SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

IOMERON® 300
IOMERON® 350
IOMERON® 400

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

IOMERON® 300
100 ml of solution contains:
Active ingredient: Iomeprol: 61.24 g
IOMERON® 350
100 ml of solution contains:
Active ingredient: Iomeprol: 71.44 g
IOMERON® 400
100 ml of solution contains:
Active ingredient: Iomeprol: 81.65 g

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

IOMEPROL, N, N'-bis(2, 3-dihydroxypropyl)-5[(hydroxyacetyl)methylamino]-2, 4, 6-triiodo-1, 3-benzenedicarboxamide, the active component of lomeron®, is a triiodinated, non-ionic, water soluble, nephrotropic, low-osmolality X-ray contrast medium with a molecular weight of 777.09, formulations of which yield contrast media of particularly low osmolality and viscosity in comparison with other non-ionic media. lomeprol has been formulated in a wide range of concentrations (up to 400 mg iodine/ml). All have proved to be extremely stable both to heat sterilization and prolonged room temperature storage, without the chelator (EDTA salt) required by other contrast agents.

Solution for injection displaying the following physico-chemical characteristics by Iodine strengths as below:

Iodine concentration mgI/mL	*Osmolality mOsmol/kg water (x ± s•t95)**	*Viscosity mPa•s (x ± s•t95)**	
	37° C	*20°C*	*37° C*
300	521 ± 24	8.1 ± 0.7	4.5 ± 0.4
350	618 ± 29	14.5 ± 1.1	7.5 ± 0.6
400	726 ± 34	27.5 ± 2.3	12.6 ± 1.1

*Steam pressure method

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Contrast medium for diagnostic radiology.

Iomeron 300 Intravenous urography (in adults and paediatrics), peripheral phlebography, CT (brain and body), cavernosography, intravenous DSA, conventional angiography, intraarterial DSA, angiocardiography (in adults and paediatrics), conventional selective coronary arteriography, interventional coronary arteriography, ERCP, arthrography, hysterosalpingography, fistulography, discography, galactography, cholangiography, dacryocystography, sialography, retrograde urethrography, retrograde pyelo-ureterography.

Iomeron 350 Intravenous urography (in adults and paediatrics), CT (body), intravenous DSA, conventional angiography, intraarterial DSA, angiocardiography (in adults and paediatrics), conventional selective coronary arteriography, interventional coronary arteriography,

arthrography, hysterosalpingography, fistulography, galactography, retrograde cholangiography, dacryocystography, sialography.

Iomeron 400 Intravenous urography (in adults including those with renal impairment or diabetes), CT (body), conventional angiography, intraarterial DSA, angiocardiography (in adults and paediatrics), conventional selective coronary arteriography, interventional coronary arteriography, fistulography, galactography, dacryocystography, sialography.

CT: Computed Tomography
DSA: Digital Subtraction Angiography
ERCP: Endoscopic Retrograde Cholangio-Pancreatography

4.2 Posology and method of administration

Posology
Dosage and rate of administration may vary depending on the clinical question, the technique to be employed, the body area to be examined, the instrumentation, as well as on the age, body size, cardiac output and patient's clinical conditions

