1205047 IDN

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GE Healthcare

OMNIPAQUE™

IOHEXOL

NAME OF THE MEDICINAL PRODUCT
OMNIPAQUE injection 300 mg I/ml, 350 mg I/ml

QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient	Strength	Content per. ml.
Iohexol (INN)	300 mg I/ml	647 mg equiv. 300 mg I
Iohexol (INN)	350 mg I/ml	755 mg equiv. 350 mg I

Iohexol is a non-ionic, monomeric, triiodinated, water-soluble X-ray contrast medium. Omnipaque in the concentration of 140 mg I/ml is isotonic with blood and tissue fluid.

The osmolality and viscosity values of Omnipaque are as follows:

Concentration	Osmolality ** Osm/kg H_2O	Viscosity (mPa·s)	
	37°C	20°C	37°C
300 mg I/ml	0.64	11.6	6.1
350 mg I/ml	0.78	23.3	10.6

** Method: Vapour - pressure osmometry.

PHARMACEUTICAL FORM
Solution for injection. For intravenous, intra-arterial and intrathecal use, and use in body cavities.
Omnipaque injection is supplied ready to use as clear, colourless to pale yellow, sterile aqueous solutions.

CLINICAL PARTICULARS

INDICATIONS
X-ray contrast medium for use in adults and children for cardioangiography, arteriography, urography, phlebography and CT-enhancement. Lumbar, thoracic, cervical myelography and computed tomography of the basal cisterns, following subarachnoid injection. Arthrography, endoscopic retrograde pancreatography, (ERP), endoscopic retrograde cholangiopancreatography (ERCP), herniography, hysterosalpingography, sialography and studies of the gastrointestinal tract.

POSOLOGY AND METHOD OF ADMINISTRATION
The dosage vary depending on the type of examination, age, weight, cardiac output and general condition of the patient and the technique used. Usually the same iodine concentration and volume is used as with other iodinated X-ray contrast media in current use.
Adequate hydration should be assured before and after administration as for other contrast media.
The following dosages may serve as a guide.

Guidelines for Intravenous use

Indication	Concentration	Volume	Comments
Urography			
adults:	300 mg I/ml or 350 mg I/ml	40 - 80 ml 40 - 80 ml	80 ml may be exceeded in selected cases
children < 7 kg	300 mg I/ml	3 ml/kg	
children > 7 kg	300 mg I/ml	2 ml/kg (max 40 ml)	
Digital subtraction angiography	300 mg I/ml	1 - 15 ml/inj.	depending on site of inj. occasionally large volumes - up to 30 ml - may be used
Phlebography (leg)	300 mg I/ml	20 - 100 ml/leg	
Digital subtraction angiography	300 mg I/ml or 350 mg I/ml	20 - 60 ml/inj. 20 - 60 ml/inj.	
CT-enhancement			
adults:	300 mg I/ml or 350 mg I/ml	100 - 200 ml 100 - 150 ml	Total amount of iodine usually 30 - 60 g
Children:	300 mg I/ml	1-3 ml/kgbw up to 40 ml	In a few cases up to 100 ml may be given

Guidelines for Intra-arterial use

Indication	Concentration	Volume	Comments
Arteriographies			
arch aortography selective cerebral aortography femoral	300 mg I/ml 300 mg I/ml 350 mg I/ml 300 mg I/ml or 350 mg I/ml	30 - 40 ml/inj 5 - 10 ml/inj 40 - 60 ml/inj 30 - 50 ml/inj	Volume pr. injection depends on the site of injection
various	300 mg I/ml	depending on type of examination	
Cardioangiography			
adults: left ventricle and aortic root inj.	350 mg I/ml	30 - 60 ml/inj.	
selective coronary arteriography	350 mg I/ml	4 - 8 ml/inj.	
children:	300 mg I/ml or 350 mg I/ml	depending on age, weight and pathology (max 8 ml/kg)	
Digital subtraction angiography	300 mg I/ml	1 - 15 ml/inj.	depending on site of inj. occasionally large volumes - up to 30 ml - may be used

Guidelines for Intrathecal use

Indication	Concentration	Volume	Comments
Cervical myelography (lumbar injection)	300 mg I/ml	7 - 10 ml	
Cervical myelography (lateral cervical injection)	300 mg I/ml	6 - 8 ml	

To minimize possible adverse reactions a total dose of 3 g iodine should not be exceeded.

