SUMMARY OF PRODUCT CHARACTERISTICS

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1. NAME OF MEDICINAL PRODUCT

Iopamiro 150mg/ml solution for injection
Iopamiro 300 mg/ml solution for injection
Iopamiro 370 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Iopamiro 150 mg/ml solution for injection
Each ml contains 306.2 mg Iopamidol. 30.62 w/v Iopamidol equivalent to 150mg iodine/ml.

Iopamiro 300 mg/ml solution for injection
Each ml contains 612 mg iopamidol. 61.2% w/v Iopamidol equivalent to 300mg iodine/ml.

Iopamiro 370 mg/ml solution for injection
Each ml contains 755.3 mg Iopamidol. 75.5% w/v Iopamidol equivalent to 370mg iodine/ml.

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear aqueous solution filled into colourless glass ampoules or bottles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

X-ray contrast medium in neuroradiology, angiography, urography, CT scanning, arthrography and fistulography.
Iopamiro 150 is also indicated for pediatric radiology.

4.2 Posology and method of administration

Neuroradiology

	Concentration (mg I/ml)	Recommended Dose (ml)
mieloradiculography	300	5-15
cisternography and ventriculography	300	5-15

Angiography

	Concentration (mg I/ml)	Recommended Dosage (ml)
cerebral arteriography	300	5-10 per bolus
coronary arteriography	370	8-15 per bolus
thoracic aortography	370	1.0-1.2/kg
abdominal aortography	370	1.0-1.2/kg
Angiocardiography	370	1.0-1.2/kg
Selective visceral arteriography	300-370	depends on the vascular area to be examined
Peripheral arteriography	300-370	40-50
Digital Subtraction Angiography	150-370	depends on the vascular area to be examined
venography (phlebography)	300	30-50

Urography

The recommended dosage for this type of investigation is 30-50 ml for adults. The less marked osmotic diuresis induced by the non ionic agent makes Iopamiro® 370 especially suitable for patients with mild or moderately severe renal insufficiency and for neonates. The new contrast medium affords diagnostically useful nephrography even in patients with major renal insufficiency.

OTHER DIAGNOSTIC PROCEDURES

	Concentration (mg I/ml)	Recommended Dosage (ml)
Contrast enhancement in CT scanning	300-370	0.5-2.0/kg
Artrography	300	depending on examination
Fistulography	300	depending on examination

For the enhancement of contrast in CT scans IOPAMIRO® may be injected intravenously as a bolus, as a drip infusion or by a combination of the two methods.
The administration as an infusion is limited to old generation CT equipment. With spiral CT and the new multislice CT, it is recommended to administer a bolus specially for investigations aiming at increasing contrast enhancement in the arterial phase.

With slow equipment infusion is recommended whilst with fast equipment bolus injection is preferable.

Method of administration

The dosage must be adapted to the examination, the age, body weight, cardiac output, renal function, general condition of the patient and the technique used. Usually the same iodine concentration and volume are used with other iodinated x-ray contrast in current use

As with all contrast media, the lowest dose necessary to obtain adequate visualisation should be used.

Non-ionic contrast media have less anti-coagulant 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 the syringe and intravascular catheters should be flushed frequently, to minimise the risk of clotting, which rarely has led to serious thromboembolic complications after procedures.

Factors such as length of procedure, catheter and syringe material, underlying disease state, and concomitant medications may contribute to the development of thromboembolic events.. Therefore, meticulous angiographic techniques are recommended including close attention to guide wire and catheter manipulation, use of manifold systems and/or three-way stopcocks, frequent catheter flushing with heparinized saline solutions, and minimizing the length of the procedure

As experience shows that warmed contrast media are better tolerated, the contrast medium should be warmed up to body temperature before administration.

No other drugs or contrast media should be mixed with the iopamidol solution for injection.

Lumbar myelography

A slow sub-arachnoid injection is made through a fine lumbar puncture needle into one of the lower lumbar interspinous spaces (L3-L4 or L4-L5). Optimum contrast appears immediately after injections and films should be obtained promptly.

Thoraco-cervical myelography

Following a slow sub-arachnoid injection the patient should be turned on his side and tilted 10°-20° head down under fluoroscopic control. In this manner it is possible to control movement of the contrast medium column into the dorsal region.

