1 PRODUCT NAME

IOMERON® (iomeprol) solution for injection 300 mg iodine per mL
IOMERON® (iomeprol) solution for injection 350 mg iodine per mL
IOMERON® (Iomeprol) solution for injection 400 mg iodine per mL

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Iomeprol 612 mg / mL (equivalent to 300 mg iodine per mL)
Iomeprol 714 mg / mL (equivalent to 350 mg iodine per mL)
Iomeprol 816 mg (equivalent to 400 mg iodine per mL)

Excipients:
Trometamol (tromethamine USP), hydrochloric acid (Ph.Eur.), water for injection (Ph.Eur.).

3 PHARMACEUTICAL FORM

Solution for injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

IOMERON® contains as its active principal iomeprol, a tri-iodinated, non-ionic contrast agent, and is for use in X ray examinations:

Iomeron 300: Intravenous urography (in adults and paediatrics), peripheral phlebography, CT (brain and body), cavernosography, intravenous DSA, conventional angiography, intra-arterial 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-ureterograpy, myelography.

Iomeron 350: *Intravenous urography (in adults and paediatrics), CT (body), intravenous DSA, conventional angiography, intra-arterial 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, intra-arterial 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, MCU: Micturating Cisto-Urethrography

4.2 Dose and method of administration

Indication	*Formulation mg (iodine)/mL*	*Proposed dosages*
Intravenous urography	300,350,400	Adults: 50 – 150 mL Neonates: 3 – 4.8 mL/kg Babies: 2.5 – 4 mL/kg Children: 1 – 2.5 mL/kg[a]
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 Children[a]
CT body	300,350,400	Adults: 100-200mL Children[a]
Cavernosography	300	Adults: Up to 100 mL
Intravenous DSA	300,350,400	Adults: 100 – 250 mL Children[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	Children: Up to 130mL[a]
Interventional	300,350,400	Adults[b] Children[a]

Indication	*Formulation mg (iodine)/mL*	*Proposed dosages*
Intra-arterial DSA		
Cerebral	300,350	Adults: 30 - 60 mL for general view; 5 - 10 mL for selective injections Children[a]
Thoracic	300	Adults[b]: 20 - 25 mL (aorta) repeat as necessary 20 mL (bronchial arteries)
Aortic arch	300,350	Adults[c]
Abdomen	250,300	Adults[c]
Aortography	300,350	Adults[c]
Trans-lumbar aortography	300	Adults[b]
Peripheral arteriography	300	Adults: Adults: 5 - 10 mL for selective injections up to 250 mL Children[a]
Interventional	300	Adults: 10-30 mL for selective injections up to 250 mL Children[a]
Angiocardiography	300,350,400	Adults[b] Children: 3-5 mL/kg
Conventional selective coronary arteriography	300,350,400	Adults: 4-10 mL 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

Indication	*Formulation mg (iodine)/mL*	*Proposed dosages*
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 pyelo-ureterography	300	Adults: 10 - 20 mL per injection
Myelography	300	Adults: 13-22 mL 10-18 mL 8-15 mL

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

4.3 Contraindications

There are no precise and absolute contraindications to the use of Iomeron.
Investigations of the female genitalia are contraindicated in suspected or confirmed pregnancy and in cases of acute inflammation.

4.4 Special warnings and precautions for use

In consideration of possible serious side effects, the use of organoiodinate contrast media should be limited to cases for which there is a precise need for contrastographic examination. The need should be evaluated on the basis of the clinical status of the patient, in particular in relation to pathologies on the cardiovascular, urinary or hepatobiliary systems. The use should be avoided in case of Waldenstroem's paraproteinemia, multiple myeloma and severe liver or renal impairment.

Contrast media designed for angiocardiographic procedures should be used in hospitals or clinics equipped and staffed for intensive care in emergencies. For other more common diagnostic procedures calling for the use of iodinized contrast media, in the institutions, where such procedures are to take place, resuscitation equipment and therapeutic measures should be immediately available.