Guidelines for Body cavities

Indication	Concentration	Volume	Comments
Arthrography	300 mg I/ml or 350 mg I/ml	5 - 15 ml 5 - 10 ml	
Hysterosal-pingography	300 mg I/ml	15 - 25 ml	
Sialography	300 mg I/ml	0.5 - 2 ml	
Gastrointestinal studies			
Oral use			
Adults:	350 mg I/ml	individual	

CONTRA INDICATIONS
Manifest thyrotoxicosis. History of serious reaction to Omnipaque.
Myelography should not be performed in the presence of significant local or systemic infection where bacteremia is likely.
Intrathecal administration of corticosteroid with Omnipaque is contra-indicated. Because of the possibility of overdosage, immediate repeat myelography in the event of technical failure is contra-indicated.

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE.
Special precautions for use of non-ionic monomeric contrast media in general:
A positive history of **allergy, asthma,** or untoward **reactions** to iodinated contrast media indicates a need for special caution. Premedication with corticosteroids or histamine H_1 and H_2 antagonists might be considered in these cases.
Iodinated contrast media may provoke **anaphylactoid** reactions or other manifestations of **hypersensitivity**. A course of action should therefore be planned in advance, with necessary drugs and equipment available for immediate treatment, should a serious reaction occur. It is advisable always to use an indwelling cannula or catheter for quick intravenous access throughout the entire X-ray procedure.
Non-ionic contrast media have less effect on the coagulation system *in vitro*, compared to ionic contrast media. When performing vascular catheterization procedures one should pay meticulous attention to the angiographic technique and flush the catheter frequently (e.g.: with heparinized saline) so as to minimize the risk of *procedure-related* thrombosis and embolism.
Adequate **hydration** should be assured before and after contrast media administration. This applies especially to patients with multiple myeloma, diabetes mellitus, renal dysfunction, as well as to infants, small children and elderly patients. Young **infants** (age < 1 year) and especially **neonates** are susceptible to electrolyte disturbance and haemodynamic alterations.
Care should also be taken in patients with **serious cardiac disease** and **pulmonary hypertension** as they may develop haemodynamic changes or arrhythmias.
Patients with **acute cerebral pathology**, tumours or a history of **epilepsy** are predisposed for seizures and merit particular care. Also **alcoholics** and **drug addicts** have an increased risk for seizures and neurological reactions. A few patients have experienced a temporary **hearing loss** or even deafness after myelography, which is believed to be due to a drop in spinal fluid pressure by the lumbar puncture per se.
To prevent acute renal failure following contrast media administration, special care should be exercised in patients with preexisting **renal impairment** and **diabetes mellitus** as they are at risk. Patients with **paraproteinemias** (myelomatosis and Waldenström's macroglobulinemia) are also at risk.
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. The inherent risk of angiography in patients with chronic pulmonary emphysema must be weighed against the necessity for performing this procedure.

Preventive measures include:
- Identification of high risk patients
- Ensuring adequate hydration. If necessary by maintaining an i.v. infusion from before the procedure until the contrast medium has been cleared by the kidneys.
- Avoiding additional strain on the kidneys in the form of nephrotoxic drugs, oral cholecystographic agents, arterial clamping, renal arterial angioplasty, or major surgery, until the contrast medium has been cleared.
- Postponing a repeat contrast medium examination until renal function returns to pre-examination levels.

