Summary of Product Characteristics

1. Name of the medicinal product
PAMIDOL 370
(Iopamidol Injection USP 370 mg I / mL)

2. Qualitative and quantitative composition
Each ml contains:
Iopamidol USP …....755.3 mg
Equivalent to 370 mg of Iodine
Water for Injection USP ….q.s.

For a full list of excipients, see section 6.1

3. Pharmaceutical form
Solution for Injection

4. Clinical particulars
4.1 Therapeutic indications
Neuro-radiology: Myeloradiculography, cisternography and ventriculography.
Angiography: Cerebral arteriography, coronary arteriography, thoracic aortography, abdominal aortography, angiocardiography, selective visceral arteriography, peripheral arteriography, venography, digital subtraction angiography (DSA), DSA of cerebral arteries, DSA of peripheral arteries, DSA of abdominal arteries.
Urography: Intravenous urography.
Contrast Enhancement CT Scanning: Arthrography and Fistulography

4.2 Posology and method of administration
Iopamidol injections are administered intrathecally in the following indications.

Neuroradiology

	Concentration (mg iodine/mL)	**Recommended dosage (mL)**
Myeloradiculography	200 – 300	5 – 15
Cisternography and Ventriculography	200 – 300	5 – 15

Iopamidol injections are administered intravascularly in the following indications.

Angiography

	Concentration (mg iodine/mL)	**Recommended dosage (mL)**
Cerebral arteriography	300	5 – 10 (bolus)
Coronary arteriography	370	8 – 15 (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	Depending on examination
Peripheral arteriography	300-370	40 – 50
Digital subtraction angiography	150-370	Depending on examination

Venography	300	30 – 50

Urography

	Concentration (mg iodine/mL)	**Recommended dosage (mL)**
Urography	300-370	30 to 50ml

The less marked osmotic diuresis induced by the non-ionic agent makes Iopamidol 370 especially suitable for the 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 iodine/mL)	**Recommended dosage (mL)**
Contrast enhancement in CT scanning	300-370	0.5 – 2.0/kg
Arthrography	300	Depending on examination
Fistulography	300	Depending on examination

Pediatric Use

Safety and Effectiveness in children has been established in pediatric angiocardiography, computed tomography (head and body) and excretory urography. Pediatric patients at higher risk of experiencing adverse events during contrast medium administration may include those having asthma, a sensitivity to medication and/or allergens, cyanotic heart disease, congestive heart failure, a serum creatinine greater than 1.5 mg/dL or those less than 12 months of age.

Pediatric Angiocardiography

Iopamidol-370 should be used. Pediatric angiocardiography may be performed by injection into a large peripheral vein or by direct catheterization of the heart. The usual dose range for single injections is provided in the following table:

Single Injection	
Usual Dose Range	
Age	***mL***
< 2 years	10-15 mL
2-9 years	15-30
10-18 years	20-50

The usual recommended dose for cumulative injections is provided in the following table:

Cumulative Injection	
Usual Recommended Dose	
Age	***mL***
< 2 years	40
2-9 years	50
5-9 years	100
10-18 years	125

Pediatric Excretory Urography

1.0 mL/kg to 3.0 mL/kg for Iopamidol-300. It should not be necessary to exceed a total dose of 30 grams of iodine.

Pediatric Computed Tomography
1.0 mL/kg to 3.0 mL/kg for Iopamidol-300. It should not be necessary to exceed a total dose of 30 grams of iodine.

Method of administration
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 the syringe and intravascular catheters should be flushed frequently, to minimize 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.

Keep Iopamidol solutions away from strong light. Exceptionally, the event of crystallization of Iopamidol solutions 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. Iopamidol 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.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Iopamidol solutions should be used only if clear and within the normal colorless to pale yellow range.

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.

Instructions for preparation (if applicable)
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Iopamidol solutions should be used only if clear and within the normal colorless to pale yellow range. Discard any product which shows signs of crystallization or damage.
It is desirable that solutions of radiopaque diagnostic agents for intravascular use be at body temperature when injected. 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.

