

Bracco. The contrast imaging specialists.

Trust Experience Choose Confidence



IOPAMIRO

iopamidol injection



Committed to Science,
Committed to You.™

- More than **2000 studies published** in peer-reviewed journals¹
- More than **380 million doses** administered worldwide¹
- **Approved in a wide range of indications (including pediatric), concentration and volumes²**
- **Proven short-term and long-term safety profile in patients with moderate-to-severe chronic kidney disease^{3,4,5,6}**

Concentration		ph	Viscosity (m Pa.s)		Density		Osmolality (mosm/g)	Osmotic pressure (atm.)
Iodine (mg/ml)	Iopamidol (g/100ml)		20°C	37°C	20°C	37°C	37°C	37°C
300	61.2	7±0.5	88	4.7	1.335	1.328	0.62	15.7
370	75.5	7±0.5	20.9	9.4	1.415	1.405	0.80	20.3

References: 1) Data on file 2) SPC 3) Solomon RJ et al. Cardiac Angiography in Renally Impaired Patients (CARE) study: a randomized double-blind trial of contrast-induced nephropathy in patients with chronic kidney disease. *Circulation*. 2007;26;115(25):3189-96. Epub 2007 Jun 11 4) Barrett BJ et al. Contrast-induced nephropathy in patients with chronic kidney disease undergoing computed tomography: a double-blind comparison of iodixanol and iopamidol. *Invest Radiol*. 2006;41:815-821. 5) Kuhn MJ et al. The PREDICT study: a randomized double-blind comparison of contrast-induced nephropathy after low- or isoosmolar. *AJR Am J Roentgenol*. 2008;191(1):151-7 6) Solomon RJ et al. The CARE Follow-up Study. Contrast-induced nephropathy and long-term adverse events: cause and effect? *Clin J Am Soc Nephrol*. 2009 Jul;4(7):1162-9



LIFE FROM INSIDE

IOPAMIRO® IOPAMIDOL - CORE SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT IOPAMIRO® IOPAMIRON® ISOVUE® SOLUSTRAS® JOPAMIRO® JOPAMIRON® NIOPAM® mg/ml injectable solution. (The trade name is different in different countries; please also see section 7).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Active ingredient	IOPAMIRO injection®	
	300 mg/ml injectable solution	370 mg/ml injectable solution
IOPAMIDOL	612.4	755.3

3. PHARMACEUTICAL FORM

injectable solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications: non-ionic, water-soluble contrast medium for radiological diagnostic procedures.

4.1.1 Neuroradiology: - Myelographic - Cisternography and Ventriculography

4.1.2.1 Angiography: - Cerebral angiography - Coronary angiography - Thoracic aortography - Abdominal aortography - Angiocardiography - Selective visceral arteriography - Peripheral arteriography - Venography

4.1.2.2 Digital subtraction angiography (D.S.A.): - cerebral artery D.S.A., peripheral artery D.S.A., abdominal D.S.A.

4.1.3 Urography: - Intravenous urography.

4.1.4 Other indications: Contrast enhancement in C. T. (computerized axial tomography) and Arthrography - Fistulography - Hysterosalpingography

4.2 Posology and method of administration

4.2.1 Neuroradiology:

4.2.2 Angiography:

	Concentration (mg l/ml)	Recommended dose (ml)
Cerebral angiography	300	5-10 per bolus
Coronary angiography	370	8-15 per bolus
Angiocardiography	370	1.0-1.2/kg
Thoracic aortography	370	1.0-1.2/kg
Abdominal aortography	370	1.0-1.2/kg
Selective visceral arteriography	300-370	according to examination
Peripheral arteriography	300-370	40-50
Digital subtraction angiography	150-370	according to examination
Venography	300	30-50

4.2.3 Urography: The recommended dose for this type of examination is 30-50 ml in adults. The reduced induction of osmotic diuresis makes Iopamidol injection® 370 mg/ml injectable solution particularly suitable for patients with mild or moderate renal insufficiency and neonates. Diagnostically useful nephrography may be obtained even in patients with severe renal insufficiency.

4.2.4 Other diagnostic procedures:

	Concentration (mg l/ml)	Recommended dose (ml)
Contrast enhancement in C.T.	300-370	0.5-2/kg
Arthrography	300	
Fistulography	300	
Hysterosalpingography	200-300-370	5-20

For contrast enhancement in C.T. scans, the contrast medium may be injected intravenously as a bolus, by infusion or by a combination of the two. For hysterosalpingography, the total dose to be injected depends on the patient's anatomical, biological and pathological condition.