Use in:
Neonates, infants, children. Young infants (age < 1 year) especially neonates are particularly susceptible to electrolyte imbalances and haemodynamic alterations. Care should be taken regarding the dosage to be used, the details of the procedure and the patient's status.
Elderly. The elderly are at special risk of reactions due to CM high dosage. Myocardial ischemia, major arrhythmias and extrasystoles are more likely to occur in these patients. The frequently encountered combination of neurological disturbances and severe vascular pathologies constitutes a serious complication. The probability of acute renal insufficiency is higher in these subjects.

Use in patients with specific pathologic conditions

Hypersensitivity to iodinated contrast media. Hypersensitivity or a previous history of a reaction to iodinated contrast media also increases the risk of recurrence of a severe reaction with non-ionic media.

Allergic disposition. It is generally agreed that adverse reactions to iodinated contrast media are more common in patients having a history of allergy: hay fever, hives and food allergy.

Asthmatic patients. The risk of bronchospasm - inducing reactions in asthmatic patients is higher after contrast media administration.

Hyperthyroidism, nodular goitre. 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 hyperthyroidism or goitre. Thyroid storms have been reported following administration of ionic contrast media.

Intra-arterial and intravenous administration

Use in patients with specific pathologic conditions

Renal failure. Preexisting renal impairment may predispose to acute renal disfunction following contrast media administration. 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 pre-examination levels. Patients on dialysis may receive CM, such as iomeprol, which may be cleared by dialysis.

Diabetes mellitus. The presence of renal damage in diabetic patients is one of the factors predisposing to renal impairment following CM administration. This may precipitate lactic acidosis in patients who are taking biguanides. As a precaution, biguanides should be stopped 48 hours prior to the CM examination and reinstated only after control of renal function has been regained.

Multiple myeloma, paraproteinaemia. The use of the product is generally contraindicated. It is necessary to consider that the presence of myelomatosis or paraproteinaemias is a factor predisposing to renal impairment following CM administration. Adequate hydration is recommended.

Phaeochromocytoma. These patients may develop severe (rarely uncontrollable) hypertensive crises following intravascular CM-usage during radiological procedures.

Severe liver and renal dysfunctions. The use of the product is generally contraindicated. It is necessary to consider that a combination of severe hepatic and renal impairment can delay CM excretion, therefore predisposing to untoward reactions.

Severe cardiovascular disease. There is an increased risk of severe reactions in individuals with severe cardiac disease and particularly in those with heart failure and coronary artery disease. The intravascular CM injection may precipitate pulmonary oedema in patients with manifest or incipient heart failure, whereas CM administration, in pulmonary hypertension and heart valvular diseases, may lead to pronounced haemodynamic changes. Ischaemic ECG changes and major arrhythmias are commonest in elderly patients and in those with preexisting cardiac disease: their frequency and severity appear to be related to the severity of cardiac impairment. Severe and chronic hypertension may increase the risk of renal damage following CM administration and the risks associated with the catheterisation procedure.

CNS disorders. Particular care should be paid to the intravascular administration of CM in patients with acute cerebral infarction, acute intracranial haemorrhage, and conditions involving bloodbrain-barrier (BBB) damage, brain oedema and acute demyelination. The presence of intracranial tumors or metastases and a history of epilepsy may increase the probability of the occurrence of convulsive seizures. Neurological symptoms due to degenerative, inflammatory or neoplastic cerebrovascular pathologies may be exacerbated by CM administration. Vasospasm and consequent cerebral ischaemic phenomena may be caused by intravascular injections of CM.
Patients with symptomatic cerebrovascular diseases, recent stroke or frequent TIA (transient ischaemic attack) have an increased risk of transient neurological complications.

Alcoholism. Acute and chronic alcoholism have been proven both experimentally and clinically to increase BBB permeability. This facilitates the passage of iodinated agents into the cerebral tissue, possibly leading to CNS disorders.
Caution must be exercised in alcoholics because of the possibility of a reduced seizure threshold.

Drug addiction. Caution must be exercised in drug addicts because of the possibility of a reduced seizure threshold.