Patients should be well hydrated prior to and following Iopamidol administration

4.3 Contraindications

Hypersensitivity to the active ingredient Iopamidol 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 for at least 30 minutes.

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 phenol barbital.

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.

General anaesthesia may be indicated in selected patients. However, a higher incidence of adverse reactions has been reported in these patients, probably due to the hypotensive effect of the anaesthetic.

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.

The risk of bronchospasm-inducing reactions in asthmatic patients is higher after contrast media administration, especially in patients taking beta-blockers.

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 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 minimized 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.

Care should be taken in renal impairment and diabetes. In these patients it is important to maintain hydration in order to minimise deterioration in renal function.

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 who are taking metformin.

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 paraproteinemia of Waldenstrom's, 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.

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.

Iopamidol 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 branchiocephalic 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.
Iopamidol 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 tumour, abscess or hematoma/hemorrhage, history of convulsive disorder, chronic 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.
The reactions reported in cases of arthrography and fistulography usually represent irritative manifestations superimposed on existing tissue inflammation.

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

4.5 Interaction 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 up take. 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.
To prevent onset of lactic acidosis in diabetic patients under treatment with oral anti-diabetic agents of the biguanides class and with moderate renal impairment undergoing elective

procedures, biguanides should be stopped 48 hours prior to the administration of the contrast medium and re-instated only after 48 hours if serum creatinine is unchanged.
In emergency patients in whom renal function is either impaired or unknown, the physician shall weigh out risk and benefit of an examination with a contrast medium. Metformin should be stopped from the time of contrast medium administration. After the procedure, the patient should be monitored for signs of lactic acidosis. Metformin should be restarted 48 hours after contrast medium if serum creatinine/eGFR is unchanged from the pre-imaging level.
Patients with normal renal function can continue to take Metformin normally.
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.
Beta-blockers may impair the response to treatment of bronchospasm induced by contrast medium.
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 sub stances 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
Neuroleptic must be absolutely avoided because they lower the seizure threshold. The same applies to analgesics, anti-emetics, 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 breastfeeding

Fertility, Pregnancy and Nursing
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 Iopamidol is safe for use in pregnant women, it should be administered only if the procedure is considered essential by the physician. Apart from the radiation exposure of the foetus, benefit-risk consideration for iodine containing contrast agent 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, Iopamidol is non-toxic in animals after oral administration. From experience gained so far, harm to the nursing infant is unlikely to occur. Stopping breastfeeding is unnecessary.

Women of Child Bearing Potential

X-ray examination of women should if possible be conducted during the preovulation 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.

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.
When examining small children or babies, do not limit fluid intake before administering a hypertonic contrast solution. Also, correct any existing water and electrolyte imbalance.
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.
In neonates, and particularly in premature neonates, it is recommended that tests of thyroid function (typically TSH and T4), should be checked 7-10 days and 1 month after the administration of iodinated contrast media because of the risk of hypothyroidism due to iodine overload.

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, dysphasia, 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, peripheral vasodilation, 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 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 trial			***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 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 infarction, Cardiac failure, Cardio-respiratory arrest, Tachycardia
Vascular disorders		Hypotension,		Circulatory

System Organ Class	*Adverse Reactions*			
	Clinical trial			*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*
		Hypertension, Flushing		collapse or shock
Respiratory, thoracic and mediastinal disorders			Pulmonary oedema, Asthma, Bronchospasm	Respiratory arrest 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 syndrome **
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

* Cardiac reactions may occur 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 – Paediatrics Population

Frequency type and severity of adverse reactions in children are similar to those in adults.