4.3 Contra-indications: There are no specific absolute contraindications for use of these substances, with the realistic exception of Waldenström's macroglobulinemia, multiple myeloma and severe liver or kidney diseases. The intrathecal use of organic iodized contrast media may be contraindicated for patients with a history of epilepsy. The presence of blood in the cerebral spinal fluid also contraindicates the use of Iopamidol injection®. In this case, the operator should carefully assess the need for the diagnostic procedure against any possible risks to the patient. Female genital tract examination is contraindicated during confirmed or suspected pregnancy and in the case of acute inflammation.

4.4 Special warnings and special precaution for use: Once opened, the bottle must be used immediately; any remaining contrast medium must be discarded. Crystals may occasionally be found in a bottle of Iopamidol injection® solution. It has been demonstrated that this is caused by a damaged or defective container, and the contents should therefore not be used. Iopamidol injection®, as with other iodinated contrast media, may react with metal surfaces containing copper (e.g. brass), so the use of equipment where the product comes into direct contact with such surfaces should be avoided. Use of contrast media must be limited to cases where there is a precise clinical indication for the procedure. Products for cardioangiographic examination may only be administered in hospitals and clinics equipped and staffed for emergency intensive care. For other, more common diagnostic procedures requiring use of contrast agents, the radiological departments, whether public or private, should be supplied at all times with all equipment and drugs necessary for treatment of any emergency situation (Ambu balloon, oxygen, antihistamines, vasoconstrictors, cortisones, etc.). Do not limit fluid intake of babies and children and correct any water or electrolyte imbalance before use of hypertonic contrast media. Radiological examinations should only be performed in patients with hyperthyroidism if the attending physician considers it absolutely necessary. In patients scheduled for thyroid examination with radioactive iodine, bear in mind that iodine uptake by the thyroid gland will be reduced for several days, sometimes up to two weeks, after use of renally excreted iodized contrast medium.

4.4.1 Neuroradiological precautions: In the event of liquid flow blockage, remove as much of the contrast agent as possible. Patients under treatment with anticonvulsants must continue treatment before and after the radiological examination. Should a convulsive seizure occur during the examination, intravenous administration of diazepam or sodium phenobarbital is recommended.

4.4.2 Angiography precautions: Advanced arteriosclerosis, hypertension, heart failure, major systemic diseases, recent cerebral embolism or thrombosis increase the risk of severe side effects

with this type of examination. During the angiocardiographic examination, special attention should be paid to the condition of the right heart and pulmonary circulation; in the event of failure, additional volumes of contrast medium may provoke circulatory overload with bradycardia and systemic hypotension. Injection of contrast medium into the right heart of cyanotic neonates with pulmonary hypertension and impaired heart function requires particular caution. During aortic arch examination, careful positioning of the catheter tip is recommended. Excess pressure from the injector into the brachiocephalic branches may cause hypotension, bradycardia and CNS injury. Likewise, excess pressure from the automatic pump in abdominal aortography may cause renal infarction, spinal cord injury, retroperitoneal hemorrhage, and intestinal infarction and necrosis. In peripheral arteriography, use of Iopamidol injection® 370 mg/ml injectable solution may cause a painful reaction, which is not found with the "300" concentration. It has been demonstrated in vitro that at equal concentrations, nonionic contrast media have a lower inhibitory effect on coagulation activity than ionic contrast media. It is therefore necessary to follow angiographic procedures correctly: catheters must be frequently washed and prolonged contact between blood and the contrast medium in catheters and syringes must be avoided.

4.5 Interaction with other medicinal products and other forms of interaction: Do not mix other drugs with the contrast medium during injection.

4.5.1 Intrathecal application: Neuroleptics must be completely avoided, as they lower the seizure threshold. The same applies to analgesics, antihistamines and phenothiazine group sedatives. Wherever possible, treatment with such drugs should be suspended at least 48 hours before administration of the contrast medium and may be resumed not earlier than 12 hours after the examination.

4.6 Pregnancy and lactation: Radiological examinations should only be performed in pregnant women if the attending physician considers it absolutely necessary.