<u>In relation to the patient</u>

Hydration. Any severe disorders of water and electrolyte balance should be corrected. Especially in patients with multiple myeloma, diabetes mellitus, polyuria, oliguria, hyperuricemia, as well as in babies, small children and elderly patients adequate hydration must be ensured before examination.

Dietary suggestions. Unless otherwise instructed by the doctor, a normal diet may be maintained on the day of the examination. Adequate fluid intake must be ensured. However, for two hours prior to the procedure the patient should refrain from eating.

Premedication. In patients with phaeochromocytoma premedication with alpha-receptor blockers is recommended because of the risk of blood pressure crises.

History of hypersensitivity. In patients with an allergic disposition, known hypersensitivity to iodinated contrast media and a history of asthma, premedication with antihistamines and/or corticoids may be considered in order to prevent possible anaphylactoid reactions.

Anxiety. Pronounced states of excitement, anxiety and pain can be the cause of side effects or intensify contrast-related reactions. These patients may be given a sedative.

Co-medication. Neuroleptics and antidepressants should be discontinued 48 hours before the examination because they reduce the seizure threshold. Treatment should not be resumed until 24 hours post-procedure. Anticonvulsant therapy must not be discontinued and should be administered in optimal dosage.

In relation to the procedure

Coagulation, Flushing of catheters. A property of non-ionic contrast media is the extremely low interference with normal physiological functions. As a consequence of this non-ionic contrast media have less anti-coagulant activity in-vitro than ionic media. Medical personnel performing vascular catheterisation procedures should be aware of this and pay meticulous attention to the angiographic technique and catheter flushing so as to minimize the risk of procedure-related thrombosis and embolism.

Observation of the patient. Intravascular administration of contrast media should, if possible, be done with the patient lying down. The patient should be kept under observation for at least 30 minutes, after the administration.

Pretesting. Sensitivity test doses are not recommended since severe or fatal reactions to contrast media are not predictable from a patient's history or a sensitivity test.

4.5 Interaction with other medicines and other forms of interaction

Thyroid function tests. Following administration of iodinated contrast media, the capacity of the thyroid tissue to take up radioisotopes for the diagnosis of thyroid disorders is reduced for up to two weeks, or even longer in individual cases.

Laboratory tests. High concentrations of contrast media in serum and urine can interfere with laboratory test results of bilirubin, proteins or inorganic substances (e.g. iron, copper, calcium, phosphate).

Interactions with oral cholecystographics. Literature search has revealed no evidence of interactions of renally excreted contrast media with oral cholecystographics contrast media.

4.6 Fertility, pregnancy and lactation

Animal studies have not shown any teratogenicity or embryotoxicity after iomeprol administration. As with other non-ionic contrast media, there are no controlled studies in pregnant women to confirm the safety for use in humans too. 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.

Contrast media are poorly excreted in human breast milk. From experience gained so far, harm to the nursing infant is unlikely to occur.

4.7 Effects on ability to drive and use machines

No data are available but, since delayed reactions can rarely occur after administration of iodinatedcontrast media, driving or operating machinery is not advisable for the first 24 hours following (contrast medium) CM examination.

4.8 Undesirable effects

The use of iodinated compounds may cause untoward effects, which are generally of mild or moderate nature, as well as more severe ones, with possible fatal anaphylactoid reactions.
Mild and moderate symptoms include heat and pain sensation (site of injection, chest, back), chills, fever, asthenia, dizziness, fainting, nausea, vomiting, sweating, pallor, dyspnoea, moderate hypotension, widespread erythema, and oedema. Furthermore agitation, headache, laryngeal oedema or nasal congestion have been described.

Skin reactions may be present in the form of acute generalized exanthematous pustulosis (AGEP), diversified rashes or diffuse pomphus formation, and sometimes itching.

More severe effects may involve the cardiovascular system, including peripheral vasodilation with pronounced hypotension, hypertension, tachycardia or bradycardia, cyanosis, dyspnea and circulatory collapse.

