SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

IOXRAY 350 mg I/mL, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Iohexol USP.....755 mg

Corresponding amount of iodine.....350 mg

For 1 mL of solution

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Injectable solution

Clear, colorless to pale yellow, viscous liquid.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

This medicinal product is for diagnostic use only.
Radiological contrast agent for use in adults and children for urography, phlebography, intravenous DSA, CT, arteriography, cardioangiography, and intra-abdominal DSA. Myelography. For use in body cavities: arthrography, ERP/ERCP, herniography, hysterosalpingography, sialography, and use in the GI tract.

4.2. Posology and method of administration

Posology

The dosage depends on the type of examination and the technique used. Generally, the same concentration and volume of iodine are used as for other iodinated radiological contrast agents currently in use.

Adequate hydration must be ensured before and after administration, as with other contrast agents. For intravenous, intra-arterial, and intrathecal use, and for use in body cavities.

The following dosages can serve as a guide:

Guidelines for intravenous use :

Indication	Concentration	Volume	Comments
Urography : Adults Children < 7 kg Children > 7 kg	 300 mg I/ml or 350 mg I/ml 240 mg I/ml or 300 mg I/ml 240 mg I/ml or 300 mg I/ml	 40-80 ml 40-80 ml 4 ml/kg bw 3 ml/kg bw 3 ml/kg bw 2 ml/kg bw	
Phlebography (legs)	240 mg I/ml or 300 mg I/ml	20-100 ml/leg	
Digital subtraction angiography : Adults Children	140 mg I/ml 300 mg I/ml or 350 mg I/ml 140 mg I/ml	Up to 3 ml per kg of body weight 20 - 60 ml/inj. 20 - 60 ml/inj. Depends on age, weight and pathology	
CT Improvement : Adults	 140 mg I/ml or 240 mg I/ml or 300 mg I/ml or 350 mg I/ml	 100-400 ml 100-250 ml 100-200 ml 100-150 ml	

Guidelines for intra-arterial use :

Indication	Concentration	Volume	Comments
Arteriographies			
Arcuate aortography	300 mg I/ml	30-40 ml/inj.	
Selective cerebral	300 mg I/ml	5-10 ml/inj.	
aortography	350 mg I/ml	40-60 ml/inj.	
Femoral	300 mg I/ml or 350 mg I/ml	30-50 ml/inj.	
Miscellaneous	300 mg I/ml	Depending on the type of exam.	
Phlebography (legs)	240 mg I/ml or 300 mg I/ml	20-100 ml/leg	
Cardioangiography			
Adults			
Injury to the left ventricle and aortic root.	350 mg I/ml	30-60 ml/inj.	
Selective coronary arteriography	350 mg I/ml	4-8 ml/injection	
Children			
	300 mg I/ml or 350 mg I/ml	Depending on age and pathology (max 8 ml/kg bw)	
Digital subtraction angiography :			
Adults	140 mg I/ml or 240 mg I/ml or 300 mg I/ml	4 - 10 ml/day. 1 - 15 ml/day. 1 - 15 ml/day.	
Children	140 mg I/ml	Depending on age, weight and medical condition	

Guidelines for intrathecal use :

Indication	Concentration	Volume	Comments
Lumbar and thoracic myelography (lumbar injection)	240 mg I/ml	8-12 ml	
Cervical myelography (lumbar injection)	240 mg I/ml or 300 mg I/ml	10-12 ml 7-10 ml	
Cervical myelography (lateral cervical injection)	240 mg I/ml or 300 mg I/ml	6-10 ml 6-8 ml	
CT cisternography (lumbar injection)	240 mg I/ml	4 - 12 ml	

To minimize potential adverse effects, the total dose of 3 g of iodine should not be exceeded.

Guidelines for body cavities :

Indication	Concentration	Volume	Comments
Arthrography	240 mg I/ml or 300 mg I/ml or 350 mg I/ml	5 - 20 ml 5-15 ml 5-10 ml	
ERP/ERCP	240 mg I/ml	20-50 ml	
Herniography ie	240 mg I/ml	50 ml	
Hysterosalpingography	240 mg I/ml or 300 mg I/ml	15 - 50 ml 15-25 ml	
Sialography	240 mg I/ml or 300 mg I/ml	0.5 - 2 ml 0.5 - 2 ml	

Gastrointestinal studies	350 mg I/ml	10-20 ml	

For elderly patients, patients with hepatic and/or renal insufficiency, the usual/suggested adult doses may be used.

