Solution for Infusion
Iopromide 499 mg/mL, 623 mg/mL and 769 mg/mL

Name of the Medicine

Proprietary Name:
ULTRAVIST 240, ULTRAVIST 300, ULTRAVIST 370

Non-proprietary Name:
Iopromide

ULTRAVIST is a non-ionic contrast medium containing iopromide as the active ingredient.

Chemically, iopromide is \(N,N'-\text{Bis}(2,3\text{-dihydroxypropyl})-2,4,6\text{-tri-iodo}-5\text{-}(2\text{-methoxyacetamido})-N\text{-methylisophthalamide}\) and has the following structural formula.

![Structural formula of iopromide](image)

- Molecular Weight: 791.12
- CAS No.: 73334-07-3
- Chemical Formula: \(C_{18}H_{24}I_{3}N_{3}O_{6}\)

Description

Iopromide is a triiodinated, non-ionic, water-soluble X-ray contrast medium.

ULTRAVIST solution for injection/infusion is a clear, colourless to pale yellow solution, free of particles and has a pH of 6.5 - 8.0. It contains no antimicrobial preservatives. ULTRAVIST also contains small amounts of trometamol, sodium calcium edetate and dilute hydrochloric acid (10%) in water for injections.
The iodine concentrations (mg I/mL) available have the following physicochemical properties:

<table>
<thead>
<tr>
<th>Property</th>
<th>ULTRAVIST 240 240 mg I/mL</th>
<th>ULTRAVIST 300 300 mg I/mL</th>
<th>ULTRAVIST 370 370 mg I/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viscosity (mPa.s or cP) at 20°C</td>
<td>4.9</td>
<td>8.9</td>
<td>22.0</td>
</tr>
<tr>
<td>Viscosity (mPa.s or cP) at 37°C</td>
<td>2.8</td>
<td>4.7</td>
<td>10.0</td>
</tr>
<tr>
<td>Osmolality at 37°C (osm/kg H2O)</td>
<td>0.48</td>
<td>0.59</td>
<td>0.77</td>
</tr>
<tr>
<td>Osmolarity at 37°C (osm/L solution)</td>
<td>0.36</td>
<td>0.43</td>
<td>0.49</td>
</tr>
<tr>
<td>Osmotic pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Density (g/mL) 20°C</td>
<td>1.262</td>
<td>1.330</td>
<td>1.409</td>
</tr>
<tr>
<td>Density (g/mL) 37°C</td>
<td>1.255</td>
<td>1.322</td>
<td>1.399</td>
</tr>
</tbody>
</table>

Solutions of ULTRAVIST injection 240 mg I/mL, 300 mg I/mL and 370 mg I/mL have osmolalities from approximately 1.1 to 2.7 times that of plasma (285 mOsmol/kg water).

**Pharmacology**

**Pharmacodynamic Properties**

The contrast-giving substance in the ULTRAVIST formulation is iopromide, a non-ionic, water-soluble derivative of triiodinated isophthalic acid with a molecular weight of 791.12 in which the firmly bound iodine absorbs the X-rays.

**Pharmacokinetics**

**General Information**

Iopromide behaves in the organism like other highly hydrophilic biologically inert, renally excreted compounds (e.g. mannitol or inulin).

**Absorption and Distribution**

Following intravenous administration, plasma concentrations of iopromide decline rapidly due to distribution into the extracellular space and subsequent elimination. The total distribution volume at steady state is about 16 L corresponding roughly to the volume of the extracellular space.

Protein binding is negligible (about 1%). There is no indication that iopromide crosses the intact blood-brain-barrier. A small amount crossed the placental barrier in animal studies (≤ 0.3% of the dose were found in rabbit fetuses).

Following intrathecal administration, maximum iodine concentrations of 4.5% of the administered dose per total plasma volume were observed after 3.8 hours.

Following administration in the biliary and/or pancreatic duct during Endoscopic Retrograde Cholangiopancreatography (ERCP), iodinated contrast agents are systemically absorbed and reach peak plasma concentrations between 1 and 4 h post administration. Maximum serum iodine levels following a mean dose of about 7.3 g iodine were about factor 40 lower compared to maximum serum levels reached after respective intravenous doses.

**Metabolism**

Iopromide is not metabolised
Excretion

The terminal elimination half-life of iopromide is approximately 2 hours, irrespective of the dose. In the dose range tested, the mean total clearance of iopromide amounts to 106 ± 12 mL/min and is similar to the renal clearance of 102 ± 15 mL/min. Thus, excretion of iopromide is almost exclusively renal. Only about 2% of the dose administered is excreted via the faecal route within 3 days.

Approximately 60% of the dose is excreted via urine within 3 hours after intravenous administration. In the mean ≥ 93% of dose was recovered within 12 hours. Excretion is essentially complete within 24 hours.