Indication	**Formulation** mg (iodine)/ml	**Proposed dosages**	
Intravenous urography	300, 350, 400	Adults:	50-150 ml
		Newborns:	3-4.8 ml/kg
		Infants < 1 year:	2.5-4 ml/kg
		Paediatric patients > 1 years:	1-2.5 ml/kg
Peripheral phlebography	300	Adults:	10-100 ml, repeat as necessary[b] (10-50 ml upper extremities; 50-100 ml lower extremities)
CT brain	300	Adults:	50-200 ml
		Paediatric patients[a]	
CT body	300, 350, 400	Adults:	100-200 ml
		Paediatric patients[a]	
Cavernosography	300	Adults:	up to 100 ml
Intravenous DSA	300, 350, 400	Adults:	100-250 ml
		Paediatric patients[a]	
CONVENTIONAL ANGIOGRAPHY			
Arteriography of upper extremities	300, 350	Adults[b]	
Arteriography of pelvis and lower extremities	300, 350, 400	Adults[b]	
Abdominal arteriography	300, 350, 400	Adults[b]	
Arteriography of descending aorta	300, 350	Adults[b]	
Pulmonary angiography	300, 350, 400	Adults:	up to 170 ml
Cerebral angiography	300, 350	Adults:	up to 100 ml
Paediatric arteriography	300	Paediatric patients:	up to 130 ml[a]
Interventional	300, 350, 400	Adults[b]	
		Paediatric patients[a]	
INTRAARTERIAL DSA			
Cerebral	300, 350	Adults:	30-60 ml for general view; 5-10 ml for selective injections
		Paediatric patients[a]	
Thoracic	300	Adults[b]:	20-25 ml (aorta) repeat as necessary, 20 ml (bronchial arteries)
Aortic arch	300, 350	Adults[c]	

Abdomen	300	Adults[c]	
Aortography	300, 350	Adults[c]	
Translumbar aortography	300	Adults[b]	
Peripheral arteriography	300	Paediatric patients[a]	
Interventional	300	Adults:	10-30 ml for selective injections up to 250 ml
		Paediatric patients[a]	
Angiocardiography	300, 350, 400	Adults[b]	
		Paediatric patients:	3-5 ml/kg
Conventional selective coronary arteriography	300, 350, 400	Adults:	4-10 ml per artery, repeat as necessary
ERCP	300	Adults:	up to 100 ml
Arthrography	300, 350	Adults:	up to 10 ml per injection
Hysterosalpingography	300, 350	Adults:	up to 35 ml
Fistulography	300, 350, 400	Adults:	up to 100 ml
Discography	300	Adults:	up to 4 ml
Galactography	300, 350, 400	Adults:	0.15-1.2 ml per injection
Dacryocystography	300, 350, 400	Adults:	2.5-8 ml per injection
Sialography	300, 350, 400	Adults:	1-3 ml per injection
Retrograde cholangiography	300, 350	Adults:	up to 60 ml
Retrograde ureterography	300	Adults:	20-100 ml
Retrograde pyelography	300	Adults:	10-20 ml per injection

[a] According to body weight and age.
[b] Do not exceed 250 ml. Single injection volume depends on the vascular area to be examined.
[c] Do not exceed 350 ml.

In elderly patients the lowest effective dose should be used.
Dietary advice - If not otherwise recommended by the physician, a normal diet and adequate fluid intake is maintained during the day preceding the examination. However, patients should avoid eating during the two hours preceding the X-ray examination.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Diagnostic procedures which involve the use of any radiopaque medium should be carried out under the direction of personnel with the prerequisite training and with a thorough knowledge of the particular procedure to be performed.
Appropriate facilities should be available for coping with any complication of the procedure, as well as for emergency treatment of severe reactions, including hypersensitivity or anaphylactic reactions, to the contrast medium itself.

In consideration of possible complications, the patient should be kept under observation for at least 30 minutes after the examination.

Risk of extravasation

Extreme caution during injection of contrast media (CM) is necessary to avoid extravasation.

Hypersensitivity

In patients with suspected or known hypersensitivity to contrast media, sensitivity test doses are not recommended, as severe or fatal reactions to contrast media are not predictable from sensitivity test.
A positive history of allergy, asthma or untoward reaction during previous similar investigations indicates a need for extra caution since, as with other contrast media, this product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. (see Section 4.8 for additional information on anaphylaxis reactions). Patients using beta-adrenergic blocking agents may

have a lower threshold for bronchospasm, especially if asthmatic, and are less responsive to treatment with beta agonists and adrenaline, which may necessitate the use of higher doses of adrenaline.

