Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Iopamigita 300mg/ml Solution for Injection/Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains 612.4 mg iopamidol, equivalent to 300 mg iodine

One vial of 20 ml solution contains 12,248 mg Iopamidol, equivalent to 6,000 mg Iodine.
One vial of 50 ml solution contains 30,620 mg Iopamidol equivalent to 15,000 mg Iodine.
One vial of 75 ml solution contains 45,930 mg Iopamidol, equivalent to 22,500 mg Iodine.
One vial of 100 ml solution contains 61,240 mg Iopamidol equivalent to 30,000mg Iodine.
One vial of 200 ml solution contains 122,480 mg Iopamidol, equivalent to 60,000 mg Iodine.
One vial of 500 ml solution contains 306,200 mg Iopamidol equivalent to 150,000 mg Iodine.

Excipient with known effect: contains maximum 8.74 mg sodium per 1 ml.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection/ infusion

Clear, colourless or light yellow solution

pH	6.5 – 7.5
Osmolality at 37°C (mOsm/kg)	630
Osmolarity at 37°C (mOsm/1)	478
Osmotic pressure 37°C (MPa)	1.59
Viscosity (mPa.s) 37°C	5.0

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Arteriography, angiocardiography, phlebography, digital subtraction angiography (DSA), computertomography contrast enhancement (CT), excretory urography.

This medicinal product is for diagnostic use only.

4.2 Posology and method of administration

For intravenous and intra-arterial injection and infusion.

Iopamigita is a diagnostic agent for single injection in the intended indications. Multiple injections or repeated examinations are possible.

4.2.1 Method of administration

The dosage is dependent on the method of examination, age, weight, function of the heart and the general condition of the patient as well as techniques applied. Usually, the same iodine concentrations and volumes as with other non-ionic

iodine containing x-ray contrast media are applied. The lowest dose which is necessary to achieve the informative results should be applied.

In impaired renal function, cardio-circulatory insufficiency as well as bad general condition, the dosage of contrast media should be kept as low as possible (see section 4.4). In these patients it is advisable to monitor renal function at least three days following the examination. Particular caution is required in patients with concomitant hepatic insufficiency and renal insufficiency, which increases the risk of retention of the contrast agent

The contrast medium should be warmed to body temperature before application. Experience has shown that a warmed contrast medium is tolerated better.

Basically, the contrast medium should be drawn up in the syringe immediately before use. In order to keep the thromboembolisation risk in connection with the examination as low as possible, contact time between blood and contrast medium should be kept as short as possible. Attention has to be paid to a careful angiographic technique as well as frequent flushing of the used catheter in sodium chloride 9 mg/ml (0.9%) solution for injection (by adding heparin, if necessary).
The contrast medium should be applied in the lying patient. Immediate repositioning must be possible. A safe venous access should be inserted before examination in case of possible emergency. As for all iodine containing contrast media, Iopamigita may only be used with all diagnostic techniques if resuscitative equipment and emergency medication are available.

After examination the patient should be kept under supervision for at least 30 minutes, during which time most undesirable effects may occur. All physicians and nursing staff must be informed of adverse reactions as well as general and medicinal emergency measures.

Dietary recommendations:
The patient should refrain from eating for 2 hours prior to the investigation in order to reduce the risk of aspiration, as nausea and vomiting are known possible adverse reactions.

Pretesting:
Pretesting using a low dose of contrast medium for hypersensitivity is not recommended, as this not meaningful and occasionally resulted in serious, sometimes fatal hypersensitivity reactions.

The dosage for children, if not indicated otherwise, depends on their age and weight and is defined by the attending physician.

This medicinal product must be exclusively administered by authorised personnel.

4.2.2 Posology

The following dose recommendations are based on general experience with non-ionic x-ray contrast media as well as clinical studies performed with iopamidol. The total volume applied should not exceed 250 ml.