If the cervical region is to be examined, the contrast medium should be run into the cervical region first, before the examination of the dorsal areas where it is progressively diluted.

Iopamiro may also be injected sub-occipitally or by lateral cervical puncture technique. Care should be taken to ensure that the contrast medium does not move intra-cranially.

After completion of direct cervical or lumbo-cervical procedures:

- Raise head of table steeply (45° angle) for about two minutes so that the contrast medium flows towards the caudal end.
- Avoid excessive and particularly active patient movement or straining, maintain the patient under close observation, quiet and in a head up position especially in the first few hours.
- Patients suspected of having a low seizure threshold should be observed during this period.
- The patient should remain supine and at bed rest during this period.
- Encourage the patient, if able, to take in fluids orally and eat.

Cerebral angiography

Any of the current techniques is suitable for radiological visualisation of the cerebral vasculature with Iopamiro 300. Carotid and vertebral angiography, performed by catheterisation or percutaneous injection techniques, require rapid injection, which, if necessary may be repeated.

Peripheral arteriography and phlebography (venography)

Iopamiro may be administered by rapid injection through a catheter into a suitable peripheral artery or vein. Percutaneous injection into the appropriate blood vessel is used for visualisation of peripheral arteries and veins.

Computer tomography enhancement

Contrast enhancement for brain scans can be achieved between one and three minutes after i.v. injection. Iopamiro 300 is also used for total body scanning examinations after i.v. administration as a bolus, as a drip infusion or by a combination of the two methods.

Urography

The contrast medium is injected intravenously and rapidly eliminated through the kidneys. In patients with severe renal failure, high dose urography should be used.

Angiocardiography, left ventriculography, selective coronary arteriography

It can also be introduced under pressure through a cardiac catheter into any of the heart chambers, or injected into large vessels for immediate visualisation.The contrast medium may also be administered during selective catheterisation of the coronary arteries.

Arthrography

Visualisation of joint cavities and articular surfaces can be achieved by either single or double contrast examination.

Digital subtraction angiography

For cardiac imaging the contrast medium may be administered intra-arterially by selectivecatheterisation to provide subtracted images. Iopamiro 370 injected intravenously either centrally or peripherally is also recommended for use in this modality.

4.3 Contraindications

Hypersensitivity to the active ingredient iopamidol and/or iodine or to any of the excipients

Intrathecal administration

The concomitant intrathecal administration of corticosteroids with Iopamidol is contraindicated. Because of overdosage considerations, immediate repeat myelography in the event of technical failure is contraindicated.

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 reaction to the contrast medium itself.

During the examination an intravenous route for emergency treatment in the event of a reaction is required.

After the administration of the contrast medium, competent personnel, drugs and equipment for emergency resuscitation must be available.

Caution during injection of contrast media is necessary to avoid extravasation.

Local tissue irritation can occur as an event of perivascular infiltration of the contrast media.

In patients who are known epileptics or have a history of epilepsy, anticonvulsant therapy should be maintained before and following myelographic procedures. In some instances anticonvulsant therapy may be increased for 48 hours before the examination. If during the procedure a convulsive crisis occurs, it is recommended to administer intravenously diazepam or phenolbarbital.

Iopamidol injection should be used with caution in patients with hypercalcaemia and cerebral vascular disease.

The risk associated with a particular investigation may be increased by conditions such as advanced arteriosclerosis and hypertension.

The administration of iodinated contrast media may aggravate the symptoms of myasthenia gravis.

As with all other contrast media this product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. Occasional severe reactions with fatal outcome have been reported.

A positive history of allergy, asthma or untoward reaction during previous similar investigations indicates a need for extra caution; the benefit should clearly outweigh the risk in such patients.

Pre-treatment with antihistamines or corticosteroids to prevent or minimise possible allergic reactions in such patients may be considered.

In patients with suspected or known hypersensitivity to contrast media, sensitivity testing is not recommended, as severe or fatal reactions to contrast media are not predictable from sensitivity tests.

The patient should also be informed that allergic reactions may develop up to several days after the procedure; in such case, a physician should be consulted immediately.