4.3. Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Manifest thyrotoxicosis.

4.4. Special warnings and precautions for use

Special precautions for the use of non-ionic monomeric contrast agents in general:

Hypersensitivity : A history of allergy, asthma, or adverse reactions to iodinated contrast agents indicates the need for particular caution. Therefore, any application of contrast agent must be preceded by a detailed medical history. In patients with an allergic diathesis and in patients with known hypersensitivity reactions, a very strict indication is required.

Premedication with corticosteroids or H1 and H2 antihistamines may be considered in patients at risk of intolerance, but it does not prevent anaphylactic shock and may even mask the initial symptoms. In patients with bronchial asthma, the risk of bronchospasm is particularly high.

The risk of serious reactions related to the use of IOXRAY is considered minor. However, iodinated contrast agents can cause severe, potentially life-threatening anaphylactic/anaphylactoid reactions, or other manifestations of hypersensitivity. Regardless of the amount and route of administration, symptoms such as angioedema, conjunctivitis, cough, pruritus, rhinitis, sneezing, and urticaria may be signs of a serious anaphylactoid reaction requiring treatment. Therefore, an action plan must be in place in advance, with the necessary medications and equipment, medical expertise, and qualified personnel readily available for immediate treatment should a serious reaction occur. In the event of impending shock, contrast agent administration must be stopped immediately, and—if necessary—specific intravenous treatment should be initiated. It is advisable to always use an indwelling cannula or catheter for rapid intravenous access throughout the radiological procedure. Patients using beta-blockers may experience atypical symptoms of anaphylaxis that could be misinterpreted as a vagal reaction. Hypersensitivity reactions usually manifest as minor respiratory or cutaneous symptoms, such as mild difficulty breathing, skin reddening (erythema), urticaria, pruritus, or facial edema. Severe reactions such as angioedema, subglottis edema, bronchospasm, and shock are rare. These reactions generally occur within one hour of contrast agent application. In rare cases, hypersensitivity may occur later (after hours or days), but these cases are rarely life-threatening and primarily affect the skin.

When performing vascular catheterization procedures, meticulous attention should be paid to the angiographic technique and the catheter should be frequently flushed (e.g., with heparinized saline) to minimize the risk of thrombosis and embolism associated with the procedure.

The examination should be as short as possible. Precautions should be taken in patients with homocystinuria (risk of thromboembolism).

Hydration : Adequate hydration must be ensured before and after administration of the contrast agent. If necessary, the patient should be hydrated intravenously until complete excretion of the contrast agent. This applies particularly to patients with dys- and paraproteinemias such as multiple myeloma, diabetes mellitus, renal dysfunction, hyperuricemia, as well as to infants, young children, elderly patients, and patients in poor general condition. In at-risk patients, water and electrolyte metabolism should be monitored, and symptoms of decreased serum calcium levels should be managed. Due to the risk of diuretic-induced dehydration, initial fluid and electrolyte rehydration is necessary to minimize the risk of acute renal failure.

Cardio-circulatory reactions : Caution should also be exercised in patients with serious heart disease / cardiovascular disease and pulmonary hypertension as they may develop hemodynamic changes or arrhythmias.

This is particularly applicable after intracoronary, left ventricular and right ventricular application of contrast agents.

Patients with heart failure, severe coronary artery disease, unstable angina, valvular heart disease, previous myocardial infarction, coronary artery bypass grafting, and pulmonary hypertension are particularly susceptible to cardiac reactions. In elderly patients and those with pre-existing heart disease, reactions with ischemic ECG changes and arrhythmias are more common. In patients with heart failure, intravasal injection of contrast agents can induce pulmonary edema.

CNS Disorders : Patients with acute brain disease, tumors, or a history of epilepsy are predisposed to seizures and require special attention. Alcoholics and drug addicts are also at increased risk of seizures and neurological reactions. Caution is advised during intravascular administration in patients with acute cerebral infarction or acute intracranial hemorrhage, as well as in patients with diseases that disrupt the blood-brain barrier, cerebral edema, acute demyelination, or advanced cerebral atherosclerosis. Neurological symptoms caused by metastases, degenerative, or inflammatory processes may be exacerbated by the application of contrast agents. Intra-arterial

injection of contrast agents may induce vasospasm, potentially leading to cerebral ischemia. Patients with symptomatic cerebrovascular disease, a history of stroke, or frequent transient ischemic attacks are at increased risk of contrast-induced neurological complications following intra-arterial injection. A few patients have experienced temporary hearing loss or even deafness after myelography, which is thought to be due to a decrease in cerebrospinal fluid pressure caused by the lumbar puncture itself.