Field of application	**Volume**	
	Sheet Film Angiography	Digital Subtraction Angiography
Arteriography		
cerebral, non-selective	Adults: 40-60 ml Children: depending on body weight and age.	Adults: 20 – 30 ml Children: depending on body weight and age.
cerebral, selective	4-12 ml	3 – 8 ml
A. pulmonalis		Adults: 25 ml per

others	Adults: Maximum of 250 ml. The volume of the single injection depends on the vascular region to be examined. Children: depending on body weight and age.	single injection; overall dose up to 170 ml Adults: 30 – 50 ml. Maximum of 250 ml. The volume of the single injection depends on the vascular region to be examined. Children: depending on body weight and age.
Angiocardiography	Adults: Maximum of 250 ml. The volume of the single injection depends on the vascular region to be examined. Children: depending on body weight and age.	
Coronary angiography	Adults: 4 - 10 ml/artery, to be repeated if required	
Phlebography	Adults: 50 ml, depending on body weight and age	
Intraveneous digital subtraction angiography (i.v. DSA)	Adults: 30 - 50 ml, to be repeated if required Children: depending on body weight and age.	
Excretory urography	Adults: 50 - 100 ml Children: 0 – 1 month: 4 - 5-(6) ml/kg 1 – 3 month: 4 ml/kg 3 – 6 month: 3.5 - 4 ml/kg 6 – 12 month: 3 – 3.5 ml/kg 12 – 24 month: 2.5 - 3 ml/kg 2 – 5 years: 2.5 ml/kg 5 – 7 years: 2 – 2.5 ml/kg 7 – 12 years: 1.5 - 2 ml/kg	
Computer tomography (CT)	Adults: 1 – 2 ml/kg body weight Children: depending on body weight and age.	
The maximum dose for 300 mg Iodine/ml is 2 ml/kg bodyweight.		

Intravenous excretory urography:
In intravenous urography it has to be considered that the physiologically low concentration capacity of the immature nephron of children's kidneys requires relatively high doses of contrast media.

Computer tomography:
Iopamigita 300 mg/ml can be administered by rapid intravenous injection, if available, by using a high pressure injector. It can also be injected by a slow infusion by hand, in particular for enhancement of the central nervous system where 5 to 10 min waiting time are necessary before taking the images. In spiral CT, especially when using multi-slice technique, a multitude of information is captured while breath is held. In order to optimize the effect of the intravenous bolus injection in the examined region (time-dependent accumulation in the single pathologically altered tissues), the use of an automatic high pressure injector and the bolus application are recommended.
The doses and application velocity of contrast media for CT depend on the organs to be examined, on the diagnostic problem and especially on the device available (e. g. scan and image build-up times). For slow-processing devices, application by infusion is recommended , for rapid scanners bolus injection is recommended.

If this medicinal product is intended to be used with an automatic application system, the suitability of the device for the intended use must be proven by the manufacturer of the medical device. Instructions for use of the medical devices must be followed absolutely. In infants and toddlers automatic application systems must not be used.

4.3 Contraindications

Manifest hyperthyreosis
Hypersensitivity to the active substance or to any of the excipients
History of major immediate or delayed skin reaction (see section 4.8) to injection of iopamidol.

4.4 Special warnings and precautions for use

This medicinal product contains maximum 8.74 mg sodium per milliliter (ml). To be taken into consideration by patients on a controlled sodium diet.

Iopamigita should only be used after precise clinical indication considering possible risk factors of the examined patient.

Strict indication and special care is required in patients with
- known allergic disposition
- latent hyperthyreosis, euthyroid goiter
- renal impairment or severe liver dysfunction
- severe cardiovascular disease
- bronchial asthma
- diabetes mellitus
- cerebral convulsive disorder
- advanced cerebral atherosclerosis
- acute cerebral infarction
- acute intracranial bleeding or conditions accompanied by impairment of the blood-cerebral barrier and cerebral oedema
- bad general condition, dehydration
- dys- or paraproteinaemia
- phaeochromocytoma

Contrast media may promote sickling in individuals who are homozygous for sickle cell disease when injected intravenously and intra-arterially

Accidental paravasal injection can lead to local swelling, pain and erythema. These symptoms usually disappear again without complications.
Raising the affected extremety and cold compresses has been proven advantageous.