Particular care should also be exercised in patients with moderate to severe impairment of renal function (as reflected by a raised blood urea). Substantial deterioration in renal function is minimised if the patient is well hydrated. Renal function parameters especially urinary output should be monitored after the examination in these patients. Pre-existing renal impairment may predispose to acute renal dysfunction following contrast media administration.

In patients with impairment of renal function, the administration of potentially nephrotoxic drugs should be avoided until the contrast medium is completely excreted. In such patients, renal function parameters should be monitored after the procedure. Further administration of contrast media should be postponed until renal function has returned to its previous level. Patients on dialysis may receive contrast media such as iopamidol, which can be removed without difficulty by dialysis.

Patients with severe hepatic, renal or combined hepato-renal insufficiency should not be examined unless absolutely indicated. Re-examination should be delayed for 5-7 days.

The presence of renal damage in diabetic patients is one of the factors predisposing to renal impairment following contrast media administration. This may precipitate lactic acidosis in patients with moderate renal impairment who are taking metformin. As a precaution, metformin (biguanides see section 4.5)should be discontinued at the time of, or prior to, the procedure and withheld for 48 hours subsequent to the procedure and re-instituted only after renal function has been re-evaluated and found to be normal.

Patients must be sufficiently hydrated before and after radiographic procedures. Patients with severe functional impairment of the liver or myocardium, myelomatosis, diabetes, polyuria or oliguria, hyperuricemia, infants, elderly patients and patients with severe systemic disease should not be exposed to dehydration.

Fluid intake should not be limited and any abnormalities of fluid or electrolyte balance should be corrected prior to use of this hypertonic solution

Patients with paraproteinaemia of Waldenström, with multiple myeloma or severely compromised hepatic and renal impairment are also more at risk: in these cases adequate hydration is recommended after contrast medium administration.

Contrast media may promote sickling in individuals who are homozygous for sickle cell disease when injected intravenously and intra-arterially. To prevent crises in patients with sickle cell disease adequate hydration should be assured and a minimal volume of low concentration should be used.

Patients with congestive heart failure should be observed for several hours following the procedure to detect delayed haemodynamic disturbances, which may be associated with a transitory increase in the circulating osmotic load. All other patients should be observed for at least 20-30 minutes after the procedure, as most of the adverse events occur in this period.

In patients undergoing angiocardiographic procedures special attention should be paid to the status of the right heart and pulmonary circulation. Right heart insufficiency and pulmonary hypertension may precipitate bradycardia and systemic hypotension, when the organic iodine solution is injected.

Right heart angiography should be carried out only when absolutely indicated.

During intracardiac and/or coronary arteriography, ventricular arrhythmias may infrequently occur.

Caution should be exercised in performing iodinated contrast-enhanced examinations in patients with, or with suspicion of, hyperthyroidism or autonomously functioning thyroid nodule(s), as thyroid storms have been reported following administration of iodinated contrast media.

Iopamiro should be used with caution in patients with hyperthyroidism. It is possible that hyperthyroidism may recur in patients previously treated for Graves' disease.

In patients scheduled for thyroid examination with a radioactive iodine tracer, one must take into consideration that iodine uptake in the thyroid gland will be reduced for several days (up to two weeks) after dosing with an iodinized contrast medium that is eliminated through the kidneys.

Patients with phaeochromocytoma may develop severe hypertensive crisis following intravascular Iopamidol. Pre-medication with α-receptor blockers is recommended.

In angiographic procedures, the possibility of dislodging plaque or damaging or perforating the vessel wall should be considered during catheter manipulation and contrast medium injection. Test injections to ensure proper catheter placements are recommended.

In examinations of the aortic arch the tip of the catheter should be positioned carefully to avoid hypotension, bradycardia and CNS injury due to excess pressure transmitted from the injector pump to the brachiocephalic branches of the aorta.

Angiography should be avoided whenever possible in patients with homocystinuria due to an increased risk of thrombosis and embolism.

In patients undergoing peripheral angiography, there should be pulsation in the artery into which the X-ray contrast medium will be injected. In patients with thromboangiitis obliterans or ascending infections in combination with serious ischemia the angiography should be performed, if at all, with special caution.