Intrathecal Administration - Adults

System Organ Class	***Adverse Reactions***			
	Clinical trial			***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***
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				Eye disorders
Cardiac disorders				Arrhythmia
Vascular disorders		Flushing		Hypertension
Respiratory, thoracic and mediastinal disorder				Respiratory arrest, Dyspnoea
Gastrointestinal disorders		Nausea, Vomiting		
Skin and sub cutaneous tissue disorders			Rash	
Musculoskeletal and connective tissue disorders		Back pain, Neck pain, Pain in		

System Organ Class	*Adverse Reactions*			
	Clinical trial			*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*
		extremity, Sensation of heaviness		
General disorders and administration site conditions				Pyrexia, Malaise, Rigors

* Anaphylaxis (anaphylactoid reactions/hypersensitivity) may occur. Anaphylactoid reactions with circulatory disturbances such a 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

Symptoms of overdosage are unlikely in patients with normal renal function unless the patient has received more than 2000 mg I / kg body weight over a limited period of time. The duration of the procedure is important for tolerance to high doses of contrast medium ($t_{1/2}$ = 2 hours). Accidental overdosage is more likely after complex angiographic procedures in children, particularly when multiple injections of contrast media are administered high concentration.

Symptoms that may occur from overdosage can be treated with antihistamines and corticosteroids, and eventual oxygen. In the case of cardiovascular disorders it may be necessary in addition to the above input of vasopressors, plasma and electrolytes, as any resulting disparity of water and electrolytes must correct treatment. The seizures can be controlled by diazepam, and tetanic crises that may arise can be controlled by injection of calcium gluconate.

Renal function should be monitored during the next 3 days. If needed, it can be used to clarify hemodialysis excess dye. There is no specific antidote.

5. Pharmaceutical properties

5.1 Pharmacodynamic properties

Intravascular injection of a radiopaque diagnostic agent opacifies those vessels in the path of flow of the contrast medium, permitting radiographic visualization of the internal structures of the human body until significant hemodilution occurs.

Following intravascular injection, radiopaque diagnostic agents are immediately diluted in the circulating plasma. Calculations of apparent volume of distribution at steady-state indicate that iopamidol is distributed between the circulating blood volume and other

extracellular fluid; there appears to be no significant deposition of iopamidol in tissues. Uniform distribution of iopamidol in extracellular fluid is reflected by its demonstrated utility in contrast enhancement of computed tomographic imaging of the head and body following intravenous administration.

5.2 Pharmacokinetic properties
The pharmacokinetics of intravenously administered iopamidol in normal subjects conform to an open two-compartment model with first order elimination (a rapid alpha phase for drug distribution and a slow beta phase for drug elimination). The elimination serum or plasma half-life is approximately two hours; the half-life is not dose dependent. No significant metabolism, deiodination, or biotransformation occurs.
Iopamidol is excreted mainly through the kidneys following intravascular administration. In patients with impaired renal function, the elimination half-life is prolonged dependent upon the degree of impairment. In the absence of renal dysfunction, the cumulative urinary excretion for Iopamidol, expressed as a percentage of administered intravenous dose is approximately 35 to 40 percent at 60 minutes, 80 to 90 percent at 8 hours, and 90 percent or more in the 72-to 96hour period after administration. In normal subjects, approximately one percent or less of the administered dose appears in cumulative 72-to 96-hour fecal specimens.

5.3 Preclinical safety data
No relevant information additional to that contained elsewhere in the Summary of Product Characteristics.

6. Pharmaceutical particulars

6.1 List of excipients
Tromethamine USP
Edetate Calcium Disodium USP
Hydrochloric Acid BP
Water for Injection USP

6.2 Incompatibilities
Not Applicable

6.3 Shelf life
4 years

6.4 Special precautions for storage
Store at a temperature not exceeding 30ºC. Protect from light & secondary X-rays.

6.5 Nature and content of container
- 50 mL clear, colorless type I glass bottle packed in a carton along with leaflet.
- 100 mL clear, colorless type I glass bottle packed in a carton along with leaflet.

6.6 Special precautions for disposal and other handling
Not Applicable

7. Marketing Authorization Holder

UNIQUE PHARMACEUTICAL LABORATORIES
(A Division of J.B. Chemicals & Pharmaceuticals Ltd.)

Neelam center, B Wing, 4th floor, Hind cycle road,
Worli, Mumbai 400 030, INDIA

8. Marketing Authorization Number
3672/3406/NMR/2017

9. Date of First Authorization/Renewal of the Authorization
Date of First Authorization: 08/11/2021

10. Date of revision of the text
27/07/2023