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im Gesundheitswesen

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**Betreff: Iopamidol – hältige Arzneispezialitäten – Änderungen der Fach- und Gebrauchsinformationen aufgrund des HBD – PSUR Worksharing Projektes**

Sehr geehrte Damen und Herren,

basierend auf der Evaluierung des PSURs im EU-HBD-worksharing Projekt (Verfahrensnummer: IE/H/PSUR/0016/002) kommt es zu der Empfehlung, folgende Ergänzungen in die **Fach- und Gebrauchsinformation** aller Iopamidol– hältige Arzneispezialitäten aufzunehmen.

Sollten diese bereits aufgenommen worden sein, betrachten Sie dieses Schreiben als gegenstandslos.

## Iopamidol oral / rectal

**4.3 - Contraindications**
Hypersensitivity to the active ingredient iopamidol and/or iodine preparations or to any of the excipients.

**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.
The risk of severe hypersensitivity reactions may be increased in patients with history of known clinical hypersensitivity to any of the ingredients, other contrast media or history of asthma or other allergic disorders.
In case of suspected perforation of the gastrointestinal tract, use only when the benefit of the information outweighs the risk.
Concomitant administration of β-blockers can exacerbate severe hypersensitivity reactions.
Aspiration of orally administered contrast medium into the tracheobronchial tree may very rarely result in pulmonary complications. Therefore, avoid use of Iopamidol solution in patients with oesophagotracheal fistula and minimise risks for pulmonary aspiration in all patients. If the contrast medium is given by nasogastric tube, the position of the tube in the stomach must be verified before administration.

Alcohol: Iopamidol solution contains 2.4 mg of ethanol per mL which may be harmful for those suffering from alcoholism, and to be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease or epilepsy.

*Special populations*
Women of child bearing potential
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.

*Paediatric population*
Newborns and infants
Infants (age<1year), and especially newborns are particularly susceptible to electrolyte imbalances and haemodynamic alterations. It is recommended that they are adequately hydrated prior to administration of Iopamidol solution.

**4.5 - Interactions with other medicaments and other forms of interaction**

Concomitant administration of β-blockers can exacerbate severe hypersensitivity reactions.
No interaction studies have been performed. There are no known interactions

**4.6 Fertility, pregnancy and lactation**

*Pregnancy*
There are no or a limited amount of data from the use of Iopamidol in pregnant women.
Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.
As a precautionary measure, it is preferable to avoid the use of Iopamidol solution during pregnancy.

*Breastfeeding*
It is unknown whether Iopamidol is excreted in human milk. A risk to newborns/infants cannot be excluded.
However, due to the low level of absorption of Iopamidol from the gastrointestinal tract, it is unlikely that a foetus could be exposed to significant levels.

*Fertility*

No effects on fertility are anticipated due to the low absorption of Iopamidol from the gastrointestinal tract following oral or rectal administration.
Reproduction studies performed in animals with Iopamidol administered parenterally revealed no evidence of impaired fertility. No studies have been performed in women.

**4.7 - Effects on ability to drive and use machines**

On the basis of the pharmacokinetic and pharmacodynamic profiles, no or negligible influence is expected with the use of Iopamidol solution on the ability to drive or use machines.

**4.8 - Undesirable effects**

The undesirable effects reported with Iopamidol solution were, in general, non-serious, mild to moderate, transient and resolved spontaneously without residual effects.
Solutions of iodinated contrast media administered oral route or by enema can cause diarrhoea due to high osmolality of these solutions.

In clinical trials, the most commonly reported adverse reactions are vomiting in adult patients (1.8%) and diarrhoea in paediatric patients (5.7%). These reactions have been reported mostly after oral administration of the contrast agent.
Signs and symptoms of anaphylactoid reactions, both localised (flushing, urticaria, rash, laryngeal oedema, dyspnoea, bronchospasm) and systemic (hypotension, shock, pulmonary oedema, circulatory arrest, respiratory arrest) are possible following administration of iodinated contrast media by routes other than intravascular, since a small fraction is normally absorbed by the intestinal mucosa. However, systemic absorption is rapid and complete if the contrast agent reaches the peritoneal cavity.