- Hydration

Sufficient hydration should be assured before and after administration of the contrast medium. If necessary, the patient should be hydrated intravenously until excretion of the contrast medium is complete.
This applies especially for patients with pre-existing disturbance of renal function, dys- and paraproteinaemia, diabetes mellitus, hyperuricaemia as well as for new-born infants, infants, toddlers, elderly patients, and patients in bad general condition. In risk patients the water and electrolyte metabolism must be controlled and symptoms of a dropping serum calcium level must be taken care of.
Due to the risk of dehydration induced by diuretics, at first, water and electrolyte rehydration is necessary to limit the risk of acute renal failure.

- Neonates and babies

Especially babies aged less than 1 year and neonates are susceptible to electrolyte disturbances and haemodynamic changes. Caution is, therefore, advised with regard to dosage of the contrast medium, conducting the examination and patient’s condition. Premature new-born infants should be monitored very carefully as application of the contrast medium can result in transient hypothyroidism.

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.

- Allergoid and anaphylactoid reactions (hypersensitivity reactions)

As with all iodinated contrast media, dose-independent non-allergic (pseudoallergic, allergoid) hypersensitivity reactions of varying severity and heterogenous symptomatology may occur following application of Iopamigita 300 mg Iodine/ml.
Usually these reactions become manifest as minor respiratory or cutaneous symptoms, such as mild difficulties of breathing, skin reddening (erythema), urticaria, pruritus or facial oedema. Severe reactions such as angio-oedema, subglottis oedema, bronchial spasm and shock are rare. These reactions usually occur within one hour following application of the contrast medium. In rare cases, hypersensitivity may occur delayed (after hours or days).
Due to the unsteady occurrence of such events they are not predictable in the individual case. It is, however, well-known that allergoid reactions are more frequent in patients with allergic disposition (allergies) and/or bronchial asthma and in patients with known hypersensitivity reactions to contrast media.
In patients with bronchial asthma especially the risk for bronchospasm is increased. Any application of a contrast medium should, therefore, be preceded by a detailed medical history with regard to the above mentioned risk factors. In patients with allergic diathesis and in patients with known hypersensitivity reactions a very strict indication is required.
In patients at risk for intolerance, premedication with antihistaminics and/or glucocorticoids was proposed; they may, however, not prevent anaphylactic shock.
There is a risk of IgE-dependent immediate allergy to the contrast agent.

- Provision for emergencies

Independent from quantity and route of administration, symptoms such as angioedema, conjunctivitis, coughing, pruritus, rhinitis, sneezing and urticaria may be indicative of a serious anaphylactoid reaction requiring treatment. Iodinated contrast media should, therefore, only be used under the precondition that treatment of emergencies is possible. This includes availability of the necessary technical and medicinal equipment, sufficient medical experience as well as skilled personnel. In principle, measures for immediate treatment of serious reactions and the required emergency supplies and equipment should be prepared. In imminent state of shock, administration of the contrast medium must be terminated immediately and - if necessary - specific intravenous treatment must be initiated. A flexible indwelling cannula or catheter (for immediate intravenous access) is recommendable during the entire X-ray examination.
Following application, the patient shall be monitored for at least ½ hour, as from experience the majority of all serious incidents occur within this timeframe.

- Disturbed thyroid function

Due to the free iodide contained in the solutions and due to the iodide released additionally by deiodination following application, iodinated contrast media influence thyroid function. This may induce hyperthyroidism or even thyreotoxic crisis in predisposed patients. In this respect patients with manifest but not yet diagnosed hyperthyroidism are at risk as well as patients with latent hyperthyroidism (often patients with nodular goiter) and patients with functional autonomy (often elderly patients, especially in regions with iodine deficiency). If administration of iodinated contrast media is planned in patients who are potentially at risk, thyroid function has to be assessed prior to the examination and hyperthyroidism or autonomy have to be excluded.
Before administering an iodinated contrast agent, make sure that the patient is not about to undergo thyroid scan or thyroid function tests or treatment with radioactive iodine, as administration of iodinated contrast agents, regardless of the route, interferes with hormone assays and iodine uptake by the thyroid gland or metastases from thyroid cancer until urinary iodine excretion returns to normal
Following injection of an iodinated contrast agent, there is also a risk of induction of hypothyroidism. There is as well a risk of hypothyroidism in neonates who have received, or whose mother has received, an iodinated contrast agent.