Renal reactions : The use of iodinated contrast agents can cause contrast-induced nephropathy, impaired renal function, or acute renal failure. To prevent these conditions following contrast administration, particular attention should be paid to patients with pre-existing renal impairment and diabetes mellitus, as they are at risk. Other predisposing factors include prior renal impairment after contrast administration, a history of kidney disease, age over 60, dehydration, advanced arteriosclerosis, decompensated heart failure, high doses of contrast agents and multiple injections, direct application of the contrast agent to the renal artery, exposure to other nephrotoxins, severe and chronic hypertension, hyperuricemia, paraproteinemias (myelomatosis and Waldenström's macroglobulinemia, plasmacytoma), or dysproteinemias. Preventive measures include:

- Identifying high-risk patients
- Ensuring adequate hydration. If necessary, by maintaining an IV infusion from before the procedure until the contrast agent is eliminated by the kidneys.
- Avoid further stressing of the kidneys in the form of nephrotoxic drugs, oral cholecystographic agents, arterial clamping, renal arterial angioplasty, or major surgery, until the contrast agent is eliminated.
- Reduce the dose to a minimum.
- Postponing a new examination with contrast medium will occur until renal function returns to pre-examination levels. Patients undergoing hemodialysis may receive contrast medium for radiological procedures. It is unnecessary to coordinate the timing of contrast medium injection with the hemodialysis session.

Diabetic patients on metformin : There is a risk of lactic acidosis when iodinated contrast agents are administered to diabetic patients treated with metformin, particularly those with impaired renal function. To reduce the risk of lactic acidosis, serum creatinine levels should be measured in diabetic patients treated with metformin before intravascular administration of iodinated contrast agents, and the following precautions should be taken in the following circumstances:

Normal serum creatinine (130 µmol/L)/impaired renal function : Metformin should be discontinued and the contrast agent examination delayed for 48 hours. Metformin should only be restarted 48 hours later if renal function is not impaired (if serum creatinine is not elevated) compared to pre-contrast values.

Emergency situations : In emergency situations where renal function is impaired or unknown, the physician must assess the benefit/risk ratio of the contrast agent examination, and the following precautions must be implemented: metformin must be discontinued. It is particularly important that the patient be fully hydrated before administration of the contrast agent and for 24 hours afterward. Renal function (e.g., serum creatinine), serum lactic acid, and blood pH should be monitored, as well as the patient for signs of lactic acidosis. A pH of 5 mmol/L is indicative of lactic acidosis. The patient should be observed for symptoms of lactic acidosis. These include vomiting, drowsiness, nausea, epigastric pain, anorexia, hyperpnea, lethargy, diarrhea, and thirst.

Hepatic reactions : There is a potential risk of transient liver dysfunction. Particular attention is required in patients with severe renal and hepatic impairment, as they may experience a significant delay in contrast agent clearance. Patients undergoing hemodialysis may receive contrast agents for radiological procedures. It is unnecessary to correlate the timing of contrast agent injection with the hemodialysis session.

Myasthenia gravis : The administration of iodinated contrast agents may worsen the symptoms of myasthenia gravis.

Pheochromocytoma : In patients with pheochromocytoma undergoing interventional procedures, alpha-blockers should be administered prophylactically to avoid a hypertensive crisis.

Thyroid Function Disruption : Due to the free iodide present in the solutions and the additional iodide released by deiodination, iodinated contrast agents affect thyroid function. This can induce hyperthyroidism or even a thyrotoxic crisis in predisposed patients with overt but undiagnosed hyperthyroidism. Patients with latent hyperthyroidism (e.g., nodular goiter) and patients with limited functional independence (often, for example, elderly patients, particularly in iodine-deficient regions) should therefore have their thyroid function assessed before the examination if such conditions are suspected. Before administering an iodinated contrast agent, it is essential to ensure that the patient is not about to undergo a thyroid scan, thyroid function tests, or radioactive iodine treatment, as the administration of iodinated contrast agents, regardless of the route, interferes with hormone assays and iodine uptake by the thyroid gland or thyroid cancer metastases until urinary iodine excretion returns to normal. Following injection of an iodinated contrast agent, there is also a risk of inducing hypothyroidism.

