Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Omnipaque 180 mg I/ml, solution for injection (polypropylene).

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Iohexol 388mg/ml equivalent to 180mg/ml iodine.
Iohexol is a non-ionic, monomeric, triiodinated, water-soluble X-ray contrast medium.

The osmolality and viscosity values of Omnipaque 180mg I/ml are as follows:

Concentration	Osmolality * Osm/kg H_2O	Viscosity (mPa·s)	
	37°C	20°C	37°C
180 mg I/ml	0.36	3.2	2.0

*Method: Vapour-pressure osmometry.
This medicinal product contains 0.012mg sodium per ml, i.e. essentially sodium free.
For a full lost of excipients, see 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
A clear, colourless to pale yellow, sterile aqueous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

X-ray contrast medium for use in lumbar and thoracic myelography and computed tomorgraphy of the basal cistern, following subarachnoid injection. CT-enhancement and plain studies of the gastrointestinal tract.

4.2 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.
For intravenous, intra-arterial and intrathecal use, and use in body cavities.

The following dosages may serve as a guide.

Guidelines for Intrathecal use:

Indication	Concentration	Volume	Comments
Lumbar and thoracic myelography (lumbar injection)	180 mg I/ml	10 - 15 ml	
CT cisternography (lumbar injection)	180 mg I/ml	5 - 15 ml	
Paediatric myelography <2 years 2-6 years >6 years	 180 mg I/ml 180 mg I/ml 180 mg I/ml	 2 - 6 ml 4 - 8 ml 6 - 12 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**
Gastrointestinal studies **Oral use** *Adults:* **Rectal use** *Children:*	 180 mg I/ml Dilute with tap water to 100-150 mg I/ml	 Individual 5-10 ml/kg b.w.	 Example: Dilute Omnipaque 180 with tap-water 1:0.5
CT- enhancement **Oral use** - *adults:* - *children:* **Rectal use** - *children*:	 Dilute with tapwater to ~6mgI/ml Dilute with tapwater to ~6mgI/ml Dilute with tapwater to ~6mgI/ml	 800 -2000 ml of the diluted solution over a period of time 15-20 ml/kg b.w. of the diluted solution individual	 Example: Dilute Omnipaque 180 with tap-water 1:30

4.3 Contraindications

Manifest thyrotoxicosis. History of serious reaction to Omnipaque.

4.4 Special warnings and precautions for use

Special precautions for use of non-ionic monomeric CM 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.

The risk of serious reactions in connection with use of Omnipaque is regarded as minor. However, 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 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 also be exercised in patients with preexisting renal impairment and diabetes mellitus as they are at risk. Patients with paraproteinaemias (myelomatosis and Waldenströms macroglobulinaemia) are also at risk.

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 patients 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 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 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 patients should rest with the head and thorax elevated by 20^{o} for one hour. Thereafter he/she may ambulate care fully 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.

4.5 Interaction with other medicinal products 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 section 4.4 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.

4.6 Fertility, pregnancy and lactation

The safety of Omnipaque for use in 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 foetus, 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 medium, 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.

4.7 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.

4.8 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 and gastrointestinal reactions like nausea, vomiting and diarrhoea may occur.

Hypersensitivity reactions are rare and usually present as mild respiratory or cutaneous symptoms like dyspnoea, 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. Severe and even toxic skin reactions have been reported.

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 represent with atypical symptoms of anaphylaxis which may be misinterpreted as a vagal reaction.

Vagal reactions giving hypotension and bradycardia are seen on very rare occasions.

Headache or fever may occur. Episodes of hypertension may also occur.
Pyrexia with rigors are seen on rare occasions.

Iodism or “iodide mumps” is a very rare complication of iodinated contrast media resulting in swelling 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 undesirable 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 amongst 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 the examination, sometimes associated with transient confusion or cortical blindness.

Serious cardiac complications, including cardiac arrest, arrhythmia, depression or signs of ischaemia, are very rare.

Post phlebographic thrombophlebitis or thrombosis is very rare. A very few cases of arthralgia have been reported.

Severe respiratory symptoms and signs (including dyspnoea, bronchospasm, laryngospasm, non-cardiogenic pulmonary oedema) and cough may occur.
Thyrotoxicosis may occur. Flushing may occur. Injection site reactions may occur.

Intrathecal use
Please first read the section labelled "General". Below, only undesirable 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.

Transient 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 undesirable events with frequency during use of non-ionic monomeric contrast media in body cavities are described.

Systemic hypersensivity 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.

4.9 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 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 medium (t½ ~ 2 hours). Accidental overdosing is most likely following complex angiographic procedures in children, particularly when multiple injections of high-concentration contrast medium are given.

If 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

X-Ray Contrast Media, ATC code: V08A B02
For most of the haemodynamic, clinical-chemical and coagulation parameters examined following intravenous injection of iohexol in healthy volunteers, no significant deviation form preinjection values has been found. The few changes observed in the laboratory parameters were minor and considered to be of no clinical importance.

5.2 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 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.

5.3 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 neurotxicity are low. The histamine release ability and the anticoagulant activity have been shown to be less than for ionic contrast media.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trometamol,
Sodium calcium edetate,
Hydrochloric acid (pH adjustment),
Water for injections.

6.2 Incompatibilities

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

6.3 Shelf life

The shelf life for polypropylene bottles is 3 years.

The product should be used immediately after opening. Any unused product must be discarded.

6.4 Special precautions for storage

Store below 30°C
Keep the container in the outer carton. Protect from secondary x-rays.
Furthermore, 10,15, and 20 ml fill volumes in polypropylene bottles may be stored at 37°C for up to 1 week prior to use. 40 and 50 ml fill volumes in polypropylene bottles may be stored at 37°C for up to 1 month prior to use.

6.5 Nature and contents of container

The product is filled in 20 and 50 ml polypropylene bottles. The bottle is a rigid stand-up bottle with a twist-off top.

The product is supplied as:

Bottle size	Pack size/Fill volume
20 ml	1 bottle of 10 ml, 10 bottles of 10 ml 1 bottle of 15 ml, 10 bottles of 15 ml 1 bottle of 20 ml, 10 bottles of 20 ml
50 ml	1 bottle of 40 ml, 10 bottles of 40 ml 1 bottle of 50 ml, 10 bottles of 50 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

For single use only. Discard any unused contents.
Like all parenteral products, Omnipaque should be inspected visually for particulate matter, discolouration and the integrity of the container prior to use. The product should be drawn into the syringe immediately before use.

7 MARKETING AUTHORISATION HOLDER

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Nycoveien 1-2
4220 Nydalen
Oslo N-0401
Norway

8 MARKETING AUTHORISATION NUMBER

PA 0735/006/022

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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