SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

OMNİPOL 300 mgI/ml Solution for I.A., I.V. Intrathecal Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance:

Each ml contains 647 mg of Iohexol equivalent to 300 mg of I.

Iohexol is a non-ionic, monomeric, water-soluble x-ray contrast medium containing three iodine atoms.

The osmolality and viscosity values of OMNIPOL 300 mgI/ml are as follows:

Concentration	Osmolality* Osm/kg H_2O 37°C	Viscosity (mPa.s)	
		20°C	37°C
300 mgI/ml	0.64	11.6	6.1

*Method: Vapor-pressure osmometry

Excipients:

Sodium calcium edetate 0,1 mg/ml.

This medicinal product contains 0.012 mg of sodium per ml.

Electrolyte concentrations (per liter):

Sodium: 0,53 mEq = 0,53 mmol

Calcium: 0,54 mEq = 0,27 mmol

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

OMNIPOL is a clear, colorless to pale yellow, sterile aqueous solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

This medicinal product is for diagnostic use only.

X-ray contrast medium for use in adults and children for angiography, urography, phlebography and computed tomography enhancement. Used in 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.

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.

Administration way:
For intravenous, intra-arterial and intrathecal use, and use in body cavities.
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:	240 mg I/ ml or 300 mg I/ml	4 ml/kg 3 ml/kg	
Children > 7 kg:	240 mg I/ ml or 300 mg I/ml	3 ml /kg 2 ml /kg	Max. 40 ml
Phlebography (leg)	240 mg I/ ml or 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-emhancement Adults:	 140 mg I/ml 240 mg I/ ml or 300 mg I/ml or 350 mg I/ml	 100-400 ml 100-250 ml 100- 200 ml 100-150 ml	 Total amount of iodine usually 30 - 60 g
Children:	240 mg I/ ml or 300 mg I/ml	2-3 ml/kg b.w (Up to 40 ml) 1-3 ml/kg b.w (Up to 40 ml)	In a few cases up to 100 ml may be given.

b.w.: Body weight

Guidelines for Intra-arterial use

Indication	Concentration	Volume	Comments
Arteriographies Arch aortography	300 mg I/ ml	30-40 ml/inj.	Volume per injection depends on the site of injection
Selective cerebral	300 mg I/ ml	5-10 ml/inj.	
Aortography	350 mg I/ ml	40-60 ml/inj.	
Femoral	300 mg I/ ml or 350 mg I/ml	30-50 ml/inj.	
Various	300 mg I/ ml	Depending on type of examination	
Cardioangiography <u>Adults:</u> Left ventricle and aortic root injection	350 mg I/ml	30-60 ml/inj.	
Selective coronary arteriography	350 mg I/ml	4-8 ml/inj.	
<u>Children:</u>	300 mg I/ml or 350 mg I/ml	Depending on age, weight and pathology.	Max. 8 ml /kg
Digital subtraction angiography	140 mg I/ml or 240 mg I/ml or 300 mg I/ml	1-15 ml/inj 1-15 ml/inj. 1-15 ml/inj.	depending on site of injection occasionally large volumes (up to 30 ml) may be used

Guidelines for Intrathecal use

Indication	Concentration	Volume	Comments
Myelography Lumbar and thoracic myelography (Lumbar injection)	180 mg I/ml or 240 mg I/ml	10-15 ml 8-12 ml	
Cervical myelography (Lumbar injection)	240 mg I/ml or 300 mg I/ml	10-12 ml 7-10 ml	
Cervical myelography (Lateral cervical injection)	240 mg I/ ml or 300 mg I/ml	6-10 ml 6-8 ml	
CT cisternography (Lumbar injection)	180 mg I/ ml or 240 mg I/ml	5-15 ml 4-12 ml	
Pediatric myelography < 2 years	180 mg I/ ml	2-6 ml	
2 - 6 years	180 mg I/ml	4-8 ml	
> 6 years	180 mg I/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
Arthrography	240 mg I/ml or 300 mg I/ml or 350 mg I/ml	5-20 ml 5-15 ml 5-10 ml	
ERP/ERCP	240 mg I/ml	20-50 ml	
Herniography	240 mg I/ml	50 ml	The dosage varies with the size of the hernia.
Hysterosalpingography	240 mg I/ml or 300 mg I/ml	15-50 ml 15-25 ml	
Sialography	240 mg I/ml or 300 mg I/ml	0.5 - 2 ml 0.5 - 2 ml	