To prevent lactic acidosis, serum creatinine level should be measured in diabetic patients treated with **metformin** prior to intravascular administration of iodinated contrast medium. Normal serum creatinine / renal function: Administration of metformin should be stopped at the time of administration of contrast medium and not resumed for 48 hours or until renal function / serum creatinine is normal. Abnormal serum creatinine / renal function: Metformin should be stopped and the contrast medium examination delayed for 48 hours. Metformin should only be restarted if renal function / serum creatinine is unchanged. In emergency cases where renal function is abnormal or unknown, the physician should evaluate the risk / benefit of the contrast medium examination, and precautions should be implemented: Metformin should be stopped, patient hydrated, renal function monitored and patient observed for symptoms of lactic acidosis.
A potential risk of transient hepatic dysfunction exists. Particular care is required in patients with severe disturbance of both renal and hepatic function as they may have significantly delayed contrast medium clearance. Patients on haemodialysis may receive contrast media for radiological procedures. Correlation of the time of contrast media injection with the haemodialysis session is unnecessary because there is no evidence that haemodialysis protects patients with impaired renal function from contrast medium induced nephropathy. The patient should not be re-exposed to contrast media before the kidney function has returned to its previous function. If contrast medium is to be given again, the patient must be adequately hydrated. The administration of iodinated contrast media may aggravate the symptoms of **myasthenia gravis**.
In patients with **phaeochromocytoma** undergoing interventional procedures, alpha blockers should be given as prophylaxis to avoid a hypertensive crisis.
Special care should be exercised in patients with **hyperthyroidism**. Patients with multinodular **goiter** may be at risk of developing hyperthyroidism following injection of iodinated contrast media. One should also be aware of the possibility of inducing transient hypothyroidism in premature infants receiving contrast media.
Extravasation of contrast media may on rare occasions give rise to local pain, and oedema, which usually recedes without sequela. However, inflammation and even tissue necrosis have been seen. Elevating and cooling the affected site is recommended as routine measures. Surgical decompression may be necessary in cases of compartment syndrome.
Observation-time:
After contrast medium administration the patient should be observed for at least 30 minutes, since the majority of serious side effects occurs within this time. However, delayed reactions may occur.
Intrathecal use:
Following **myelography** the patient should rest with the head and thorax elevated by 20° for one hour. Thereafter he/she may ambulate carefully but bending down must be avoided. The head and thorax should be kept elevated for the first 6 hours if remaining in bed. Patients suspected of having a low seizure threshold should be observed during this period. Outpatients should not be completely alone for the first 24 hours.

INTERACTIONS WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION
Use of iodinated contrast media may result in a transient impairment of renal function and this may precipitate lactic acidosis in diabetics who are taking **metformin** (see Special warnings and special precautions for use).
Patients treated with **interleukin-2** less than two weeks previously have been associated with an increased risk for delayed reactions (flu-like symptoms or skin reactions).
All iodinated contrast media may interfere with tests on thyroid function, thus the iodine binding capacity of the thyroid may be reduced for up to several weeks.
High concentrations of contrast media in serum and urine can interfere with **laboratory tests** for bilirubin, proteins or inorganic substances (e.g. iron, copper, calcium and phosphate). These substances should therefore not be assayed on the day of examination.

PREGNANCY AND LACTATION
The safety of Omnipaque for use in human pregnancy has not been established. An evaluation of experimental animal studies does not indicate direct or indirect harmful effects with respect to reproduction, development of the embryo or fetus, the course of gestation and peri- and postnatal development.
Since whenever possible, radiation exposure should be avoided during pregnancy, the benefits of an X-ray examination, with or without contrast media, should be carefully weighed against the possible risk. Omnipaque should not be used in pregnancy unless the benefit outweighs risk and it is considered essential by the physician.
Contrast media are poorly excreted in human breast milk and minimal amounts are absorbed by the intestine. Harm to the nursing infant is therefore unlikely.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
It is not advisable to drive a car or use machines during the first 24 hours following **intrathecal examination**.

UNDESIRABLE EFFECTS
General (applies to all uses of iodinated contrast media):
Below are listed possible general side effects in relation with radiographic procedures which include the use of non-ionic monomeric contrast media. For side effects specific to mode of administration, please refer to these specific sections.
Undesirable effects associated with the use of iodinated contrast media are usually mild to moderate and transient in nature, and less frequent with non-ionic than with ionic contrast media. Serious reactions as well as fatalities are only seen on very rare occasions.
The most frequent adverse event is a **mild, general sensation** such as a feeling of warmth or a transient metallic taste.
Abdominal discomfort/pain is very rare (incidence <1:1000) and **gastrointestinal reactions** like nausea or vomiting are rare (incidence <1:100, but >1:1000) and gastrointestinal reactions like nausea, vomiting and diarrhea may occur.
Hypersensitivity reactions are rare and usually present as mild respiratory or cutaneous symptoms like dyspnoe, rash, erythema, urticaria, pruritus and angioedema. They may appear either immediately after the injection or up to a few days later. Severe manifestations such as laryngeal oedema, bronchospasm or pulmonary oedema are very rare.
Anaphylactoid reactions may occur irrespectively of the dose and mode of administration and mild symptoms of hypersensitivity may represent the first signs of a serious reaction. Administration of the contrast medium must be discontinued immediately and, if necessary, specific therapy instituted via the vascular access. Patients using **beta blockers** may present with atypical symptoms of anaphylaxis which may be misinterpreted as a vagal reaction.
Vagal reactions giving hypotension and bradycardia are seen in very rare occasions.
Severe **skin reactions** such as Stevens-Johnsons or toxic epidermal necrolysis are seen very rarely.
Pyrexia with rigors are seen on rare occasions.
Iodism or "iodide mumps" is a very rare complication of iodinated contrast media resulting in swelling

