OMNIpaque®

(iohexol) Injection

DESCRIPTION

OMNIpaque is provided as a sterile, pyrogen-free, colorless to pale-yellow solution, in an 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:

\[
\text{HOCH}_2\text{CH}_2\text{CH}_2\text{OH} \quad \text{HOCH}_2\text{CH}_2\text{CH}_2\text{OH} \quad \text{HOCH}_2\text{CH}_2\text{CH}_2\text{OH} \quad \text{HOCH}_2\text{CH}_2\text{CH}_2\text{OH}
\]

OMNIpaque is provided as a sterile, pyrogen-free, colorless to pale-yellow solution, in an Imaging Bulk Package, in the following iodine concentrations: 300 and 350 mg Iodine/mL. An Imaging Bulk Package is used to dispense multiple single doses, utilizing a transfer set cleared for use with this contrast agent in this Imaging Bulk Package. OMNIpaque 300 contains 667 mg of iohexol equivalent to 300 mg of organic iodine per mL; and OMNIpaque 350 contains 755 mg of iohexol equivalent to 350 mg of organic iodine per mL. Each milliliter of iohexol solution contains 1.21 mg tromethamine and 0.1 mg edetate calcium disodium with the pH adjusted between 6.8 and 7.7 with hydrochloric acid or sodium hydroxide. All solutions are sterilized by autoclaving and contain no preservatives. Iohexol solution is sensitive to light and therefore should be protected from exposure. The available concentrations have the following physical properties:

<table>
<thead>
<tr>
<th>Concentration (mg Iodine/mL)</th>
<th>Osmolality* (mOsm/kg water)</th>
<th>Osmolarity (mOsm/L)</th>
<th>Absolute Viscosity (cp)</th>
<th>Specific Gravity</th>
</tr>
</thead>
<tbody>
<tr>
<td>300</td>
<td>672</td>
<td>465</td>
<td>11.8</td>
<td>6.3</td>
</tr>
<tr>
<td>350</td>
<td>844</td>
<td>541</td>
<td>20.4</td>
<td>10.4</td>
</tr>
</tbody>
</table>

* By vapor-pressure osmometry.

INDICATIONS AND USAGE

CT SCANNING OF THE HEAD

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

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

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

CT SCANNING OF THE BODY

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

INDICATIONS AND USAGE

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

CT SCANNING OF THE HEAD

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

Tumors

OMNIpaque may be useful to investigate the presence and extent of certain malignancies such as: gliomas including malignant gliomas, glialblastomas, astrocytomas, oligodendrogliomas and gangliogliomas, ependymomas, medulloblastomas, meningiomas, neuromas, pinealomas, pituitary adenomas, carcinopharyngiomas, germinomas, and metastatic lesions. The usefulness of...
contrast enhancement for the investigation of the retrolubar space and in cases of low grade or infiltrative gloma 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 vena cava following contrast media administration has resulted in false-positive diagnosis in a number of otherwise normal studies.

Nonneoplastic Conditions

OMNIPAQUE may be beneficial in the image enhancement of nonneoplastic lesions. Cerebral infarctions of recent onset may be better visualized with contrast enhancement, while some infarctions are obscured if contrast medium is used. The use of iodinated contrast media results in enhancement in about 60 percent of cerebral infarctions studied from one to four weeks from the onset of symptoms. Sites of active infection may also be enhanced following contrast medium administration. Arteriovenous malformations and aneurysms will show contrast enhancement. For these vascular lesions the enhancement is probably dependent on the iodine content of the circulating blood pool. Hematomas and intraparenchymal 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 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 (i.e., tumor extension) or may help to define suspicious lesions seen with unenhanced CT (i.e., pancreatic cyst).