- Anxiety conditions

Conditions of marked agitation, anxiety or pain may increase the risk of side-effects or contrast media-related reactions. A sedative may be administered in the case of marked anxiety.

- Cardio-circulatory diseases

Patients with cardio-circulatory diseases are at higher risk for serious changes in cardiac haemodynamics and

electrophysiology (pacing and conduction). This is especially applicable following intracoronary, left and right ventricular application of contrast media (see also section 4.8).
Patients with cardiac insufficiency, severe coronary heart disease, instable angina pectoris, valvular diseases, previous myocardial infarction, coronary bypass and pulmonary hypertension are especially predisposed for cardiac reactions.
In elderly patients and patients with pre-existing cardiac diseases reactions with ischemic changes in the ECG and arrhythmia occur more frequently.
In patients with cardiac insufficiency intravasal injection of contrast media can induce pulmonary oedema.

- Disturbance of renal function

Reversible renal failure can occur. A history of renal disease, preceding renal failure following application of contrast media, existing renal insufficiency, diabetic nephropathy, age over 60 years, dehydration, advanced arteriosclerosis, decompensated cardiac insufficiency, high doses of contrast media and multiple injections, direct application of contrast media to the renal artery, exposition to further nephrotoxins, severe and chronic hypertension, hyperuricaemia and paraproteinaemia (e. g. plasmocytoma, macroglubulinaemia) are predisposing factors.
The following preventive measures are recommended: assuring sufficient hydration prior to and during application of the contrast medium, preferably by intravasal infusion until renal excretion of the contrast medium is complete, avoidance of additional exposure of the kidneys (nephrotoxic medicinal products, renal arterial angioplasty, major surgery etc.), dose reduction to a minimum.
Repeated examination with a contrast medium should only be performed when the renal function has returned to the base level.
Iodinated contrast media can be administered to dialysis patients as they are eliminated by dialysis.

- Diabetes mellitus

In patients treated with metformin: As the intravascular administration of iopamidol can lead to renal failure, metformin must be discontinued prior to, or at the time of the test and not be reinstituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal (see section 4.5).

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 and take precautions: withdrawal of metformin treatment, hydration, monitoring of renal function, serum lactate as well as pH and monitoring of the patient with regard to signs of lactacidosis.

- Coagulopathy

Catheter angiography with contrast media is connected with the risk to induce thromboembolic events. In vitro, non-ionic contrast media have a weaker coagulation inhibiting effect than ionic contrast media. During catheterization it should be considered that besides the contrast medium numerous other factors may also influence the development of thromboembolic events. These are: duration of the examination, number of injections, type of catheter and syringe material, existing underlying diseases und concomitant medication. In order to minimize the examination-related risk for thromboembolism, an especially thorough angiographic method and frequent irrigation of the used catheters shall be observed, the examination shall be kept as short as possible.
Caution is also advised in patients with homocysteinuria (risk of induction of thromboembolia).

- CNS disturbances

Caution is advised in intravasal application to patients with acute cerebral infarction or acute intracranial bleeding as well as in patients with diseases causing disturbance of the blood-brain barrier, in patients with cerebral oedema or acute demyelinisation. Intracranial tumors or metastases and epilepsy may induce an increased occurrence of seizures following application of a contrast medium. Neurological symptoms caused by metastases, degenerative or inflammatory processes can be aggravated by application of contrast media. Intraarterial injection of contrast media may induce vasospasm with resulting cerebral ischaemic phenomenons. Patients with symptomatic cerebrovascular diseases, previous stroke or frequent transitory ischemic attacks are at increased risk for contrast medium-induced neurological complications following intra-arterial injection.

- Alcoholism/drug dependency

Acute or chronic alcoholism can increase permeability of the blood-brain barrier and thus possibly cause contrast medium-induced CNS reactions.