Anxiety states : A sedative may be administered in cases of marked anxiety.

Sickle cell disease : Contrast agents may promote sickle cell disease in people homozygous for sickle cell disease when injected intravenously and intra-arterially.

Other risk factors : Among patients with autoimmune diseases, cases of severe vasculitis or Stevens-Johnson

syndrome have been observed. Severe vascular and neurological diseases, particularly in elderly patients, are risk factors for reactions to contrast agents.

Extravasation : Extravasation of the contrast agent can, in rare cases, lead to local pain, edema, and erythema, which generally resolve without sequelae. However, inflammation and even tissue necrosis have been observed. Elevating and cooling the affected site is recommended as routine measures. Surgical decompression may be necessary in cases of compartment syndrome. Observation Time: Patients should be kept under close observation for 30 minutes after the last injection, as the majority of serious reactions occur during this time. Coagulopathy: Catheter angiography with contrast agent carries a risk of inducing thromboembolic events. In vitro, nonionic contrast agents have a weaker coagulation-inhibiting effect than ionic contrast agents. During catheterization, it should be considered that, in addition to the contrast agent, many other factors can also influence the development of thromboembolic events. This includes the duration of the examination, the number of injections, the type of catheter and syringe material, any existing underlying diseases, and any concomitant medications.

Intrathecal use : After myelography, the patient should rest with their head and chest elevated at a 20° angle for one hour. Afterward, they may move around cautiously, but should avoid bending over. The head and chest should remain elevated for the first 6 hours if the patient is bedridden. Patients suspected of having a low seizure threshold should be observed during this period. Outpatients should not be left completely alone for the first 24 hours.

Cerebral arteriography : In patients with advanced arteriosclerosis, severe hypertension, cardiac decompensation, advanced age, and a history of cerebral thrombosis or embolism and migraine, cardiovascular reactions such as bradycardia and increased or decreased blood pressure may occur more frequently.

Arteriography : Depending on the procedure used, damage to the artery, vein, aorta and adjacent organs, pleurocentesis, retroperitoneal hemorrhage, spinal cord injury and symptoms of paraplegia may occur.

Pediatric population :

Transient hypothyroidism has been reported in premature infants, newborns, and other children following the administration of iodinated contrast agents. Premature infants are particularly sensitive to the effects of iodine. Thyroid function should be checked in newborns during the first week of life after the mother received iodinated contrast agents during pregnancy. It is recommended to repeat thyroid function tests at 2 to 6 weeks of age, especially in low birth weight or premature newborns. Adequate hydration should be ensured before and after contrast agent administration, particularly in infants and young children. Nephrotoxic medications should be discontinued. The age-related reduction in glomerular filtration rate in infants may also result in delayed excretion of contrast agents. Young infants (age < 1 year) and especially newborns are sensitive to electrolyte disturbances and hemodynamic alterations.

4.5. Interactions with other medicinal products and other forms of interaction

The use of iodinated contrast agents may cause transient alterations in renal function, which may precipitate lactic acidosis in diabetics taking metformin.

Patients treated with interleukin-2 and interferons less than two weeks prior have been associated with an increased risk of delayed reactions (erythema, flu-like symptoms or skin reactions).

The concomitant use of certain neuroleptics or tricyclic antidepressants may reduce the seizure threshold and thus increase the risk of contrast-induced seizures.

Treatment with β-blockers may lower the threshold for hypersensitivity reactions, as well as require higher doses of β-agonists when treating hypersensitivity reactions.

Beta-blockers, vasoactive substances, angiotensin-converting enzyme inhibitors, and angiotensin receptor antagonists can reduce the effectiveness of cardiovascular compensation mechanisms for variations in blood pressure.

All iodinated contrast agents can interfere with thyroid function tests, as the thyroid's iodine uptake capacity may be reduced for several weeks.

High concentrations of contrast agents in serum and urine can interfere with laboratory tests for bilirubin, proteins, or inorganic substances (e.g., iron, copper, calcium, and phosphate). Therefore, these substances should not be measured on the day of the examination.

4.6. Fertility, pregnancy and breastfeeding

Pregnancy

The safety of IOXRAY during human pregnancy has not been established. Evaluation of experimental studies in animals does not indicate direct or indirect harmful effects with respect to reproduction, embryo-fetal development, the course of pregnancy, or peri- and postnatal development.