CONTRAINDICATIONS

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

WARNINGS—General

INTRAVASCULAR ADMINISTRATION

Nonionic iodinated contrast medium inhibit blood coagulation, in vitro, less than ionic contrast medium. Clotting has been reported when blood remains in contact with syringes containing nonionic contrast media. Serious, fatal, thromboembolic events causing myocardial infarction and stroke have been reported with both ionic and nonionic contrast media. The use of plastic syringes in place of glass syringes has been reported to decrease but not eliminate the likelihood of in vitro clotting. OMNIPAQUE may be used with extreme care in patients with severe functional disturbances of the liver and kidneys, severe thyrotoxicosis, or myelomatosis. Diabetics with a serum creatinine level above 3 mg/dl should not be examined unless the possible benefits of the examination clearly outweigh the additional risk. OMNIPAQUE is not recommended for use in patients with anuria. Radiopaque contrast agents are potentially hazardous in patients with multiple myeloma or other paraproteinemia, particularly in those with therapeutically resistant anuria. The possibility of an idiosyncratic reaction in susceptible patients should always be considered (see ADVERSE REACTIONS: Intravascular—General). The susceptible population includes, but is not limited to, patients with a history of a previous contrast medium injection of any contrast media, may be more accurate than pretesting in predicting potential adverse reactions. A positive history of allergies or hypersensitivity does not arbitrarily contraindicate the use of a contrast agent where a diagnostic procedure is thought essential, but caution should be exercised (see ADVERSE REACTIONS: Intravascular—General). Premedication with antihistamines or corticosteroids in these patients should be considered. Pretreatment does not prevent serious life-threatening reactions, but may reduce both their incidence and severity. Even though the osmolality of OMNIPAQUE is low compared to diatrizoate or iothalamate-based ionic agents of comparable iodine concentration, the potential for interaction in the circulatory osmotic load in patients with congestive heart failure may cause serious cardiovascular reactions. Iohexol may increase the risk of anaphylactoid reactions, particularly in susceptible patients. Injection of any contrast medium in patients with advanced vascular disease, diabetic patients, and in susceptible non-diabetic patients (often elderly with preexisting renal disease), infants and small pediatric patients. Dehydration in these patients seems to be enhanced by the osmotic diuretic action of urographic agents. It is believed that overnight fluid restriction prior to excretory urography generally does not provide better visualization in normal patients. Premedication should be instituted prior to and following administration of any contrast medium, including ioxanol.

Acute renal failure has been reported in diabetic patients with diabetic nephropathy and in susceptible non-diabetic patients (often elderly with preexisting renal disease). Therefore, careful consideration of the potential risks should be given before performing radiographic procedure in these patients. The possibility of a reaction, including serious, life-threatening, fatal, anaphylactoid or cardiovascular reactions should always be considered (see ADVERSE REACTIONS: Intravascular—General). It is of utmost importance that a course of action be carefully planned in advance for immediate treatment of serious reactions, and that adequate and appropriate personnel be readily available in case of any reaction. The possibility of an idiosyncratic reaction in susceptible patients should always be considered (see ADVERSE REACTIONS: Intravascular—General). The susceptible population includes, but is not limited to, patients with a history of a previous reaction to contrast media, patients with a known sensitivity to ioxanol 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 pretesting methods. However, pretesting cannot be relied upon to predict severe reactions and may itself be hazardous for the patient. It is suggested that a thorough medical history with emphasis on allergy and hypersensitivity, prior to the injection of any contrast media, may be more accurate than pretesting in predicting potential adverse reactions. A positive history of allergies or hypersensitivity does not arbitrarily contraindicate the use of a contrast agent where a diagnostic procedure is thought essential, but caution should be exercised (see ADVERSE REACTIONS: Intravascular—General). Premedication with antihistamines or corticosteroids in these patients should be considered. Pretreatment does not prevent serious life-threatening reactions, but may reduce both their incidence and severity. Even though the osmolality of OMNIPAQUE is low compared to diatrizoate or iothalamate-based ionic agents of comparable iodine concentration, the potential for interaction in the circulatory osmotic load in patients with congestive heart failure may cause serious cardiovascular reactions. Iohexol may increase the risk of anaphylactoid reactions, particularly in susceptible patients.

Information for Patients

Patients receiving injectable radiopaque diagnostic agents should be instructed to:

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

Drug/Laboratory Test Interaction

If iodine-containing isotopes are to be administered for the diagnosis of thyroid disease, the iodine-binding capacity of thyroid tissue may be reduced for up to 2 weeks after contrast medium administration. Thyroid function tests which do not depend on iodine estimation, eg, T3 resin uptake or direct thyroid assays, are not affected. Many radiopaque contrast agents are incompatible in vitro with some antibiotics and many other drugs; therefore, no other pharmaceuticals should be administered within the same venous or arterial syringe as the Omnipaque.