- Further risk factors

Following application of contrast media to patients with plasmocytoma or paraproteinaemia renal insufficiency may occur. Sufficient hydration is obligatory.
In patients with phaeochromocytoma severe, occasionally uncontrollable hypertensive crisis can develop following intravasal application of a contrast medium. In patients with phaeochromocytoma pre-treatment with alpha receptor blockers is, therefore, recommended.
The symptoms of myasthenia gravis may be increased by iodinated contrast media.
Among patients with autoimmune diseases cases of serious vasculitis or Stevens-Johnson-like syndromes were observed.
Severe vascular and neurological diseases which are present especially in elderly patients, are risk factors for the occurrence of reactions to contrast media.
In severe renal insufficiency, an additional severe hepatic impairment can induce serious delayed excretion of the contrast medium, occasionally requiring haemodialysis.

The following precautions and warnings shall be observed for the different modes of application:

- Cerebral arteriography

In patients with advanced arteriosclerosis, severe hypertension, cardiac decompensation, senility, and previous cerebral thrombosis or embolism and migraine, special caution is advised as cardiovascular reactions such as bradycardia and increases or decreases in blood pressure may occur more often.

- Peripheral arteriography

There should be pulsation in the artery into which the contrast medium will be injected. In the presence of obliterative thrombangiitis or ascending infection in combination with severe ischaemia angiography should be performed with special caution, if at all.

- Arteriography of the aorta

Depending on the applied technique, injury of the aorta and adjacent organs, pleurocentesis, retroperitoneal bleeding, spinal cord injury and symptoms of paraplegia may occur.

- Coronary arteriography and ventriculography

During coronary arteriography and left ventriculography, cardiac decompensation, serious arrhythmia. ischaemia and myocardial infarction may occur.

It is absolutely necessary that the examination is performed by specialized staff and that electrocardiograph and sufficient equipment for reanimation and cardioversion are available. During the entire examination, ECG and vital function should be monitored routinely.

Angiocardiography of right ventricle in paediatric patients:
Special precaution should be taken in cyanotic newborns with pulmonary hypertension and cardiac dysfunction.
Supraaortic angiography:
Supraaortic angiography should be performed with special attention to the introduction of the catheter. High pressures of the automatic pump can provoke renal infarction, spinal cord lesions, retroperitoneal bleeding, intestinal infarction and necrosis. Renal function should be measured once angiography is concluded. In case of angiography, women should be explored during the pre-ovulation phase of cycle if possible.

- Phlebography

In patients with suspected thrombosis, phlebitis, severe ischaemia, local infection or complete venous occlusion special caution is advised. X-ray fluoroscopy is recommended in order to avoid extravasation.

4.5 Interaction with other medicinal products and other forms of interaction

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

The application of X-ray contrast media may induce transient impairment in renal function which may cause lactate acidosis in patients with diabetes mellitus treated with metformin (see section 4.4).

In patients taking beta-blockers, hypersensitivity reactions such as drop of blood pressure, bradycardia and bronchospasm may occur more intensely, especially in the presence of bronchial asthma. In addition it should be considered that patients taking beta-blockers may need higher doses of beta-agonists as they possibly do not respond to standard doses used for the treatment of hypersensitivity reactions.
Beta-blockers, vasoactive substances, angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists: These medicinal products induce decreased efficacy of cardiovascular compensation mechanisms of blood pressure changes: the doctor must be informed before injection of the iodinated contrast agent and resuscitation equipment must be at hand.

Medicinal products reducing seizure threshold (e.g. phenothiazine derivates, analeptic agents, tricyclic antidepressants, monoamine oxidase inhibitors, neuroleptic agents) can favour a convulsive seizure especially in patients suffering from epilepsy or focal brain damage. As far as justified by physician's treatment with such medicinal products should be discontinued 48 hours before and up to 24 hours after cerebral angiography in these patients.

In patients being treated with interferons and interleukins, known contrast medium reactions such as erythema, fever and/or flu-like symptoms may occur more frequently and above all delayed. The reason is not know so far.

Metformin: in diabetic patients (see section 4.4 Special precautions for use - Renal insufficiency).