Since radiation exposure should be avoided whenever possible during pregnancy, the benefits of a radiological examination, with or without contrast medium, must be carefully weighed against the potential risks. IOXRAY should not be used during pregnancy unless the benefits outweigh the risks and the physician deems it essential. In addition to avoiding radiation exposure, the sensitivity of the fetal thyroid gland to iodine must be considered when assessing the risks and benefits.

Thyroid function should be checked in all newborns during the first week of life after the mother received iodinated contrast agents during pregnancy. Repeat thyroid function tests are recommended at 2 to 6 weeks of age, particularly in low birth weight or premature infants.

Breastfeeding

Contrast agents are excreted in small amounts in human breast milk, and minimal quantities are absorbed by the intestine. Breastfeeding can be continued normally when iodinated contrast agents are administered to the mother. The amount of iohexol in breast milk excreted 24 hours after injection was 0.5% of the weight-adjusted dose in one trial. The amount of iohexol ingested by the infant during the first 24 hours after injection corresponds to only 0.2% of the pediatric dose.

4.7. Effects on the ability to drive vehicles and use machinery

Driving or operating machinery is not recommended for one hour after the last injection or for 24 hours following the intrathecal procedure. However, individual assessment should be made if post-myelographic symptoms persist.

4.8. Undesirable effects

General information (applies to all uses of iodinated contrast agents) :

The possible general side effects associated with radiographic procedures, including the use of nonionic monomeric contrast agents, are listed below. For side effects specific to the route of administration, please refer to those specific sections. Hypersensitivity reactions can occur regardless of the dose and route of administration, and mild symptoms may represent the first signs of a severe anaphylactoid reaction/shock. Contrast agent administration should be stopped immediately, and if necessary, specific treatment should be initiated via vascular access. A transient increase in S-creatinine is common after the administration of iodinated contrast agents; contrast-induced nephropathy may occur.

Iodis or "iodide mumps" is a very rare complication of iodinated contrast agents resulting in swelling and tenderness of the salivary glands for up to about 10 days after the examination.

The frequencies indicated are based on internal clinical documentation and large-scale published studies involving more than 90,000 patients.

The frequency of adverse effects are defined as follows:

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) and not known (cannot be estimated from the available data).

Immune system disorders :

Rare: Hypersensitivity (including dyspnea, rash, erythema, urticaria, pruritus, skin reaction, conjunctivitis, cough, rhinitis, sneezing, vasculitis, angioedema, laryngeal edema, laryngospasm, bronchospasm or non-cardiogenic pulmonary edema).

They can appear either immediately after the injection or up to a few days later, and may indicate the onset of shock. Skin reactions related to hypersensitivity can appear up to a few days after the injection.

Not known: Anaphylactic/anaphylactoid reaction, anaphylactic/anaphylactoid shock

Nervous system disorders :

Rare: Headaches

Very rare: Dysgeusia (transient metallic taste)

Not known: Vasovagal syncope

Heart problems :

Rare: Bradycardia, Vascular disorders

Very rare: Hypertension, hypotension

Gastrointestinal disorders :

Uncommon: Nausea

Rare: Vomiting

Very rare: Diarrhea, abdominal pain/discomfort

Unknown: Salivary gland hypertrophy

General disorders and administration site abnormalities :

Frequent: sensation of heat

Uncommon: hyperhidrosis, feeling cold, vasovagal reactions

Rare: pyrexia

Very rare: chills (feeling cold)

Intravascular use (intra-arterial and intravenous use) :

Please read the section entitled "General Information" first. Only common adverse reactions associated with the intravascular use of non-ionic monomeric contrast agents are described below. The nature of the adverse reactions specifically observed during intra-arterial use depends on the injection site and the administered dose. Selective arteriography and other procedures in which the contrast agent reaches a particular organ at high concentrations may be associated with complications in that organ.

Blood and lymphatic system disorders :

Unknown: Thrombocytopenia

Endocrine disorders :

Not known: Thyrotoxicosis, transient hypothyroidism

Psychiatric disorders :

Not known: Confusion, agitation, restlessness, anxiety

Nervous system disorders :

Rare: Dizziness, paresis, paralysis, photophobia, drowsiness

Very rare: Convulsions, impaired consciousness, stroke, sensory abnormalities (including hypoesthesia), paresthesia, tremors.