Reference ID: 4080358
suppression have been uncommonly reported following iodinated contrast media
administration to adult and pediatric patients, including infants. Some patients were
treated for hypothyroidism. Skin and Subcutaneous Tissue Disorders: Reactions
range from mild (e.g. rash, erythema, pruritus, urticaria and skin discoloration) to
severe: (e.g. Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN),
acute generalized exanthematous pustulosis (AGEP) and drug reaction with
eosinophilia and systemic symptoms (DRESS)). Allergic reactions: asthmatic attacks,
flushing, rash, and conjunctival symptoms; cardiac reactions such as urticaria with or
without pruritus, as well as pleomorphic rashes, sneezing and lacrimation,
anaphylactic reactions and anaphylactic shock. Fatalities have occurred, due to this
or unknown causes. Signs and symptoms related to the respiratory system: pulmonary
or laryngeal edema, bronchospasm, dyspnea; or to the nervous system: restlessness,
tremors, convulsions. Other reactions: flushing, pain, warmth, metallic taste, nausea,
vomiting, anxiety, headache, confusion, pallor, weakness, sweating, localized areas
of edema, especially facial cramps, neutropenia, and dizziness. Immediate or
delayed rashes can occur, sometimes accompanied by hyperpyrexia. Infrequently,
“iodism” (salivary gland swelling) from organic iodinated compounds appears two
days after exposure and subsides by the sixth day.

General Adverse Reactions to Contrast Media

Physicians should remain alert for the occurrence of adverse effects in addition to
those discussed above. The following reactions have been reported after administration
of intravascular iodinated contrast media. Reactions due to technique: hematomas and
eechymoses.

Hemodynamic reactions: vein cramp and thrombophlebitis following intravenous
injection. Cardiovascular reactions: Cardiac arrhythmias, reflex tachycardia, chest
pain, cough, hypotension, hypertension, peripheral vasodilatation, shock,
and cardiac arrest. Renal reactions: Transient proteinuria, oliguria or anuria. Endocrine
reactions: Thyroid function tests indicative of hyperthyroidism or transient thyroid

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DOSAGE AND ADMINISTRATION

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

OMNIPAQUE Injection (Iohexol)

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

<table>
<thead>
<tr>
<th>Head Imaging by Injection:</th>
<th>70 mL to 150 mL (21 g Iodine to 65 g Iodine) of OMNIPAQUE 300 (300 mg Iodine/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Imaging by Injection:</td>
<td>50 mL to 200 mL (15 g Iodine to 60 g Iodine) of OMNIPAQUE 300 (300 mg Iodine/mL)</td>
</tr>
<tr>
<td></td>
<td>60 mL to 100 mL (21 g Iodine to 35 g Iodine) of OMNIPAQUE 350 (350 mg Iodine/mL)</td>
</tr>
</tbody>
</table>

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

| Head and body Imaging by Injection: | 1mL/kg to 2mL/kg (with maximum = 3mL/kg, maximum single dose = 35g Iodine (116mL)] |

Dosage for infants and children should be administered in proportion to age and body weight.

DIRECTIONS FOR USE

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

a. The OMNIPAQUE Imaging Bulk Package is to be used only in a room designated for radiological procedures that involve intravascular administration of a contrast agent.

b. Transfer OMNIPAQUE from the Imaging Bulk Package utilizing aseptic technique. Prior to penetrating the container closure, swab the face of the container stopper with 70% isopropyl alcohol. The container closure may be penetrated only one time with a suitable sterile component of the iodinated contrast media transfer set cleared for use with this Imaging Bulk Package.

c. Once the Imaging Bulk Package is punctured, do not remove it from the work area during the entire period of use, and maintain the bottle in an inverted position such that container contents are in continuous contact with the dispensing set.

d. After the container closure is punctured, if the integrity of the Imaging Bulk Package and the delivery system cannot be assured through direct continuous supervision, discard the Imaging Bulk Package and all associated disposables for the iodinated contrast media transfer set.

e. A maximum time of 8 hours from initial closure entry is permitted to complete fluid transfer. Discard any unused OMNIPAQUE injection 8 hours after initial puncture of the Imaging Bulk Package.

f. Do not heat the container beyond 37°C, after the closure has been entered.

HOW SUPPLIED

OMNIPAQUE 300
500 mL in +PLUSPAK™ (polymer bottle), boxes of 10 Imaging Bulk Packages (NDC 0407-3413-72)

OMNIPAQUE 350
500 mL in +PLUSPAK™ (polymer bottle), boxes of 10 Imaging Bulk Packages (NDC 0407-3414-72)

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

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

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