The benefits should clearly outweigh the risks in such patients and appropriate resuscitative measures should be immediately available. The primary treatments are as follows:

Effect	**Major Symptoms**	**Primary Treatment**
Vasomotor effect	warmth nausea/vomiting	reassurance
Cutaneous	scattered hives severe urticaria	H_1 -antihistamines H_2 -antihistamines
Bronchospastic	wheezing	oxygen Beta-2-agonist inhalers
Anaphylactoid reaction	angioedema urticaria bronchospasm hypotension	oxygen IV fluids adrenergics (iv epinephrine) Inhaled beta-2-adrenergics antihistamines (H_1-and H_2- blockers) corticosteroids
Hypotensive	hypotension	iv fluids
Vagal reaction	hypotension bradycardia	iv fluids iv atropine

From: Bush WH; The Contrast Media Manual; Katzburg RW Ed.; Williams and Wilkins; Baltimore 1992; Chapter 2 p 23

Hydration

Patients must be well hydrated, and any relevant abnormalities of fluid or electrolyte balance should be corrected prior to and following contrast media injection. Especially patients with severe functional impairment of the kidneys, liver or myocardium, myelomatosis or other paraproteinaemias, sickle cell disease, diabetes mellitus, polyuria, oliguria, hyperuricaemia, neonates, infants, elderly patients, and patients with severe systemic disease should not be exposed to dehydration. Caution should be exercised in hydrating patients with underlying conditions that may be worsened by fluid overload, including congestive heart failure.

Cardiovascular diseases

Care should be taken in severe cardiac disease particularly heart failure and coronary artery disease. The intravascular contrast media injection may precipitate pulmonary oedema in patients with manifest or incipient heart failure, whereas in patients with pulmonary hypertension and valvular heart diseases, contrast media administration may lead to pronounced haemodynamic changes.

Thyroid function and thyroid function tests

The small amount of free inorganic iodide that may be present in contrast media might have some effects on thyroid function. These effects appear more evident in patients with latent or overt hyperthyroidism or goitre. Hyperthyroidism or even thyroid storms have been reported following administration of iodinated contrast media.

Thyroid function tests indicative of hypothyroidism or transient thyroid suppression have been reported following iodinated contrast media administration to adult and paediatric patients, including infants. Some patients were treated for hypothyroidism. See also section on Paediatric population.

Myasthenia gravis

The administration of iodinated contrast media may aggravate myasthenia signs and symptoms.

CNS Disorders and neurological symptoms

Particular care is needed in patients with acute cerebral infarction, acute intracranial haemorrhage and any conditions involving damage to the blood brain barrier, brain oedema or acute demyelination. Convulsive seizures are more likely in patients with intracranial tumours or metastases or with a history of epilepsy.

Neurological symptoms related to cerebrovascular diseases, intracranial tumours/metastases or degenerative ischaemic or inflammatory pathologies may be exacerbated by CM adminitsration. There is an increased risk of transient neurological complications in these patients , and those with symptomatic cerebrovascular disease (e.g. stroke, transient ischaemic attacks).
Vasospasm and consequent cerebral ischaemic phenomena may be caused by intravascular injection of CM.
Anticonvulsant therapy should not be discontinued.

Contrast induced encephalopathy
Encephalopathy has been reported with the use of iomeprol (see section 4.8).
Contrast encephalopathy may manifest with symptoms and signs of neurological dysfunction such as headache, visual disturbance, cortical blindness, confusion, seizures, loss of coordination, hemiparesis, aphasia, unconsciousness, coma and cerebral oedema within minutes to hours after administration of iomeprol, and generally resolves within days.
The product should be used with caution in patients with conditions that disrupt the integrity of the blood brain barrier (BBB), potentially leading to increased permeability of contrast media across the BBB and increasing the risk of encephalopathy. If contrast encephalopathy is suspected, administration of iomeprol should be discontinued and appropriate medical management should be initiated.