Gastrointestinal studies			
Oral use			
Adults:	180 mg I/ml or 350 mg I/ml	Individual Individual	
Children: Oesophagus	300 mg I/ml or 350 mg I/ml	2-4 ml/kg b.w. 2-4 ml/kg b.w.	Max. dose 50 ml Max. dose 50 ml
Ventricle / follow through	140 mg I/ml	4-5 ml/kg b.w.	
Premature:	350 mg I/ml	2-4 ml/kg b.w.	
Rectal use Children:	140 mgI/ml or dilute with tap water to 100-150 mg I/ml	5-10 ml/kg b.w	Example: Dilute OMNIPOL 300 or 350 with tap-water 1:1 or 1:2.
Contrast enhancement in computed tomography			
Oral use			
Adults:	Dilute with tap water to 6 mg I/ml	800 - 2000 ml of the diluted solution over a period of time	Example: Dilute OMNIPOL 300 or 350 with tap-water 1:50.
Children:	Dilute with tap water to 6 mg I/ml	15-20 ml/kg b.w. of the diluted solution	
Rectal use Children:	Dilute with tap water to 6 mg I/ml		

b.w.: Body weight

4.3. Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Manifest thyrotoxicosis.
- Myelography in cases of significant local or systemic infection where bacteremia is likely to occur.
- Because of overdosage considerations, immediate repeat myelography in the event of technical failure
- The concomitant intrathecal administration of corticosteroids with OMNIPOL.

4.4. Special warnings and 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.

The risk of serious reactions in connection with use of OMNIPOL is regarded as minor. However, iodinated contrast media may provoke serious, life-threatening, fatal anaphylactic/anaphylactoid reactions or other manifestations of hypersensitivity such as hay fever, food allergies. Precaution should therefore be taken 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.

An accurate evaluation of the risk/benefit ratio is needed in the presence of blood in the cerebrospinal fluid in order to avoid risk to the patient.

Patients using β-blockers may present with atypical symptoms of anaphylaxis which may be misinterpreted as vagal reaction.

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 with e.g. 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.
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. Caution is required in patients with multipl sclerosis. Temporary hearing loss or deafness experienced by a few patients after myelography is believed to be due to a drop in spinal fluid pressure by the lumbar puncture.

Elderly patients may present a greater risk following myelography. For this reason, the need for treatment in this group of patients should be carefully evaluated, special attention must be paid to dose and concentration of the medium and technique used and to the patient's hydration status.

Care must be taken to avoid intracranial administration of the drug in large doses or as a concentrated bolus. In addition, preventive measures should be taken to prevent rapid progression of intracranial levels of the drug (for example, to prevent active mobility of the patient). Direct intracisternal or ventricular administration of standard radiography (not computed tomography) should be avoided.

Use of iodinated contrast media may cause contrast induced nephropathy, impairment of renal function or acute renal failure. To prevent these conditions 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 paraproteinaemias (myelomatosis and Waldenströms macroglobulinaemia) are also under 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.

Diabetic patients receiving metformin
There is a risk of the development of lactic acidosis when iodinated contrast agents are administered to diabetic patients treated with metformin, particular in those with impaired renal function.

To reduce the risk of lactic acidosis, serum creatinine level should be measured in diabetic patients treated with metformin prior to intravascular administration of iodinated contrast medium and the following precautions undertaken in the following circumstances:

Normal serum creatinine (<130 µmole/liter)/normal renal function: Administration of metformin should be stopped at the time of administration of contrast medium and should not be resumed for 48 hours. Metformin should only be restarted if renal function/serum creatinine remains stable in the normal range.

Abnormal serum creatinine (>130 µmol/litre)/impaired renal function: Metformin should be stopped and the contrast medium examination delayed for 48 hours. Metformin should only be restarted 48 hours later if renal function is not diminished (if serum creatinine is not increased) compared to pre-contrast values.