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

In the diagnosis and treatment of thyroid diseases, Iodine substituted x-ray contrast media can reduce receptivity of the thyroid gland for radio-isotopes for 2 - 6 weeks. When renal scintigraphy using an injection of radiopharmaceutical secreted by the renal tubule is planned, it should preferably be performed before injection of the contrast agent.

4.6 Fertility, pregnancy and lactation

There are no adequate data from use of iopamidol in pregnant women.
For reproduction toxicity in animals see section 5.3.

As during pregnancy x-ray exposure should be avoided as far as possible, wether with or without a contrast agent, the benefit of x-ray examination has to be considered carefully.
Apart from radiation exposure of the fetus, benefit-risk-consideration after application of a iodine-containing contrast agent should also take into account the sensitivity of the fetal thyroid towards iodine, since acute iodine overload following administration of an iodinated contrast agent to the mother can induce fetal thyroid dysfunction.

Low amounts of iodinated contrast agents are secreted into the breast milk. Occasional administration to the mother is accociated with a low risk of adverse effects for the infant. However, as a precautionary measure, it is preferable to suspend breast feeding for 24 hours after administration of a iodinated contrast agent.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Undesirable effects in connection with the intravasal use of iodine-containing contrast media are usually mild to moderate and transient. However, severe reactions and in some cases possibly life-threatening reactions can occur that require rapid and effective emergency treatment.

The most commonly reported reactions are urticaria, nausea, vomiting, pruritus and dyspnoea.

ADRs are reported according to the following frequencies:

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 estimate from the available data)

System Organ Class	**Undesirable effects**
Immune system disorders	
Common:	Allergoid and/or anaphylactoid reactions: Angioedemas, conjunctivitis, coughing, pruritus, rhinitis, sneezing and urticaria (These reactions, which can occur with a delay in time and regardless of the amount administered and the method of administration, may be indicative of the beginning of a state of shock.)
Endocrine disorders	
Not known:	Dysfunction of metabolic condition in manifest hyperthyroidism through thyreotoxic crisis
Nervous system disorders	
Rare: *Not known:*	Cerebral angiography and other procedures in which the contrast medium enters the arterial blood in the brain in a high concentration: Agitation, confusion, amnesia, speech, sight and hearing disorders, epileptic fits, shaking, pareses, paralyses, paraesthesia, photophobia, transient blindness, coma and somnolence Thromboembolic events that resulted in a stroke Transient complications such as dizziness and headache
Cardiac disorders	
Very rare:	Clinically relevant disorders of blood pressure, heart rate, cardiac rhythm or cardiac function and cardiac arrest
Vascular disorders	
Rare:	Thromboembolic events have been reported during catheter angiographic examinations, which resulted in a cardiac infarction
Respiratory, thoracic and mediastinal disorders	
Common: *Rare:* *Very rare:*	Transient changes in respiratory rate, shortness of breath and respiratory distress as well as coughing Bronchospasm, laryngospasm and laryngeal oedema Pulmonary oedema or respiratory arrest
Gastrointestinal disorders	
Common: *Rare:* *Very rare:*	Nausea, vomiting, impaired taste Abdominal complaints Swelling of salivary glands (iodide mumps)
Skin and subcutaneous tissue disorders	
Common:	Oedemas, flush, urticaria, rash, pruritus and erythema

Very rare:	Toxic skin reactions in the form of a mucocutaneous syndrome (e.g. Stevens-Johnson or Lyell's syndrome). So far a causal relationship has not been established.
Renal and urinary Disorders	
Rare:	Renal function disorders extending to acute kidney failure, particularly in patients whose renal function was already impaired
General disorders and administration site conditions	
	General disorders:
Rare:	Serious life-threatening reactions (including fatalities) that require emergency treatment and are associated with vital functions of the cardiovascular system, usually in connection with respiratory and central nervous reactions
Very rare:	Feeling warmth, changes in body temperature (fever), headache, feeling unwell, sweating, a cold feeling and vasovagal reactions Thrombophlebitis and venous thromboses
	Administration site conditions:
Very rare:	Inflammation and tissue necrosis
Not known:	Extravasation local pain and oedemas

Severe anaphylactic/anaphylactoid reactions in the form of shock are characterised by a massive fall in blood pressure, tachycardia, dyspnoea, agitation, cyanosis, pallor, cold sweats, clouding or loss of consciousness and respiratory and circulatory arrest. The fall in blood pressure may also be connected with bradycardia (vasovagal reaction), from which tachycardia usually develops over time.