In patients undergoing venography, special caution should be exercised in patients with suspected phlebitis, serious ischaemia, local infections, or a complete venous occlusion.

Serious neurological events have been observed following direct injection of contrast media into cerebral arteries or vessels supplying the spinal cord or in angiocardiography due to inadvertent filling of the carotids.

Iopamiro should be administered with caution in elderly patients, in patients with symptomatic cerebrovascular diseases, recent stroke, or frequent TIA, altered permeability of the blood-brain barrier, increased intracranial pressure, suspicion of intracranial tumor, abscess or hematoma/hemorrhage, history of convulsive disorder, alcoholism or multiple sclerosis. Patients with these conditions have an increased risk of neurological complications.

Vasospasm and subsequent cerebral ischemic phenomena may be caused by intra-arterial injections of contrast media

Intrathecal administration

An accurate evaluation of the risk/benefit ratio is needed if from clinical history there is a previous history of epilepsy or in the presence of blood in the cerebrospinal fluid or presence of local or systemic infection where bacteremia is likely.

The contrast medium should be removed as much as possible in case of spinal fluid blockage.

Use in Special Populations

Newborns, children

Infants (age<1 year), and especially newborns 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

In paediatric roentgenology, one should proceed with great caution when injecting the contrast medium into the right heart chambers of cyanotic neonates with pulmonary hypertension and impaired cardiac function.

Elderly

The elderly are at special risk of reactions due to reduced physiological functions, especially when high dosage of contrast medium is used. Myocardial ischemia, major arrhythmias and premature ventricular complexes are more likely to occur in these patients. The probability of acute renal insufficiency is higher in these patients.

Women of child-bearing potential

X-ray examination of women should if possible be conducted during the pre-ovulation phase of the menstrual cycle and should be avoided during pregnancy.

Appropriate investigations and measures should be taken when exposing women of child-bearing potential to any X-ray examination, whether with or without contrast medium.

4.5 Interactions with other medicinal products and other forms of interaction

Following administration of iopamidol, the capacity of the thyroid tissue to take up iodine is reduced for 2-6 weeks.

Thyroid function tests: use of iodinated contrast media may interfere with tests for thyroid function which depend on iodine estimations, such as Protein Binding Iodine and radioactive iodine uptake. As a consequence they will not accurately reflect thyroid function for up to 16 days following administration of iodinated contrast media. Thyroid function tests not depending on iodine estimations, e.g. T3 resin uptake and total or free thyroxine (T4) assays are not affected.

The administration of an X-ray contrast medium in diabetic patients with nephropathy who are taking biguanides may precipitate lactic acidosis.

To prevent onset of lactic acidosis in diabetic patients with moderate renal impairment and under treatment with oral anti-diabetic agents of the biguanide class, biguanides should be stopped 48 hours before the administration of the contrast medium and re-instated only after renal function has been demonstrated to have returned to pre-examination values (see section 4.4).

Arterial thrombosis has been reported when Iopamidol was given following papaverine.

Cardiac and/or hypertensive patients under treatment with diuretics, ACE-inhibitors, and/or beta-blocking agents are at higher risk of adverse reactions when administered iodinated contrast media.

In patients receiving beta-blockers there is an elevated risk of more severe anaphylactoid reactions.

The administration of vasopressors strongly potentiates the neurological effect of the intra-arterial contrast media.

Renal toxicity has been reported in patients with liver dysfunction who were given oral cholecystographic agents followed by intravascular contrast agents. Therefore, administration of intravascular contrast agents should be postponed in patients who have recently been given a cholecystographic contrast agent.

Contrast media may interfere with laboratory tests for bilirubin, proteins or inorganic substances (e.g. iron, copper, calcium, phosphate). These substances should not be assayed during the same day following the administration of contrast media.

Following administration of iopamidol atypical adverse reactions e.g. erythema, fever and flu symptoms have been reported in patients treated with interleukin-2.

Intrathecal administration

Neuroleptics must be absolutely avoided because they lower the seizure threshold. The same applies to analgesics, antiemetics, antihistamines and sedatives of the phenothiazine group. Whenever possible, treatment with such drugs should be discontinued at least 48 hours before administration of the contrast medium and treatment can be resumed not earlier than 24 hours afterwards.