Emergency cases: In emergency cases where renal function is impaired or unknown, the physician should evaluate the risk/benefit of the contrast medium examination, and the following precautions should be implemented: Metformin should be stopped. It is particularly important that the patient is fully hydrated prior to contrast medium administration and for 24 hours afterwards. Renal function (e.g. serum creatinine), serum lactic acid and blood pH should be monitored.

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 medium 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 medium 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.

Extravasation of contrast medium 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.

Repeat procedure: If in the clinical judgment of the physician, repeat procedure is required, a suitable interval of time between administrations should be observed to allow for normal clearance of the drug from the body.

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.

Pediatric Population

Transient hypothyroidism has been reported in premature infants, neonates and in other children after administration of iodinated contrast media. Premature infants are particularly sensitive to the effect of iodine. It is advisable to monitor thyroid function. Thyroid function

should be checked in neonates during the first week of life, following administration of iodinated contrast agents to the mother during pregnancy.

Especially in infants and small children, adequate hydration should be assured before and after contrast media administration. Nephrotoxic medication should be suspended. The age dependent reduced glomerular filtration rate in infants can also result in delayed excretion of contrast agents.

Young infants (age < 1 year) and especially neonates are susceptible to electrolyte disturbance and haemodynamic alterations.

This medicinal product contains less than 1 mmol (23 mg) of sodium per ml, i.e. it is essentially "sodium free".

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.).

Patients treated with interleukin-2 less than two weeks previously have been associated with an increased risk for delayed reactions (skin reactions or flu-like symptoms).

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.

Drugs that lower the seizure threshold, especially phenothiazine derivatives (including antihistamines and anti-nausea drugs) are not recommended for use with OMNIPOL. MAO inhibitors, tricyclic antidepressants, central nervous system stimulants, psychoactive drugs should not be used concomitantly. Such drugs should be discontinued at least 48 hours before the start of myelography and should not be used for at least 24 hours after the procedure. Prophylaxis with anticonvulsant drugs should be evaluated in patients who are taking these drugs and undergoing non-elective procedures.

4.6. Pregnancy and lactation

General advice
Pregnancy category: B

Women with childbearing potential/Contraception
Care should be exercised in women with childbearing potential.

Pregnancy
The safety of OMNIPOL for use in pregnancy has not been established.

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. OMNIPOL should not be used in pregnancy unless the benefit outweighs risk and it is considered essential by the physician.

Lactation
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. Breast feeding may be continued normally when iodinated contrast media are given to the mother. The amount of iohexol in breast milk excreted in 24 hours after injection was 0.5% of the weight adjusted dose in a trial. The amount of iohexol ingested by the baby in the first 24 hours after injection corresponds to only 0.2% of the pediatric dose.

Fertility
There are no adequate data in human.

4.7. Effects on ability to drive and use machines
No studies on the ability to drive or use machines have been performed. However, it is not advisable to drive a car and use machines for one hour after the last injection or for 24 hours following intrathecal examination (see section 4.4). However, individual judgement must be performed if there are persistent post-myelographic symptoms.

4.8. Undesirable effects

General (undesirable effects related to all uses of iodinated contrast media)
Below are listed possible general side effects in relation with radiographic procedures, which include the use of nonionic monomeric contrast media. Side effects specific to mode of administration are given in specific sections.

Hypersensitivity reactions may occur irrespective of the dose and mode of administration and mild symptoms may represent the first signs of a serious anaphylactoid reaction/shock. In such case, administration of the contrast medium must be discontinued immediately and, if necessary, specific therapy instituted via the vascular access.

A transient increase in S-creatinine is common after iodinated contrast media, contrast induced nephropathy may occur.

Iodism or "iodide-induced mumps-like reaction" 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.

The listed frequencies are based on internal clinical documentation and published large scale studies, comprising more than 90,000 patients.