4.7 Effects on ability to drive and use machines: Nothing to report.

4.8 Undesirable effects: Use of organic iodine compounds may cause secondary undesired effects and anaphylactic or medication-type shock: nausea, vomiting, widespread erythema, generalized sensation of heat, headache or symptoms of coryza of laryngeal edema, fever, sweating, asthenia, dizziness, pallor, dyspnea, or mild hypotension. Skin reactions may occur as various types of rash or widespread blister formation. More severe reactions involving the cardiovascular system, such as peripheral vasodilation with pronounced hypotension, tachycardia, dyspnea, agitation, cyanosis and loss of consciousness may require emergency treatment.

4.8.1 Neuroradiology: Clinical studies have shown good general tolerability, especially by the central nervous system. Side effects have been reported: headache, sometimes with delayed onset, nausea, vomiting, pain at the injection site, generally mild and of short duration; more rarely, dizziness, neck stiffness, lumbar pain, sciatic-type pain in the legs, often as transient worsening of existing symptoms, and temperature increase. Exceptionally, patients have developed muscle spasms or generalized convulsions, sometimes relating to an epilepsy under treatment with neuroleptics and involuntary overdose. Very rare cases of transitory mental confusion have been observed.

4.8.2 Angiography: Use of Iopamidol in cerebral angiography may provoke side effects, generally mild and of short duration. A sense of heat around the face and neck is often experienced. Headache is rarely reported. Cardiovascular reactions may be common: transitory bradycardia and systemic hypotension, not requiring treatment. It should be borne in mind that severe neurological reactions may arise as direct complications of existing patient pathologies. These reactions may vary and include tonic/clonic convulsions, aphasia, fainting, transient narrowing of field of vision, hemiparesis and coma. In peripheral arteriography, use of Iopamidol injection® 370 mg/ml injectable solution may cause a painful reaction, which is not experienced with the "300" concentration.

4.8.3 Urography: Side effects which may arise in connection with intravenous urography are as described in paragraph 4.8.

4.8.4 Other diagnostic procedures: Reactions reported for arthrography and fistulography are usually related to worsening of an existing inflammatory condition. Vaso-vagal manifestations may arise during hysterosalpingography.

4.9 Overdose: Most side effects (see point 4.8) are not dose-dependent and may require therapeutic intervention as specified in point 4.4. In the event of voluntary or accidental administration of higher than normal doses, excretion should be facilitated by ensuring patient hydration, as clearance almost totally occurs via the kidney. In the event of renal insufficiency, whether pre-existing or manifesting after contrast medium introduction, dialysis will eliminate the contrast medium.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties: Pharmacotherapeutic category: Radiological contrast media: hydrosoluble, nephrotropic, low osmolality. ATC code: V08AB04 Iopamidol is a non-ionic radio-opaque hydrosoluble substance with strongly reduced toxicity and no teratogenic effects. Its use at doses 2 to 4 times higher than for clinical use provoked transient bradycardia and hypotension in dogs, followed by mild hypertension and increased respiratory frequency. Base values were returned to in 2-4 minutes.

5.2 Pharmacokinetic properties: Excretion: the vast majority is via renal route. In dogs, 93-95% of the administered dose was excreted renally and 0.5% through the biliary route in 7-10 hours. In humans, more than 90% of the dose is excreted by the urinary route in 24 hours. Blood half life in the excretion phase (T • B) is approximately 60 minutes in dogs and 90-120 minutes in humans. Intrathecal administration leads to circulation in the blood, peaking from 90-150 mins, with almost total excretion within 24 hours. Iopamidol does not undergo detectable metabolic processes in animals or humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients: Trometamol, Sodium calcium edetate, Hydrochloric acid (d=1.18), Water for injection

6.2 Incompatibilities: See point 4.5

6.3 Shelf life: 5 years

6.4 Special precautions for storage: The expiry date refers to the product stored correctly in intact packaging.

Protect from light. See point 4.4

6.5 Nature and contents of container: Type I or II glass vials or bottles with halobutyl stoppers and aluminium crimp seal.

6.6 Instruction for use/handling: See point 4.2.

7. MARKETING AUTHORISATION INFORMATION

The product name, the Marketing Authorisation Holder, Number, and Date of Approval may be different in different Countries. Volumes, presentations, and indications may also differ. Refer to Local Summary of Product Characteristics. Please contact Bracco Imaging SpA - Via Egidio Folli, 50 20134 Milano- Italy for further information.