4.9 Overdose

In case of accidental overdose or considerable renal dysfunction, iopamidol can be removed from the organism by extracorporeal dialysis.

If an undesired reaction occurs, administering contrast medium has to be stopped immediately. Treatment follows the clinical picture. Besides general reanimation measures, medication might be advisable, e.g. general treatment (antihistaminic, corticosteroids, oxygenotherapy),treatment of cardiovascular disorders (vasopressors, plasma, electrolites),treatment of convulsions (diazepam),treatment of tetanic crisis (calcic gluconate), Renal function should be monitored at least the following 3 days after overdose.. It has to be considered that in patients receiving beta-blockers simultaneously, adrenalin and volume substitution have a minor effect.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: x-ray contrast media, iodinated; watersoluble, nephrotropic, low osmolar x-ray contrast media

ATC code: V08A B04

X-rays are absorbed by iodine atoms in a stable bound state. The contrast giving effect is based on this absorption.

5.2 Pharmacokinetic properties

After intravenous injection, the contrast medium distributes into the intravasal and interstitial space within a few

minutes together with a simultaneous renal elimination.

After 120 minutes approx. 50% of the injected contrast medium is excreted with the urine; in case of renal impairment this period of time is prolonged accordingly.

Due to its hydrophilic character, there is practically no binding of iopamidol to plasma proteins and cell membranes are not penetrated. It is not possible that iopamidol penetrates the intact blood-brain-barrier.

The heterotopy excreted proportion is small. In animal experiments (dog and rabbit) only 0.07 – 0.32% of the applied dose were found in the bile.

There is no evidence of biotransformation.
Serum protein binding is negligible

5.3 Preclinical safety data

Intravenous LD_{50}-values in various animal species were determined to be approximately 15-35 fold the maximum clinical dose.

Reproduction Toxicology
There is no evidence for a teratogenic potential of iopamidol. Doses above 1.5 g Iodine/kg/day showed embryotoxic effects in rats and a reduced number of living foetuses and weight of the foetuses. Reduced weight of the foetuses was also observed in rabbits with a dose of 2 g Iodine/kg/day. The fertility of rats as well as the peri- and postnatal development of their offspring was not affected. However, reversible spermatogenesis disorders have been observed in mice after single application of iopamidol.

Mutagenic Potential
Iopamidol did not show any mutagenic effects in a series of in vitro- and in vivo-tests.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trometamol
Edetate calcium disodium (dihydrate)
Water for injections
Hydrochloric acid 36 % (for pH-adjustment)

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years

Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C. Contents not used in a patient during one single investigation as well as contents of a 500 ml vial not used within 24 hours during two investigations in one single patient, must be discarded.

6.4 Special precautions for storage

Store in the original package in order to protect from light. Protect from x-rays.
Do not refrigerate or freeze.

6.5 Nature and contents of container

Iopamigita 300 mg/ ml solution for injection and infusion is available in package sizes as follows:

- Glass vials type I with bromobutyl rubber closure and aluminium caps for single use 10 and 30 vials containing 20 ml solution for injection and infusion each
- Glass vials type II with bromobutyl rubber closure and aluminium caps for single use

10 and 30 vials each containing 50 ml solution for injection and infusion
10 and 30 vials each containing 75 ml solution for injection and infusion
10 and 30 vials each containing 100 ml solution for injection and infusion
10 and 20 vials each containing 200 ml solution for injection and infusion.
1 and 6 vials each containing 500 ml solution for injection and infusion

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Each container is for single patient use only.

Prior to use, the solution has to be inspected visually. Only solutions without visible signs of deterioration or particles may be used.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

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

Agfa Healthcare Imaging Agents GmbH
Am Coloneum 4
50829 Köln
Germany

8 MARKETING AUTHORISATION NUMBER

PA 1504/2/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 22nd February 2013

10 DATE OF REVISION OF THE TEXT