4.6 Fertility, pregnancy and lactation

X-ray examination of women should if possible be conducted during the pre-ovulation phase of the menstrual cycle and should be avoided during pregnancy; also, since it has not been demonstrated that Iopamiro is safe for use in pregnant women, it should be administered only if the procedure is considered essential by the physician. Apart from radiation exposure of the foetus, benefit-risk consideration for iodine-containing contrast agents should also take into account the sensitivity of the foetal thyroid towards iodine.

Iodine-containing X-ray contrast agents are excreted into the breast milk in low amounts. From animal experience, Iopamiro is non toxic in animals after oral administration. Although, no serious adverse reactions have been reported in nursing infants, Iopamiro should be administered to lactating women only if considered essential by the physician.

4.7 Effects on ability to drive and use machines

There is no known effect on the ability to drive and operate machines. However, because of the risk of early reactions, driving or operating machinery is not advisable for one hour following the last intravascular injection.

Driving or operating machinery is not advisable for 6 hours following intrathecal administration.

4.8 Undesirable effects

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.

Anaphylaxis (anaphylactoid reactions/hypersensitivity) may manifest with: mild localized or more diffuse angioneurotic oedema, tongue oedema, laryngospasm or laryngeal oedema, dysphagia, pharyngitis and throat tightness, pharyngolaryngeal pain, cough, conjunctivitis, rhinitis, sneezing, feeling hot, sweating increased, asthenia, dizziness, pallor, dyspnoea, wheezing, bronchospasm, and moderate hypotension. Skin reactions may occur in the form of various types of rash, diffuse erythema, diffuse blisters, urticaria, and pruritus. These reactions, which occur irrespective of the dose administered and the route of administration, may represent the first signs of incipient state of shock. Administration of the contrast medium must be discontinued immediately and – if necessary – specific treatment initiated via a venous access.

Following intravascular administration, in most cases reactions occur within minutes of dosage. However, delayed reactions, usually involving skin, may occur, mostly within 2-3 days, more rarely within 7 days, after the administration of the contrast medium .

After intrathecal administration, most side effects occur with a delay of some hours due to the slow absorption from the site of administration and distribution to the whole body. Reactions usually occur within 24 hours after injection.

More severe reactions involving the cardiovascular system such as vasodilatation with pronounced hypotension, tachycardia, dyspnoea, agitation, cyanosis and loss of consciousness (syncope) may require emergency treatment.

Intravascular administration –Adults

The safety of Iopamidol injection through intravascular administration was evaluated in 2,548 adult patients involved in clinical trials.

In clinical trials, the most commonly reported adverse reactions are headache (1.5 %), nausea (1.2%) and feeling hot (3.5%) after intravascular administration; headache (18.9%) after intrathecal administration.

The adverse reactions reported in clinical trials among 2,680 adult subjects and 35 paediatric patients, and from post marketing surveillance are presented in the tables below by frequency and classified by MedDRA system organ classes

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. The adverse reactions are classified by System Organ Class and frequency, using the following convention: Very common (≥ 1/10), Common (≥ 1/100 to < 1/10), Uncommon (≥ 1/1,000 to < 1/100), Rare (≥ 1/10,000 to < 1/1,000), Very rare (< 1/10,000), not known (cannot be estimated from the available data)

System Organ Class	**Adverse Reactions**			
	Clinical Trials			**Post-marketing Surveillance**
	Common (≥1/100 to <1/10)	**Uncommon (≥1/1,000 to <1/100)**	**Rare (≥≥1/10,000 to <1/1,000)**	**Frequency unknown***
Blood and lymphatic system disorders				Thrombocytopenia
Immune system disorders				Anaphylaxis, Anaphylactoid reaction
Psychiatric disorders			Confusional state	
Nervous system disorders	Headache	Dizziness, Taste alteration	Paraesthesia	Coma, Transient ischaemic attack, Syncope, Depressed level of consciousness or loss of consciousness, Convulsion,
Eye disorders				transient blindness, Visual disturbance, Conjunctivitis, Photophobia
Cardiac disorders		Cardiac dysrhythmias such as extrasystoles, atrial fibrillation, ventricular tachycardia and ventricular fibrillation**	Bradycardia	Myocardial ischaemia or infarction, Cardiac failure, Cardio-respiratory arrest, Tachycardia
Vascular disorders		Hypotension, Hypertension, Flushing		Circulatory collapse or shock
Respiratory, thoracic			Pulmonary oedema,	Respiratory arrest,