Not known: transient motor dysfunction (including speech disorder, aphasia, dysarthria), contrast-induced transient encephalopathy (including transient memory loss, coma, stupor, retrograde amnesia), disorientation, cerebral edema.

Eye disorders :

Rare: Vision impairment

Unknown: Transient cortical blindness

Ear and labyrinth disorders :

Not known: Transient hearing loss

Heart problems :

Rare: arrhythmia (including bradycardia, tachycardia).

Very rare: myocardial infarction. Undetermined: serious cardiac complications (including cardiac arrest, cardiorespiratory arrest), heart failure, coronary artery spasm, cyanosis, chest pain

Vascular disorders :

Very rare: hot flashes

Not known: shock, arterial spasm, thrombophlebitis and venous thrombosis

Respiratory, thoracic and mediastinal disorders:

Frequent: transient changes in respiratory rate, respiratory distress

Rare: cough, respiratory arrest

Very rare: dyspnea

Not known: severe respiratory symptoms and signs, pulmonary edema, acute respiratory distress syndrome, bronchospasm, laryngospasm, apnea, aspiration, asthma attack.

Gastrointestinal disorders :

Rare: Diarrhea

Not known: Worsening of pancreatitis, acute pancreatitis

Skin and subcutaneous tissue disorders :

Rare: Skin rash, itching, hives

Not known: bullous dermatitis, Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, drug eruption with eosinophilia and systemic symptoms, psoriasis flare-up, erythema, drug eruption, skin exfoliation.

Musculoskeletal and connective tissue disorders :

Not known: Arthralgia, muscle weakness, musculoskeletal spasm

Disorders of the renal and urinary system :

Rare: Impaired renal function, including acute renal failure.

General disorders and administration site abnormalities :

Uncommon: pain and discomfort.

Rare: asthenic states (including malaise, fatigue).

Not known: Administration site reactions, including extravasation, back pain.

Injury, poisoning, and procedural complications :

Unknown: Iodism

Intrathecal use :

Please read the "General Information" section first. Below, only common adverse effects during intrathecal use of non-ionic monomeric contrast agents are described.

Adverse effects following intrathecal administration may be delayed and appear several hours or even days after the procedure. Their frequency is similar to that of lumbar puncture alone. Headaches, nausea, vomiting, or dizziness can largely be attributed to a loss of pressure in the subarachnoid space resulting from leakage at the puncture site. Excessive removal of cerebrospinal fluid should be avoided to minimize this pressure loss.

Psychiatric disorders :

Not known: Confusion, agitation.

Nervous system disorders :

Very common: Headaches (which can be severe and prolonged)

Uncommon: Aseptic meningitis (including chemical meningitis).

Rare: Convulsions, dizziness

Not known: Abnormal electroencephalogram, meningism, status epilepticus, contrast-induced transient encephalopathy (including transient memory loss, coma, stupor, retrograde amnesia), motor dysfunction (including speech disorder, aphasia, dysarthria), paresthesia, hypoesthesia, and sensory disturbances.

Eye disorders :

Not known: transient cortical blindness, photophobia

Ear and labyrinth disorders :

Not known: transient hearing loss

Gastrointestinal disorders :

Common: Nausea, vomiting

Musculoskeletal and connective tissue disorders :

Rare: Neck pain, back pain

Unknown: Muscle spasm

General disorders and administration site abnormalities :

Rare: Pain in the extremities

Unknown: Administration site issues

Use in body cavities :

Please read the section entitled "General Information" first. Below, only adverse events with a frequency when using non-ionic monomeric contrast agents in body cavities are described.

Endoscopic retrograde cholangiopancreatography (ERCP) :

Gastrointestinal disorders :

Common: pancreatitis, increased blood amylase

Oral use :

Gastrointestinal disorders :

Very common: Diarrhea

Common: Nausea, vomiting

Uncommon: Abdominal pain.

Hysterosalpingography (HSG) :

Gastrointestinal disorders :

Very common: lower abdominal pain

Arthrography :

Musculoskeletal and connective tissue disorders :

Not known: Arthritis

General disorders and administration site abnormalities :

Very common: Herniographic pain:

General disorders and abnormalities at the administration site :

Unknown: Post-procedure pain

(c) Description of selected adverse effects

Thromboembolic complications have been reported in association with contrast-enhanced angiography of the coronary, cerebral, renal, and peripheral arteries. The contrast agent may have contributed to these complications.