In acute and chronic alcoholism the increase in blood brain barrier permeability facilitates the passage of the contrast medium into cerebral tissue possibly leading to CNS disorders. There is a possibility of a reduced seizure threshold in alcoholics.

In patients with a drug addiction there is also the possibility of a reduced seizure threshold.

Severe cutaneous adverse reactions
Severe cutaneous reactions (SCARs) including Steven-Johnson (SJS), toxic epidermal necrolysis (TEN), acute generalized exanthematous pustulosis (AGEP) and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported in association with the intravascular administration of iodinated contrast agents (see Section 4.8). At the time of administration patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, Iomeron should be stopped immediately. If the patient has developed a serious reaction such as SJS, TEN, AGEP or DRESS with the use of Iomeron, administration of Iomeron must not be restarted to this patient at any time.

Phaeochromocytoma
Patients with phaeochromocytoma may develop severe, occasionally uncontrollable hypertensive crises during intra-arterial administration. Premedication with an alpha and beta receptor blocker is recommended in these patients.

Pronounced excitement, anxiety and pain can cause side effects or intensify reaction to the contrast medium. A sedative may be given.

Renal impairment
In patients with moderate to severe impairment of renal function, attention should be paid to renal function parameters before re-examining the patient with a contrast media.

Preventive measures include:
- identification of high-risk patients;
- ensuring adequate hydration before CM administration, preferably by maintaining I.V. infusion before and during the procedure and until the CM has been cleared by the kidneys;
- avoiding whenever possible, the administration of nephrotoxic drugs or major surgery or procedure such as renal angioplasty, until the CM has been cleared;
- postponing a new contrast agent examination until renal function returns to the same level as before the examination.

Contrast media may cause transient renal impairment that may precipitate lactic acidosis in diabetic patients treated with biguanides (see section 4.5).

Paediatric population

Thyroid Dysfunction in Pediatric Patients 0 to 3 Years of Age

Thyroid dysfunction characterized by hypothyroidism or transient thyroid suppression has been reported after both single exposure and multiple exposures to iodinated contrast media (ICM) in pediatric patients 0 to 3 years of age.

Younger age, very low birth weight, prematurity, underlying medical conditions affecting thyroid function, admission to neonatal or pediatric intensive care units, and congenital cardiac conditions are associated with an increased risk of hypothyroidism after ICM exposure. Pediatric patients with congenital cardiac conditions may be at the greatest risk given that they often require high doses of contrast during invasive cardiac procedures.

An underactive thyroid during early life may be harmful for cognitive and neurological development and may require thyroid hormone replacement therapy. After exposure to ICM, individualize thyroid function monitoring based on underlying risk factors, especially in term and preterm neonates.

Elderly

The elderly are at special risk of reactions due to CM high dosage. A combination of neurological disturbances and vascular pathologies present a serious complication.

Precautions for dedicated exams

Angiography

Non-ionic contrast media have less anticoagulant activity in vitro than ionic media. Meticulous attention should therefore be paid to angiographic technique. Non ionic media should not be allowed to remain in contact with blood in a syringe, and intravascular catheters should be flushed frequently to minimise the risk of clotting which, rarely, has led to serious thromboembolic complications.

Intravascular administration should be performed, if possible, with the patient lying down. The patient should be kept in this position and closely observed for at least 30 minutes after the procedure since the majority of severe incidents occur with this time.

4.5 Interaction with other medicinal products and other forms of interaction

Use of the product may interfere with tests for thyroid function.

Vasopressor agents should not be administered prior to iomeprol.

To prevent onset of lactic acidosis in diabetes patients under treatment with oral anti-diabetic agents of the biguanide class (Metformin), these agents should be stopped in the following scenarios; prior to an intraarterial contrast medium administration with first pass renal exposure, in patients with eGFR less than 30 ml/1.73m^2 receiving intravenous contrast medium, or intra-arterial contrast medium with second pass renal exposure, or in patients with acute kidney injury, and re-instated only after 48 hours if renal function has not changed significantly.