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and tenderness of the salivary glands for up to approximately 10 days after the examination.
Intravascular use (Intraarterial and Intravenous use):
Please first read the section labelled "General". Below, only undesireable events with frequency during intravascular use of non-ionic monomeric contrast media are described.
The nature of the undesirable effects specifically seen during intraarterial use depend on the site of injection and dose given. Selective arteriographies and other procedures in which the contrast medium reaches a particular organ in high concentrations may be accompanied by complications in that particular organ.
Distal **pain or heat sensation** in peripheral angiography is common (incidence >1:10).
A transient increase in S-creatinine is common after iodinated contrast media, but usually of no clinical relevance. Renal failure is very rare. However, renal failure may occur in high risk patients and among such patients fatalities have been reported.
Arterial spasm may follow injection into coronary, cerebral or renal arteries and result in transient ischaemia.
Neurological reactions are very rare. They may include seizures or transient motor or sensory disturbances.
On very rare occasions the contrast medium may cross the blood-brain barrier resulting in uptake of contrast medium in the cerebral cortex being visible on CT-scanning until the day following examination, sometimes associated with transient confusion or cortical blindness.
Cardiac complications, including cardiac arrest, arrythmias, depression or signs of ischaemia **are very rare**.
Post phlebographic thrombophlebitis or thrombosis is very rare. A very few cases of **arthralgia** has been reported. Severe respiratory symptoms and signs including dyspnoea, bhroncospsm, laryngospasm, non-cardiogenic pulmonary oedemal and cough may occur.
Thyrotoxicosis may occur.
Flushing may occur.
Injection site reaction may occur.
Intrathecal use:
Please first read the section labelled "General". Below, only undesireable events with frequency during intrathecal use of non-ionic monomer contrast media are described.
Undesirable effects following intrathecal use may be delayed and present some hours or even days after the procedure. The frequency is similar to lumbar puncture alone.
Headache, nausea, vomiting or dizziness are common and may largely be attributed to pressure loss in the subarachnoid space resulting from leakage at the puncture site. Some of these patients may experience a severe headache lasting for several days. Excessive removal of cerebrospinal fluid should be avoided in order to minimize pressure loss.
Mild local **pain, paraesthesia** and **radicular pain** occasionally (incidence <1:10, but >1:100) occur at the site of injection. **Cramping and pain** in the lower limbs are seen on very rare occasions.
Meningeal irritation giving photophobia and meningism happens occasionally. Frank chemical meningitis appear on very rare occasions.
The possibility of an infective meningitis should also be considered.
On very rare occasions, manifestations of **transient cerebral dysfunction** are seen. These include seizures, transient confusion or transient motor or sensory dysfunction. Changes in the EEG may be noted in a few of these patients.
Transients blindness may occur. Neck pain may occur.
Injection site reaction may occur.
Use in Body Cavities:
Please first read the section labelled "General". Below, only undesireable events with frequency during use of non-ionic monomeric contrast media in body cavities are described.
Systemic hypersensitivity reactions are rare.
Endoscopic Retrograde Choleangio Pancreatography (ERCP): Some elevation of amylase levels is common. Post ERCP renal opacification is seen on rare occasions and is associated with an increased risk of post ERCP **pancreatitis**. Rare cases of necrotizing pancreatitis have also been described.
Oral use: Gastrointestinal upset occasionally occur.
Hysterosalpingography (HSG): Transient **pain** in the lower abdomen is common.
Arthrography: Post procedural pain is common. Frank arthritis is rare. The possibility of infective arthritis should be considered in such cases.
Herniography: Mild postprocedural pain is common.