The frequencies of undesirable effects are defined as follows:

Very common (≥ 1/10), Common (≥ 1/100- < 1/10), Uncommon (≥ 1/1.000- < 1/100), Rare (≥ 1/10.000- < 1/1.000), Very rare (< 1/10.000) and Not known (cannot be estimated from the available data)

Immune system disorders
Rare: Hypersensitivity (including dyspnea, rash, erythema, urticaria, pruritus, skin reaction, vasculitis, angioneurotic oedema, laryngeal oedema, laryngospasm, bronchospasm or non-cardiogenic pulmonary oedema). They may appear either immediately after the injection or up to a few days later.
Not known: Anaphylactic/anaphylactoid reaction, anaphylactic/anaphylactoid shock

Nervous system disorders
Rare: Headache
Very rare: Gysgeusia (transient metallic taste)
Not known: Syncope vasovagal

Cardiac disorders
Rare: Bradycardia

Vascular disorders
Very rare: Hypertension, hypotension

Gastrointestinal disorders
Uncommon: Nausea
Rare: Vomiting
Very rare: Diarrhea, abdominal pain/discomfort
Not known: Salivary gland enlargement

General disorders and administration site conditions
Common: Feeling hot
Rare: Fever
Very rare: Shivering (chills)

Injury and poisoning
Not known: Iodism

INTRAVASCULAR USE (intra-arterial and intravenous use)

Please first read the section labelled "General". Below, only undesirable events with frequency during intravascular use of nonionic monomeric contrast media are described.

The nature of the undesirable effects specifically seen during intraarterial use depends 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.

Immune system disorders
Not known: Severe pustular or exfoliative or bullous skin lesions

Endocrine disorders
Not known: Thyrotoxicosis, transient hypothyroidism

Psychiatric disorders
Not known: Confusion

Nervous system disorders
Rare: Dizziness
Very rare: Seizures, disturbance in consciousness, encephalopathy, stupor, sensory abnormalities (including hypoaesthesia), paraesthesia, tremor.
Not known: Transient motor dysfunction (including speech disorder, aphasia, dysarthria), transient memory loss, disorientation, coma and retrograde amnesia.

Eye disorders:
Not known: Transient cortical blindness

Ear and Labyrinth Disorders
Not known: Transient hearing loss

Cardiac disorders
Rare: Arrhythmia (including bradycardia, tachycardia).
Very rare: Myocardial infarction
Not known: Severe cardiac complications (including cardiac arrest, cardio-respiratory arrest), spasm of coronary arteries, chest pain

Vascular disorders
Very rare: Flushing
Not known: Shock, arterial spasm, ischemia, thrombophlebitis and thrombosis

Respiratory, thoracic and mediastinal disorders
Rare: Cough
Very rare: Dyspnea, non-cardiogenic pulmonary oedema
Not known: Severe respiratory symptoms and signs, bronchospasm, laryngospasm, asthma attack

Gastrointestinal disorders
Rare: Diarrhea
Not known: Aggravation of pancreatitis, acute pancreatitis

Skin and subcutaneous tissue disorders
Not known: Bullous dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms, psoriasis flare-up

Musculoskeletal and connective tissue disorders
Not known: Arthralgia

Renal and urinary disorders
Rare: Impairment of renal function including acute renal failure

General disorders and administration site conditions
Common: Feeling hot
Uncommon: Pain and discomfort
Rare: Asthenic conditions (including malaise, fatigue).
Not known: Administration site reactions, including extravasation, back pain

INTRATHECAL USE
Please first read the section labelled "General". Below, only undesirable events with frequency during intrathecal use of nonionic monomeric 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 may largely be attributed to pressure loss in the sub-arachnoid space resulting from leakage at the puncture site. Excessive removal of cerebrospinal fluid should be avoided in order to minimize pressure loss.

Psychiatric disorders
Not known: Confusion

Nervous system disorders
Very common: Headache (may be severe and prolonged)
Uncommon: Aseptic meningitis (including chemical meningitis).
Rare: Seizures, dizziness
Not known: Electroencephalogram abnormal, meningism, transient contrast-induced encephalopathy including transient memory loss, coma, stupor and retrograde amnesia, motor dysfunction (including speech disorder, aphasia, dysarthria), paraesthesia, hypoesthesia and sensory disturbance

Eye disorders:
Not known: Transient cortical blindness, photophobia

Ear and Labyrinth Disorders
Not known: Transient hearing loss

Gastrointestinal disorders
Common: Nausea, vomiting

Musculoskeletal and connective tissue disorders
Rare: Neck pain, back pain
Not known: Muscle spasm

General disorders and administration site conditions
Rare: Pain in extremity
Not known: Administration site conditions

USE IN BODY CAVITIES

Please first read the section labelled "General". Below, only undesirable events with frequency during use of nonionic monomeric contrast media in body cavities are described.