Allergy-like reactions to contrast media are more frequent and may manifest as delayed reactions in patients treated with immuno-modulators, like Interleukin-2 (IL-2).

Consider the discontinuation of treatment with drugs that lower the seizure threshold until 24 hours post-procedure for intrathecal use and patients with blood-brain barrier disorders (see CNS Disorders in section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies have not indicated any harmful effects with respect to the course of pregnancy or on the health of the unborn or neonate. The safety of iomeprol in human pregnancy however has not been established. Therefore avoid in pregnancy unless there is no safer alternative.

Since, wherever possible, exposure to radiation should be avoided during pregnancy, the benefits of any X-ray examination, whether with or without contrast material, should for this reason alone be carefully weighed against the possible risk.

In neonates who have been exposed to iodinated contrast media in utero, it is recommended to monitor thyroid function (see section 4.4).

Breastfeeding

No human data exist concerning the excretion of iomeprol in breast milk. Animal studies have demonstrated that the excretion of iomeprol in breast milk is similar to that of other contrast agents and that these compounds are only minimally absorbed by the gastrointestinal tract of the young. Adverse effects on the nursing infant are therefore unlikely to occur.

Stopping breastfeeding is unnecessary.

4.7 Effects on ability to drive and use machines

There is no known effect on the ability to drive and operate machines.

4.8 Undesirable Effects

General

The use of iodinated contrast media may cause untoward side effects. They are usually mild to moderate and transient in nature. However, severe and life-threatening reactions sometimes leading to death have been reported. In most cases, reactions occur within minutes of dosing but at times reactions may occur at later time.

Anaphylaxis (anaphylactoid/hypersensitivity reactions) may manifest with various symptoms, and rarely does any one patient develop all the symptoms. Typically, in 1 to 15 min (but rarely after as long as 2 h), the patient complains of feeling abnormal, agitation, flushing, feeling hot, sweating increased, dizziness, increased lacrimation, rhinitis, palpitations, paresthesia, pruritus, sore throat and throat tightness, dysphagia, cough, sneezing, urticaria, erythema, mild localised oedema, angioneurotic oedema and dyspnoea due to glottic/laryngeal/ pharyngeal oedema and/or spasm manifesting with wheezing and bronchospasm.
Nausea, vomiting, abdominal pain, and diarrhoea are also reported.
These reactions, which can occur independently of the dose administered or the route of administration, may represent the first signs of circulatory collapse.
Administration of the contrast medium must be discontinued immediately and, if needed, appropriate specific treatment urgently initiated via venous access.
Severe reactions involving the cardiovascular system, such as vasodilatation, with pronounced hypotension, tachycardia, dyspnoea, agitation, cyanosis and loss of consciousness progressing to respiratory and/or cardiac arrest may result in death. These events can occur rapidly and require full and aggressive cardio-pulmonary resuscitation.
Primary circulatory collapse can occur as the only and/or initial presentation without respiratory symptoms or without other signs or symptoms outlined above.

The adverse reactions reported in clinical trials among 4,903 adult patients and from post-marketing surveillance are represented in the tables below by frequency and classified by MedDRA system organ class. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

4.8.1 Intravascular administration

Adult patients involved in clinical trials with intravascular administration of Iomeprol were 4,739.