System Organ Class	Adverse Reactions			
	Clinical Trials			Post-marketing Surveillance
	Common (≥1/100 to <1/10)	**Uncommon (≥1/1,000 to <1/100)**	**Rare (≥≥1/10,000 to <1/1,000)**	**Frequency unknown***
and mediastinal disorders			Asthma, Bronchospasm	Respiratory failure, Acute respiratory distress syndrome, Respiratory distress, Apnoea, Laryngeal oedema, Dyspnoea
Gastrointestinal disorders	Nausea	Vomiting, Diarrhea, Abdominal pain, Dry mouth		Salivary hypersecretion, Salivary gland enlargement
Skin and subcutaneous tissue disorders		Rash, Urticaria, Pruritus, Erythema, Sweating increased		Face oedema, muco-cutaneous syndromes ***
Musculoskeletal and connective tissue disorders		Back pain	Muscle spasms	Musculoskeletal pain, Muscular weakness
Renal and urinary disorders		Acute renal failure		
General disorders and administration site conditions	Feeling hot	Chest pain, Injection site pain****, Pyrexia, Feeling cold		Rigors, Pain, Malaise
Investigations		Blood creatinine increased		Electrocardiogram change including ST segment depression

* Since the reactions were not observed during clinical trials with 2,548 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.

** Cardiac reactions may occur as consequences of the coronary catheterization procedural hazard: these complications include coronary artery thrombosis and coronary artery embolism.

*** As with other iodinated contrast media, very rare cases of muco-cutaneous syndromes, including Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome) and erythema multiforme, have been reported following the administration of Iopamidol

**** Injection site pain and swelling may occur. In the majority of cases it is due to extravasation of contrast medium. These reactions are usually transient and result in recovery without sequelae. However, inflammation and even skin necrosis have been seen on very rare occasions. In isolated reports extravasation led to the development of compartment syndrome

Intravascular administration – Pediatric Population
Frequency type and severity of adverse reactions in children are similar to those in adults.

Intrathecal administration - Adults

The safety of Iopamidol injection through intrathecal administration was evaluated in 132 adult patients.

System Organ Class	Adverse Reactions			
	Clinical Trials			Post-marketing Surveillance
	Very common (≥ 1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Frequency unknown*
Infections and infestations				Meningitis aseptic, Meningitis bacterial as consequence of the procedural hazard
Immune system disorders				Anaphylaxis, Anaphylactoid reaction**
Psychiatric disorders				Confusional state, Disorientation, Agitation, Restlessness
Nervous system disorders	Headache			Coma, Paralysis, Convulsion, Syncope, Depressed level of consciousness or loss of consciousness, Meningism, Dizziness, Paraesthesia, Hypoaesthesia
Eye disorders				Transient blindness
Cardiac disorders				Arrhythmia
Vascular disorders		Flushing		Hypertension
Respiratory, thoracic and mediastinal disorders				Respiratory arrest, Dyspnoea
Gastrointestinal disorders		Nausea, Vomiting		
Skin and subcutaneous tissue disorders			Rash	
Musculoskeletal and connective tissue disorders		Back pain, Neck pain, Pain in extremity, Sensation of heaviness		
General disorders and administration site conditions				Pyrexia, Malaise, Rigors

* Since the reactions were not observed during clinical trials with 132 patients, best estimate is that their relative occurrence is uncommon (≥1/1,000 to <1/100).
The most appropriate MedDRA term is used to describe a certain reaction and its symptoms and related conditions

System Organ Class	Adverse Reactions			
	Clinical Trials			Post-marketing Surveillance
	Very common (≥ 1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Frequency unknown*

** Anaphylaxis (anaphylactoid reactions/hypersensitivity) may occur. Anaphylactoid reactions with circulatory disturbances such as severe blood pressure decrease leading to syncope or cardiac arrest and life threatening shock are much less common after intrathecal administration than after intravascular administration.