OVERDOSE
Preclinical data indicate a high safety margin for Omnipaque and no fixed upper dose level has been established for routine intravascular use. Symptomatic overdosing is unlikely in patients with normal renal function unless the patient has received an excess of 2000 mg I/kg body-weight over a limited period of time. The duration of the procedure is important for the renal tolerability of high doses of contrast media ($t_{1/2}$ ~ 2 hours). Accidental overdosing is most likely following complex angiographic procedures in children, particularly when multiple injections of contrast medium with high-concentration are given.
In cases of overdose, any resulting water- or electrolyte imbalance must be corrected. Renal function should be monitored for the next 3 days. If needed, haemodialysis may be used for clearance of excessive contrast medium. There is no specific antidote.

PHARMACOLOGICAL PROPERTIES
PHARMACODYNAMIC PROPERTIES
For most of the haemodynamic, clinical-chemical and coagulation parameters examined following intravenous injection of iohexol in healthy volunteers, no significant deviation from preinjection values has been found. The few changes observed in the laboratory parameters were minor and considered to be of no clinical importance.

PHARMACOKINETIC PROPERTIES
Close to 100 per cent of the intravenously injected iohexol is excreted unchanged through the kidneys within 24 hours in patients with normal renal function. The maximum urinary concentration of iohexol appears within approximately 1 hour after injection. The elimination half-life is approximately 2 hours in patients with normal renal function.
No metabolites have been detected.
The protein binding of Omnipaque is so low (less than 2 %), that it has no clinical relevance and can therefore be neglected.

PRECLINICAL SAFETY DATA
Iohexol has a very low acute intravenous toxicity in mice and rats. Animal studies have shown that iohexol has a very low protein binding, and is well tolerated by the kidneys. The cardiovascular and neurotoxicity are low. The histamine release ability and the anticoagulant activity have been shown to be less than for ionic contrast media.

PHARMACEUTICAL PARTICULARS
LIST OF EXCIPIENTS
The following excipients are included:
Trometamol, sodium calcium edetate, hydrochloric acid (pH adjustment) and water for injections.
The pH of the product is 6.8 - 7.6.

INCOMPATIBILITIES
Although no incompatibility has been found, Omnipaque should not be directly mixed with other drugs. A separate syringe should be used.

SHELF LIFE
See expiry date printed on the label.

STORAGE CONDITIONS
Glass vial:
Omnipaque should be stored according to instructions on the label. The product in glass vial may be stored at temperature below 30 °C.
Polypropylene bottles:
50, 75 and 100 ml polypropylene bottles keep at temperature below 30 °C. Stored at 37 °C for up to 1 month prior to use.

NATURE AND CONTENT OF CONTAINER
Glass vial:
The product is filled in injection vial 20 ml. The container is made of colourless highly resistant borosilicate glass (Ph. Eur. Type I), closed with chlorobutyl rubber stoppers (Ph. Eur. Type I), and sealed with combined "flip off seal/tear off seal - flat plast disc".
Polypropylene bottles:
The product is filled in polypropylene bottles.
The bottle of 50 ml is rigid stand-up bottles with a twist-off top.

PRESENTATIONS

Glass vial	
300 mg I/ml	6 vials of 20 ml

Polypropylene bottles	
300 mg I/ml	10 bottles of 50 ml l 10 bottles of 100 ml
350 mg I/ml	10 bottles of 50 ml 10 bottles of 75 ml 10 bottles of 100 ml

INSTRUCTIONS FOR USE/HANDLING
Like all parenteral products, Omnipaque should be inspected visually for particulate contamination, discolouration and the integrity of the container prior to use.
The product should be drawn into the syringe immediately before use. Vial is intended for single use only, any unused portions must be discarded.
Omnipaque may be warmed to body temperature (37°C) before administration.

Manufactured by:
GE Healthcare (Shanghai) Co., Ltd
No. 1 Niudun Road,
China (Shanghai) Pilot Free Trade Zone
Shanghai, 201203,
P.R. China

Imported and distributed by:
PT Menarini Indria Laboratories
Bekasi, Indonesia

DATE OF (PARTIAL) REVISION OF THE TEXT
August 2023

HARUS DENGAN RESEP DOKTER.
No. Reg.:
Glass vial
300 mg I/20 ml DKI.....
Polypropylene bottle
300 mg I/50 ml DKI.....
300 mg I/100 ml DKI.....
350 mg I/50 ml DKI.....
350 mg I/75 ml DKI.....
350 mg I/100 ml DKI.....