Adults

System Organ Class	Adverse Reactions			
	Clinical Trials			Post-marketing Surveillance
	Common (≥1/100 to <1/10)	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10,000 to <1/1000)	Frequency unknown*
Blood and lymphatic system disorders				Thrombocytopenia Haemolytic anaemia
Immune system disorders				Anaphylactoid reaction
Endocrine disorders				Hyperthyroidism
Psychiatric disorders				Anxiety Confusional state
Nervous system disorders		Headache Dizziness	Presyncope	Coma Transient ischaemic attack Paralysis Syncope Convulsion Loss of consciousness Dysarthria Paresthesia Amnesia Somnolence Taste abnormality Contrast induced encephalopathy***
Eye disorders				Blindness transient Visual disturbance Conjunctivitis Lacrimation increased Photopsia
Cardiac disorders			Bradycardia Tachycardia Extrasystoles	Cardiac arrest Myocardial infarction Cardiac failure Angina pectoris Arrhythmia Ventricular or atrial fibrillation Atrioventricular block
Vascular disorders		Hypertension	Hypotension	Circulatory collapse or shock Flushing Pallor Cyanosis Coronary artery thrombosis Coronary artery embolism Vasospasm**** Ischemia****
Respiratory, thoracic and mediastinal disorders		Dyspnoea		Respiratory arrest Acute respiratory distress syndrome (ARDS) Pulmonary oedema Laryngeal oedema Pharyngeal oedema Bronchospasm Asthma Cough Pharynx discomfort Laryngeal discomfort Rhinitis Dysphonia

System Organ Class	Adverse Reactions			
	Clinical Trials			Post-marketing Surveillance
	Common (≥1/100 to <1/10)	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10,000 to <1/1000)	Frequency unknown*
Gastrointestinal disorders		Nausea Vomiting		Diarrhoea Abdominal pain Salivary hypersecretion Dysphagia Salivary gland enlargement
Skin and subcutaneous tissue disorders		Erythema Urticaria Pruritus	Rash	Acute generalized exanthematous pustulosis Angioedema Sweating increased Stevens-Johnson's syndrome Toxic epidermal necrolysis Erythema multiforme Drug Reaction with Eosinophilia and Systemic Symptoms
Musculoskeletal and connective tissue disorder			Back pain	Arthralgia
Renal and urinary disorders				acute kidney injury*****
General disorders and administration site conditions	Feeling hot	Chest pain Injection site warmth and pain	Asthenia Rigors Pyrexia	Injection site reaction** Coldness local Malaise Thirst
Investigations			Blood creatinine increased	Electrocardiogram ST segment elevation Electrocardiogram abnormal

* Since the reactions were not observed during clinical trials with 4,739 patients, best estimate is that their relative occurrence is rare (≥1/10,000 to <1/1000).

The most appropriate MedDRA term is used to describe a certain reaction and its symptoms and related conditions.

** Injection site reactions comprise injection site pain and swelling. In the majority of cases they are due to extravasation of contrast medium. These reactions are usually transient and result in recovery without sequelae. Cases of extravasation with inflammation, skin necrosis and even development of compartment syndrome have been reported.

***Encephalopathy may manifest with symptoms and signs of neurological dysfunction such as headache, visual disturbance, cortical blindness, confusion, seizures, loss of coordination, hemiparesis, aphasia, unconsciousness, coma, brain oedema.

**** Vasospasm and consequent ischaemia have been observed during intra-arterial injections of contrast medium, in particular after coronary and cerebral angiography often procedurally related and possibly triggered by the tip of the catheter or excess catheter pressure.

*****Transient renal failure with oliguria, proteinuria and an increase in serum creatinine may develop, particularly in patients with impaired renal function. In case of extravasal injection a tissue reaction may develop in rare cases.

Paediatric patients

There is limited experience with paediatric patients. The clinical trial paediatric safety database comprises 184 patients. The Iomeprol safety profile is similar in children and adults.

Transient hypothyroidism may occur in neonates, especially in preterm or low birth weight neonates, and children (0-3 years), when exposed to iomeprol.

4.8.2 Administration to body cavities

After injection of an iodinated contrast media in body cavities, contrast media are slowly absorbed from the area of administration into the systemic circulation and subsequently cleared by renal elimination.

Blood amylase increased is common following ERCP. Very rare cases of pancreatitis have been described.

The reactions reported in cases of arthrography and fistulography usually represent irritative manifestations superimposed on pre-existing conditions of tissue inflammation.