*Adult patients*

Adverse reactions derived from clinical trials in 269 adult patients who received Iopamidol by either oral or rectal route of administration and from post-marketing spontaneous reporting are tabulated below.

| **System Organ Class** | **Adverse Reactions** | | |
|---|---|---|---|
| | **Clinical Trials** | | **Spontaneous reporting** |
| | **Common ≥1/100 to <1/10** | **Uncommon ≥ 1/1,000 to < 1/100** | **Frequency not known** |
| Immune system disorders | | | Anaphylactoid reaction |
| Vascular disorders | | Hypotension | |
| Gastrointestinal disorders | Vomiting | Diarrhoea,<br>Abdominal discomfort | |

*Paediatric patients*

The table below lists the adverse reactions derived from clinical trials conducted in 335 paediatric patients, who received Iopamidol by either oral or rectal route of administration. No cases were received as post-marketing spontaneous reporting.

| **System Organ Class** | **Adverse Reactions** | |
|---|---|---|
| | **Clinical Trials** | |
| | **Common ≥1/100 to <1/10** | **Uncommon ≥1/1000 to <1/100** |
| Gastrointestinal disorders | Diarrhoea | Nausea,<br>Vomiting |

**4.9 - Overdose**

The contrast agent is very poorly absorbed by the gastrointestinal tract; therefore, any accumulation of the contrast medium in humans due to overdosage is negligible.
In the event of overdose, treatment is directed toward the support of all vital functions and prompt institution of symptomatic therapy.

# Solution for Injection (IV IT)

**4.2 – Posology and 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 should not be allowed to remain in contact with blood in the syringe or intravascular catheters which should be flushed frequently to minimize the risk of clotting and thromboembolic events during angiographic techniques.
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
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.

Caution during injection of contrast media is necessary to avoid extravasation

**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 (see section 4.5 Interactions with other medicaments and other forms of interaction).
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.
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.
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.
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 20-30minutes after the procedure as most of the adverse events occur within this period.
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.
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
Care should be exercised in patients with moderate to severe impairment of renal function.
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 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
Patients on dialysis may receive contrast media such as iopamidol, which can be removed without difficulty by dialysis.
The presence of renal damage in diabetic patients is one of the factors predisposing to acute renal impairment following intravascular contrast media administration. This may precipitate lactic acidosis in patients who are taking biguanides. (see section 4.5).
As experience shows that warmed contrast media are better tolerated, the contrast medium should be warmed up to body temperature before administration
The risk associated with a particular investigation may be increased by conditions such as advanced arteriosclerosis and hypertension.
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.

Great caution should be paid when injecting the contrast medium into the heart chambers, especially in cyanotic neonates with pulmonary hypertension and impaired cardiac function
During intracardiac and/or coronary arteriography, ventricular arrhythmias may infrequently occur.

Patients who are known epileptic or have a history of epilepsy should have their medicine maintained. In some instances, anticonvulsant therapy may be increased for 48 hours before the examination
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.
It is possible that hyperthyroidism may recur in patients previously treated for Graves' disease.
In patients with hyperthyroidism, the radiological examination should be performed only if thought necessary by the physician.
In patients scheduled for thyroid examination and/or treatment with a radioactive iodine tracer, iodine update in the thyroid gland will be reduced for several days, sometimes up to 2 weeks after dosing with an iodinated contrast medium that is eliminated through the kidneys.
Use of this product might interfere with tests for thyroid function.
Patients with phaeochromocytoma can develop severe hypertensive crises following intravascular iopamidol administration. Premedication with □-receptor blockers is recommended.

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.
To prevent crises in patients with sickle cell disease adequate hydration should be assured and a minimal volume of low concentration should be used.
Local tissue irritation can occur in the case of perivascular infiltration of the contrast media.
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 placement 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 ischaemia 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.
The administration of iodinated contrast media may aggravate the symptoms of myasthenia gravis.
Iopamidol injection should be used with caution in patients with hypercalcaemia and cerebral vascular disease.
No other drugs or contrast media should be mixed with iopamidol solution for injection.
Iopamidol should be administered with caution 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.
Vasospasm and subsequent cerebral ischemic phenomena may be caused by intra-arterial injections of contrast media.

*Neuroradiology*
The contrast medium should be removed as much as possible in case of spinal fluid blockage.
Anticonvulsant therapy should be maintained before and following myelographic procedures in patients who are known to suffer from convulsions.
If during the procedure a convulsive crisis occurs , it is recommended to administer intravenously diazepam or phenolbarbital.
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 operator should evaluate in those cases the diagnostic need against possible risk to the patient 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. The patient should remain supine and at bed rest during this period Encourage the patient, if able, to take in fluids orally and eat .

