Dental Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

CC:
NDA 18-956/S-028
HFD-160/DIVFIL
HFC-130/JAllen with labeling
HFD-80 with labeling
HFD-160/Love
HFD-160/Chow
HFD-161/McCort/Kummerer
Acknowledgements: Jones-06-23-93/Chow-06-23-93/Cheever-06-21-93
drafted by: Steve McCort 6-18-93
F/T by: Jo 07-1-93 18956.S28
Concurrence JC/6/29/93 AEJ/6/23/93 CHOW/6/23/93
SUPPLEMENT APPROVAL
Sterling Drug Inc.
81 Columbia Turnpike
Rensselaer, New York 12144

Attention: Franklin J. Rosenberg, Ph.D.
Vice President, Drug Regulatory Affairs
Sterling Research Group

Dear Dr. Rosenberg:

Reference is made to your supplemental new drug application (S-020) dated November 3, 1988 submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for the diagnostic radiopaque agent Omnipaque (iohexol) Injection. We acknowledge the receipt of your amendments dated March 17, May 24 and June 15, 1989 and your additional communication dated November 11, 1988.

Reference is also made to your supplemental new drug application (S-021) dated December 7, 1988 submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Omnippique (iohexol) Injection. We acknowledge the receipt of your amendments dated May 24 and June 15, 1989.

Supplemental application S-020 provides for the use of Omnipaque 180 and Omnipaque 210 in pediatric myelography. In addition, Omnipaque 210 represents an additional strength of iohexol providing 210 milligrams of iodine per milliliter for intrathecal administration to be supplied in vials containing 10 and 15 milliliters.

Supplemental application S-021 provides for the oral use of Omnipaque 350 in adults for pass-thru examination of the gastrointestinal tract and for the oral use of diluted Omnipaque Injection in adults for contrast enhanced computed tomography of the abdomen.

We have completed our review of these supplemental new drug applications as amended including the submitted draft labeling and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the draft labeling submitted on June 15, 1989. Accordingly, the applications are approved, effective on the date of this letter.
The final printed labeling (FPL) must be identical to the draft labeling submitted on June 15, 1989. Marketing of the product for the new indications with FPL that is not identical to the draft labeling may render the product misbranded and an unapproved new drug. Please individually mount seven copies of the FPL on heavy weight paper or similar material and submit a total of twelve copies to FDA as soon as available. This submission should be designated for administrative purposes as "FPL for the Approved Supplemental Applications 18-956/S-020 and S-021". Approval of this submission by FDA is not required before the labeling may be used.

In addition, we would appreciate your submitting copies of the introductory promotional and/or advertising material that you propose to use for this new indication. Please submit one copy to this division and a second, along with a copy of the package insert, directly to:

Division of Drug Advertising and Labeling (HFD-240)
Room 10B-04
5600 Fishers Lane
Rockville, Maryland 20857

Please submit all proposed materials in draft or mock-up form, not final print. Also, please do not use form FD-2253 for this submission; this form is for routine use, not proposed materials.

Please submit one market package of Omnipaque 210 when it is available.

Should additional information relating to the safety and effectiveness of this drug product become available prior to our receipt of the final printed labeling, revision of that labeling may be required.

We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 314.81 for an approved NDA.

Sincerely yours,

John F. Palmer, M.D.
Acting Director
Division of Radiopharmaceuticals, Surgical and Dental Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research