Hypersensitivity reactions are rare, generally mild and in the form of skin reactions. However, the possibility of severe anaphylactoid reactions cannot be excluded.

As with other iodinated contrast media, pelvic pain and malaise may occur after hysterosalpingography.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

4.9 Overdose

The effects of overdose on the pulmonary and cardiovascular systems may become life-threatening. Treatment consists of support of the vital functions and prompt use of symptomatic therapy. Iomeprol does not bind to plasma or serum proteins and is therefore dialyzable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: V08AB10

Iomeprol is a low osmolality, non-ionic organic molecule with radio-opacity conferred by an iodine content of 49% of the molecular weight. It is formulated for use as an intravascular/intracavitary contrast medium in concentrations of up to 400mg iodine per ml. Even at this concentration the low viscosity allows delivery of high doses through thin catheters.

5.2 Pharmacokinetic properties

The pharmacokinetics of intravascularly administered iomeprol are similar to those of other iodinated contrast media and conform to a two-compartment model with a rapid distribution and a slower elimination phase. In healthy subjects, the mean distribution and elimination half-lives of iomeprol were 0.5 hours and 1.9 hours respectively.

Distribution volume is similar to that of extra cellular fluid. There is no significant serum protein binding and iomeprol is not metabolized.

Elimination is almost exclusively through the kidneys (90% of the dose recovered in the urine within 96 hours of its administration) and is rapid (50% of an intravascularly administered dose within 2 hours).

5.3 Preclinical safety data

Pre-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction.

Results from studies in rats, mice and dogs demonstrate that iomeprol has an acute intravenous or intra-arterial toxicity similar to that of the other non-ionic contrast media, as well as a good systemic tolerability after repeated intravenous administrations in rats and dogs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Trometamol, hydrochloric acid 32%, water for injection.

6.2 Incompatibilities
No other drug should be mixed with the contrast medium.

6.3 Shelf life
The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage
Protect from light.

6.5 Nature and contents of container
Colourless Type I glass vials or bottles.
Pack sizes:
Iomeron 300: 50, 75, 100, 200 or 500 ml of solution.
Iomeron 350: 100, 250 or 500 ml of solution.
Iomeron 400: 50, 75, 100 or 200 ml of solution.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Bottles containing contrast media solution are not intended for the withdrawal of multiple doses. The rubber stopper should never be pierced more than once. The use of proper withdrawal cannulae for piercing the stopper and drawing up the contrast medium is recommended.

Before use, examine the product to assure that the container and closure have not been damaged. Do not use the solution if it is discoloured or particulate matter is present.

The contrast medium should not be drawn into the syringe until immediately before use. Withdrawal of contrast agents from their containers should be accomplished under aseptic conditions with sterile syringes.
Sterile techniques must be used with any intravascular injection, and with catheters and guidewires. If non-disposable equipment is used, scrupulous care should be taken to prevent residual contamination with traces of cleansing agents.

It is desirable that solutions of contrast media for intravascular use should be at body temperature when injected.

Any residue of contrast medium in the syringe must be discarded. Solutions not used in one examination session or waste material, such as the connecting tubes, should be disposed in accordance with local requirements.

Bottles of 500 ml should be used in conjunction with an injector system. After each patient examination, the connecting tubes (to the patient) and relevant disposable parts should be disposed because they could be contaminated with blood.
At the end of the sessions, the left over solution in the bottle and in the connecting tubes as well as any disposable parts of the injector system should be discarded. Any additional instructions from the respective equipment manufacturer must also be adhered to.

7. MARKETING AUTHORISATION HOLDER

Dexcel Ltd., 1 Dexcel street, Or Akiva 3060000, Israel

8. MARKETING AUTHORISATION NUMBERS

Iomeron 300: 103-45-28521-11
Iomeron 350: 103-46-28522-11
Iomeron 400: 103-47-28523-11

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