*Use in Special Populations*
*Newborns, children*
Infants (age<1year), 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
*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

Womenofchild-bearingpotential
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 medicaments and other forms of interaction

To prevent onset of lactic acidosis in diabetic patients 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).
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.
Following administration of iopamidol, the capacity of the thyroid tissue to take up iodine is reduced for 2-6 weeks.
Arterial thrombosis has been reported when iopamidol was given following papaverine
The administration of vasopressors strongly potentiates the neurological effects of 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 bililrubin, proteins or inorganic substances (e.g. iron, copper, calcium, and phosphate). These substances should not be assayed during the same day following the administration of contrast media.
In patients receiving beta-blockers there is an elevated risk of more severe anaphylactoid reactions.
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 should be avoided as they lower the seizure threshold. This is also true for drugs such as analgesics, antiemetics, antihistaminics, or sedatives of the phenothiazine group.
Wherever possible the therapy with such drugs must be discontinued at least 48 h before the radiological investigation and treatment can be resumed not earlier than 24 h afterwards

**4.6 - Pregnancy and Lactation**
The safety of iopamidol injection during pregnancy has not been established. Since radiation exposure during pregnancy should be avoided anyway, regardless of whether a contrast agent is used or not, the benefit of X-ray examination has to be considered carefully. 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.

**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**
Side effects are usually mild to moderate and transient in nature; however, rare severe and life-threatening reactions, sometimes leading to death, have been reported.
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.
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.

4.8.1 Intravascular administration
Adult subjects
Adult patients involved in clinical trials with intravascular administration of Iopamidol were 2,548, of whom 1,597 with intra-arterial and 951 with intravenous administration.

| **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 | | | | Blindness transient, 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 and mediastinal disorders | | | Pulmonary oedema, Asthma, Bronchospasm | Respiratory arrest, Respiratory failure, Acute respiratory distress syndrome, Respiratory distress, Apnoea, Laryngeal oedema, |
| Gastrointestinal disorders | Nausea | Vomiting, Diarrhea, Abdominal pain, Dry mouth | | Salivary hypersecretion, Salivary gland enlargement |
| Skin and subcutaneous tissue disorders | | Rash, Urticaria, | | Face oedema |
| | | Pruritus, Erythema, Sweating increased | | |
| 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 dysrhythmias may occur mostly after cardiac angiographic and coronary catheterization procedures

Coronary artery thrombosis has been reported as a complication of coronary catheterization procedures. Other cardiac reactions which may occur as a consequence of the procedural hazard include coronary artery dissection.

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.
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.
Injection site pain and swelling may occur. On very rare occasions extravasation of contrast medium led to inflammation (manifested with local erythema, oedema and blisters), skin necrosis and compartment
syndrome.
As with other iodinated contrast media, very rare cases of mucocutaneous syndromes, including Stevens- Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome) and erythema multiforme, have been
reported following the administration of Iopamidol.
Paediatric patients
The Iopamidol safety profile is similar in children and adults.

4.8.2. Intrathecal administration
Adult subjects
Adult patients involved in clinical trials with intrathecal administration of Iopamidol were 132.

| **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 |
| Immune system disorders | | | | Anaphylaxis, Anaphylactoid reaction |
| Psychiatric disorders | | | | Confusional state, Disorientation, Agitation, Restlessness |

| | | | | |
|---|---|---|---|---|
| Nervous system disorders | Headache | | | Coma,<br>Paralysis,<br>Convulsion,<br>Syncope,<br>Depressed level of consciousness or loss of consciousness,<br>Meningism,<br>Dizziness,<br>Paraesthesia,<br>Hypoaesthesia |
| Eye disorders | | | | Blindness transient |
| Cardiac disorders | | | | Arrhythmia |
| Vascular disorders | | Flushing | | Hypertension |
| Respiratory, thoracic and mediastinal disorders | | | | Respiratory arrest,<br>Dyspnoea |
| Gastrointestinal disorders | | Nausea,<br>Vomiting | | |
| Skin and subcutaneous tissue disorders | | | Rash | |
| Musculoskeletal and connective tissue disorders | | Back pain,<br>Neck pain,<br>Pain in extremity,<br>Sensation of heaviness | | |
| General disorders and administration site conditions | | | | Pyrexia,<br>Malaise,<br>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.

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. Also less common than after intravascular administration are the respiratory (dyspnoea or respiratory distress in the form of bronchospasm) and mucocutaneous manifestations (urticaria, angioneurotic oedema, and other skin reactions like rash).

Paediatric patients
The Iopamidol safety profile is similar in children and adults.

4.8.3. Use in body cavities

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 and fistulography 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, hemodialysis 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.

Oben angeführte Textabschnitte stellen eine Mindestanforderung dar, zusätzliche nationale Hinweise in diesen Abschnitten sind zu belassen.