Cardiac complications, including acute myocardial infarctions, have been reported during or after contrast-enhanced coronary angiography. Elderly patients or patients with severe coronary artery disease, unstable angina, and left ventricular dysfunction were at higher risk.

In very rare cases, the contrast agent can cross the blood-brain barrier, leading to absorption of the contrast agent into the cerebral cortex, which can cause neurological reactions. These may include seizures, transient motor or sensory disturbances, transient confusion, transient memory loss, and encephalopathy.

Anaphylactoid reaction and anaphylactoid shock can lead to profound hypotension and associated symptoms and signs such as hypoxic encephalopathy, renal and hepatic failure.

In several cases, extravasation of the contrast agent caused local pain and edema, which generally resolved without sequelae. Inflammation, tissue necrosis, and compartment syndromes have occurred.

Pediatric patients :

Transient hypothyroidism has been reported in premature infants, newborns, and other children following the administration of iodinated contrast agents. Premature infants are particularly sensitive to the effects of iodine. Transient hypothyroidism has been reported in a breastfed premature infant. The breastfeeding mother was repeatedly exposed to IOXRAY. Especially in infants and young children, adequate hydration must be ensured before and after administration of the contrast agent. Nephrotoxic medications should be discontinued. The age-related reduction in glomerular filtration rate in infants may also result in delayed excretion of contrast agents.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions is important. It allows for continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals should report any suspected adverse reactions using the FRILAB reporting form available under the pharmacovigilance tab on the website: www.frilab.ch

4.9. Overdose

Preclinical data indicate a high safety margin for IOXRAY, and no fixed upper dose level has been established for routine intravascular use. Symptomatic overdose is unlikely in patients with normal renal function unless the patient has received an excess of 2000 mg I/kg body weight over a limited period of time. The duration of the procedure is important for renal tolerance of high doses of contrast agent (t½ ~ 2 hours). Accidental overdose is most likely following complex angiographic procedures in children, particularly when multiple injections of high-concentration contrast agent are performed.

In case of overdose, any resulting fluid or electrolyte imbalance must be corrected. Renal function should be monitored for the following 3 days. If necessary, hemodialysis may be used to remove excess contrast medium. There is no specific antidote.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Class pharmacotherapeutic Radiological contrast agents, iodinated, code ATC : V08AB02 .

For most hemodynamic, clinical-chemical, and coagulation parameters examined after intravenous injection of iohexol in healthy volunteers, no significant deviations from pre-injection values were observed. The few changes observed in laboratory parameters were minor and considered to be of no clinical significance.

5.2. Pharmacokinetic properties

Approximately 100% of intravenously injected iohexol is excreted unchanged by the kidneys within 24 hours in patients with normal renal function. The maximum urinary concentration of iohexol is reached approximately 1 hour after injection.

No metabolites were detected. IOXRAY's protein binding is very low (less than 2%).

5.3. Preclinical safety data

Iohexol exhibits very low acute toxicity via intravenous administration in mice and rats. Animal studies have shown that iohexol binds very little to proteins and is well tolerated by the kidneys.

6. PHARMACEUTICAL PARTICULARS

6.1. List of the excipients

Tromethamine, Disodium Calcium Edetate, Hydrochloric Acid, Water for Injection

6.2. Incompatibilities

Without object.

6.3. Shelf life

30 months.

6.4. Special precautions for storage

Store at a controlled room temperature between 20°C and 25°C, with an excursion to 15-30°C. Do not freeze. Protect from light and secondary X-rays. Keep out of reach of children.

6.5. Nature and contents of container

IOXRAY 350: 50 and 100 mL in a glass bottle; box of 1

6.6. Special precautions for disposal and handling

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

7. OPERATORS AND MANUFACTURERS

Operator of the export marketing authorization

FRILAB SA

17, rue des Pierres du Niton

1207 Geneva SWITZERLAND

Manufacturer

LIVEALTH BIOPHARM PVT LTD

Administrative site :

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Mumbai – 400056, Maharashtra

India

Manufacturing site :

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Hingna, Nagpur – 440028 Maharashtra

India

8. DATE OF REVISION OF THE TEXT

May 2023

9. DOSIMETRY

Without object.

CONDITIONS FOR PRESCRIPTION AND DISPENSING

List I