The intravenous or intra-arterial injection of contrast agents may cause symptoms related to CNS disturbances: tremor, muscular spasms, mental confusion, loss of consciousness, disturbances of visual field, muscular palsies, aphasia, convulsive seizures, and coma. However symptoms are usually mild, of short duration and self-limiting. More severe neurological sequelae may be the result of complications of a pre-existing pathology.

A transient renal failure with oliguria, proteinuria and an increase of serum creatinine level may arise, particularly in patients with pre-existing impairment of renal function.

Pain, haemorrhage and oedema may arise at the site of injection. In the case of extravasation a tissue reaction may ensue, but this is rare.

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/}

4.9 Overdose

Overdose may lead to life-threatening adverse effects mainly through effects on the pulmonary and cardiovascular system. For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

Treatment

Treatment of overdosage is directed toward the support of all vital functions, and prompt institution of symptomatic therapy. Iomeprol does not bind to plasma or serum proteins and is therefore dialyzable.

LD_{50} values (g iodine/kg) for iomeprol in animals are:

Intravenous administration:	19,9 (19,3 – 20,5) (mouse) 14,5 (13,2 - 16,0) (rat) >12,5 (dog)
intraperitoneal:	26,1 (13,1 - 29,2) (mouse)

	10 (8,9 - 11,3) (rat)
Intracerebral:	1,3 (1,2 - 1,5) (mouse)
Intracisternal:	> 1,2 (rat)
Intracarotid:	5,8 (4,64 - 7,25) (rat)

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

IOMERON® contains as its active principal iomeprol, a tri-iodinated, non-ionic contrast agent, and is for use in X ray examinations

5.2 Pharmacokinetic properties

The pharmacokinetics, tolerability and diagnostic efficacy of iomeprol in solutions containing up to 400 mg iodine/ml have been determined in healthy volunteers and patients requiring urographic, angiographic, computed tomography (CT) and body cavity examinations. There were no clinically significant changes in laboratory test values and vital signs.

The pharmacokinetics of iomeprol, for intravascular administration, when described by a two-compartment model, shows a rapid phase for drug distribution and a slower phase for drug elimination. In 18 healthy volunteers the mean half-lives of the distribution and elimination phases of iomeprol were 23 ± 14 (s) min and 109 ± 20 (s) min, respectively, with an excretion of 50% by the urinary tract within 2 hours after the administration.

5.3 Preclinical safety data

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. After intravenous administration in rats iomeprol is distributed between plasma and the extracellular space. It does not bind to plasma proteins. It is not metabolised and is eliminated almost exclusively through the kidneys. In the rat 94% of the administered dose is found unchanged in the urine within the first 8 hours.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Iomeprol, trometamol (tromethamine USP), hydrochloric acid (Ph.Eur.) and water for injection (Ph.Eur.).

6.2 Incompatibilities

In order to avoid possible incompatibilities, contrast media must not be mixed with other drugs.

6.3 Shelf life

Five years.

6.4 Special precautions for storage

Protect from light. Although the sensitivity of iomeprol to X-rays is low, it is advisable to store the product out of reach of ionizing radiation.

Vials 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 cannulas for piercing the stopper and drawing up the contrast medium is recommended. The contrast medium should not be drawn into the syringe until immediately before use. Solutions not used in one examination session must be discarded.

6.5 Nature and contents of container

Iomeron is packaged in bottles made of Type II glass (Ph.Eur). The bottles are closed with halobutyl stoppers and an aluminium crimp seal.

IOMERON 300	Vials 20 mL Bottles 50 mL Bottles 100 mL
IOMERON 350	Bottles 50 mL Bottles 100 mL Bottles 200 ml
IOMERON 400	Bottles 50 mL Bottles 100 mL

6.6 Special precautions for disposal

None

7 MEDICINE SCHEDULE

General Sale Medicine

8 SPONSOR

Regional Health Limited
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North Shore Mail Centre
Auckland
Ph: (09) 414-0040, Fax: (09) 414-0041

9 DATE OF FIRST APPROVAL

9 June 1994

10 DATE OF REVISION OF THE TEXT

19 March 2019

SUMMARY OF CHANGES

Format amended to the current European SmPC specification using Medsafe template v 1.1 March 2017. No changes to text.