Body cavity administration

The majority of the reactions occur some hours after the contrast administration due to the slow absorption from the area of administration and distribution in the whole organism.

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

The reactions reported in cases of arthrography usually represent irritative manifestations superimposed on existing tissue inflammation.

Systemic hypersensitivity is rare, generally mild and in the form of skin reactions. However, the possibility of severe anaphylactoid reactions cannot be excluded.

4.9 Overdose

Dosages exceeding the specific package insert dose are not recommended, as they might lead to life-threatening adverse effects.

If needed, haemodialysis can be used to eliminate Iopamidol from the body.

Treatment of overdosage is directed toward the support of all vital functions and prompt institution of symptomatic therapy.

Intravascular

In the event of accidental intravascular overdose in humans, the water and electrolyte losses must be compensated by infusion. Renal function should be monitored for at least three days.

Intrathecal

Signs of intrathecal overdose may be: ascending hyperreflexia or tonic-clonic spasms, up to generalized seizures, and, in severe cases of central involvement, hyperthermia, stupor and respiratory depression.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group; ATC code: V08A B04

5.1 Pharmacodynamic properties

Iopamidol is contrast medium belonging to the generation of non-ionic compound whose solubility is due to the presence of hydrophilic substitutes in the molecule. This results in a solution of low osmolality when compared with ionic media.

Iopamidol has been shown to be effective as an X-ray contrast medium in neuroradiology, angiography, venography, arthrography, urography, cerebral angiography and left ventriculography

and coronary arteriography. Its toxicity particularly cardiac and CNS toxicity are less than those of ionic contrast media.

5.2 Pharmacokinetic properties

The pharmacokinetics of Iopamidol conform to an open two compartment pharmacokinetic model with first order elimination.

Distribution volume is equivalent to extra-cellular fluid.

Elimination is almost completely through the kidneys. Less that 1% of the administered dose has been recovered in the faeces up to 72 hours after dosing. Elimination is rapid; up to half the administered dose may be recovered in the urine in the first two hours of dosing.

After intrathecal administration peak plasma level is within 90 - 150 minutes, and total excretion in 24 hours in humans

There is no evidence of biotransformation.

Serum protein binding is negligible.

5.3 Preclinical safety data

No adverse effects can be predicted from animal toxicology studies other than those documented from human use of iopamidol.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients are: trometamol, hydrochloric acid and edetate calcium disodium.

6.2 Incompatibilities

No other drug should be mixed with the contrast medium.

6.3 Shelf life

5 years.

6.4 Special warnings and precautions for storage

Protect from light.

6.5 Nature and contents of container

Iopamiro 150 - Boxes of 1 bottle, 50 ml.

Iopamiro 300 - Boxes of 1 bottle, 50 ml, Boxes of 1 bottle, 100 ml, Boxes of 1 bottle, 200 ml.

Iopamiro 370 - Boxes of 1 bottle, 50 ml, Boxes of 1 bottle, 100 ml, Boxes of 1 bottle, 200 ml.

6.6 Special precautions for disposal and other handling

Discard if the solution is not clear of particulate matter.

Exceptionally, the event of crystallisation of Iopamiro could occur. It has been shown that such a phenomenon is caused by a damaged or defective container and therefore the product should not be used in this case. The bottle, once opened, must be used immediately.

Any residue of contrast medium must be discarded.

Iopamiro, as other iodinated contrast media, can react with metallic surfaces containing copper (e.g. brass), therefore the use of equipment, in which the product comes into direct contact with such surfaces, should be avoided.

7. MARKETING AUTHORISATION HOLDER

Manufactured for Bracco s.p.a., Via Egidio Folli 50 - 20134 Milano, Italy
by Patheon Italia S.p.A., Via Morolense 87 - 03013 Ferentino (FR), Italy
Imported by Dexxon Ltd., 1 Dexcel St., Or Akiva 30600

8. MARKETING AUTHORISATION NUMBER

Iopamiro 150- 054 61 26773 11
Iopamiro 300- 020 40 24483 11
Iopamiro 370- 020 41 24526 11

9. DATE OF REVISION OF THE TEXT

The format of this leaflet was determined by the Ministry of Health (MOH) and its content was checked and approved by the MOH in 24.04.2013.