Endoscopic Retrograde Cholangiopancreatography (ERCP)

Gastrointestinal disorders

Common: Pancreatitis, blood amylase increased

Oral use:

Gastrointestinal disorders

Very common: Diarrhea

Common: Nausea, vomiting

Uncommon: Abdominal pain

Hysterosalpingography (HSG):

Gastrointestinal disorders

Very common: Lower abdominal pain

Arthrography:

Musculoskeletal and connective tissue disorders

Not known: Arthritis

General disorders and administration site conditions

Very common: Pain

Herniography:

General disorders and administration site conditions

Not known: Post procedural pain

Description of selected adverse reactions

Thrombo-embolic complications have been reported in connection with contrast-enhanced angiography of coronary, cerebral, renal and peripheral arteries. The contrast agent may have contributed to the complications (see section 4.4).

Cardiac complications including acute myocardial infarction have been reported during or after contrast-enhanced coronary angiography. Elderly patients or patients with severe coronary artery disease, unstable angina pectoris and left ventricular dysfunction had a higher risk (see section 4.4).

In very rare occasions the contrast medium may cross the blood-brain barrier resulting in uptake of contrast medium in the cerebral cortex. This may cause neurological reactions. They may include convulsions, transient motor or sensory disturbances, transient confusion, transient memory loss, and encephalopathy (see section 4.4).

Anaphylactoid reaction and anaphylactoid shock may lead to profound hypotension and related symptoms and signs like hypoxic encephalopathy, renal and hepatic failure (see section 4.4).

In several cases, extravasation of contrast media has caused local pain and oedema. These cases usually recede without sequelae. Inflammation, tissue necrosis and compartment syndrome have occurred (see section 4.4).

Additional information on special populations

Pediatric patients:
Transient hypothyroidism has been reported in premature infants, neonates and in other children after administration of iodinated contrast media. Premature infants are particularly sensitive to the effect of iodine. Transient hypothyroidism in a premature breast fed infant has been reported. The nursing mother was repeatedly exposed to OMNIPOL (see section 4.4).

Especially in infants and small children, adequate hydration should be assured before and after contrast media administration. Nephrotoxic medication should be suspended. The age dependent reduced glomerular filtration rate in infants can also result in delayed excretion of contrast agents.

4.9. Overdose and therapy
Preclinical data indicate a high safety margin for OMNIPOL 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, hemodialysis may be used for clearance of excessive contrast medium. There is no specific antidote.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties
Pharmacotherapeutic group: X-Ray Contrast Media
ATC Code: V08AB02
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.

5.2. Pharmacokinetic properties

Absorption:
For intravenous administration.

Distribution:
The protein binding of OMNIPOL is very low (less than 2%) and it has no clinical relevance. It can be neglected.

Biotransformation
There is no evidence of biotransformation. No metabolites have been detected.

Elimination:
Close to 100% 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.

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

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 pre- and postnatal development.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Trometamol
Sodium calcium edetate
Hydrochloric acid/Sodium hydroxide (pH adjustment)
Water for injection

6.2. Incompatibilities

In the absence of compatibility studies, OMNIPOL must not be mixed with other medicinal products. A separate syringe should be used.

6.3. Shelf-life

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

6.4. Special precautions for storage
Store at room temperature below 25^{o}C, protect from light and secondary x-rays. Keep the product in outer packaging.

6.5. Nature and contents of container
European Pharmacopoeia Type I grade, colorless durable borosilicate glass bottles. Bottle volumes are 1x50 ml and 1x100 ml. Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling
It is disposable. Any unused portion must be discarded.
Like all parenteral products, OMNIPOL should be inspected visually for particulate matter, discoloration and the integrity of the container prior to use.

As the product does not contain a preservative, it should be drawn into the syringe immediately before use.

Do not throw away drugs that have expired or are not used! Deliver to the collection system determined by the Ministry of Environment and Urbanism.

7. MARKETING AUTHORISATION HOLDER
Name: POLİFARMA İLAÇ SANAYİ VE TİC. A.Ş.
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8. MARKETING AUTHORISATION NUMBER
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Date of first authorisation: 21.06.2016
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