After intrathecal administration for lumbar myelography, elimination of iopromide from plasma is prolonged with a terminal elimination half-life of 14.9 ± 17 hours. Approximately 80% of iopromide is excreted renally within 72 hours.

Following administration into the biliary and/or the pancreatic duct for ERCP, urinary iodine serum concentrations returned to pre-dose levels within 7 days.

Linearity/Non-linearity

The pharmacokinetic parameters of iopromide in humans change dose proportionally (e.g. Cmax, AUC) or are dose independent (e.g. Vss, t1/2)

Characteristics in Special Patient Populations

Patients with Renal Impairment

In patients with impaired renal function, the plasma half-life of iopromide is prolonged according to the reduced glomerular filtration rate.

The plasma clearance was reduced to 49.4 mL/min/1.73 m² (CV = 53%) in mildly and moderately impaired patients (80 > CLCR > 30 mL/min/1.73 m²) and to 18.1 mL/min/1.73 m² (CV = 30%) in severely impaired patients not depending on dialysis (CLCR = 30 – 10 mL/min/1.73 m²).

The mean terminal half-life is 6.1 hours (CV = 43%) in mildly and moderately impaired patients (80 ≥ CLCR > 30 mL/min/1.73 m²) and 11.6 hours (CV = 49%) in severely impaired patients not depending on dialysis (CLCR = 30 – 10 mL/min/1.73 m²).

The amount recovered in urine within 6 h post dose was 38% in mildly to moderately impaired patients and 26% in severely impaired patients, compared to more than 83% in healthy volunteers. Within 24 h post dose the recovery was 60% in mildly to moderately and 51% in severely impaired patients, compared to more than 95% in healthy volunteers.

Iopromide can be eliminated by haemodialysis. Approximately 60% of the iopromide dose is removed during a 3 hours dialysis.

Patients with Hepatic Impairment

Elimination is not affected by impaired liver function because iopromide is not metabolised and only 2% of the dose is excreted in the faeces.

Indications

For diagnostic use

ULTRAVIST 240/300/370

For intravascular use and use in body cavities.
Contrast enhancement in computerised tomography (CT), arteriography and venography, intravenous/intra-arterial digital subtraction angiography (DSA), intravenous urography, use for ERCP, arthrography and examination of other body cavities.

ULTRAVIST 240: Also for intrathecal use.
ULTRAVIST 370: Especially for angiocardiography.
ULTRAVIST 300/370: Not for intrathecal use.

Contraindications

ULTRAVIST should not be administered to patients with known hypersensitivity or previous reaction to iodinated contrast media or any excipients. Immediate repeat myelography, in the event of technical failure, is contraindicated because of overdosage considerations (see recommendation under Dosage and Administration).

Precautions

Risk-benefit should be considered before use of ULTRAVIST when any of the following medical problems exist.

For All Indications

*Hypersensitivity Reactions*

ULTRAVIST can be associated with anaphylactoid/hypersensitivity or other idiosyncratic reactions characterised by cardiovascular, respiratory and cutaneous manifestations.

Allergy-like reactions ranging from mild to severe reactions including shock are possible (see Adverse Effects). Most of these reactions occur within one hour of administration. However, delayed reactions (after hours to days) may occur.

The risk of hypersensitivity reactions is higher in case of:

- previous reaction to contrast media
- history of bronchial asthma or other allergic disorders

However, such reactions are irregular and unpredictable in nature.

Patients who experience such reactions while taking beta blockers may be resistant to treatment effects of beta agonists. In the event of a severe hypersensitivity reaction, patients with cardiovascular disease are more susceptible to serious or even fatal outcomes.

Due to the possibility of severe hypersensitivity reactions after administration, post-procedure observation of the patient is recommended.

Preparedness for institution of emergency measures is necessary for all patients. Premedication with a corticosteroid regimen may be considered in patients with an increased risk of acute allergy-like reactions, patients with a previous moderate or severe acute reaction, asthma or allergy requiring medical treatment.

*Thyroid Dysfunction*

Particularly careful risk/benefit judgement is required in patients with known or suspected hyperthyroidism or goitre, as iodinated contrast media may induce hyperthyroidism or thyreotoxic crisis in these patients. Iodinated contrast media should not be given to patients with manifest hyperthyroidism. Testing of thyroid function prior to ULTRAVIST administration
and preventive thyreostatic medication may be considered in patients with known or suspected hyperthyroidism.

In neonates, specially preterm infants, who have been exposed to ULTRAVIST, either through the mother during pregnancy or in the neonatal period, it is recommended to monitor thyroid function, as an exposure to excess iodine may cause hypothyroidism, possibly requiring treatment.

**CNS Disorders**

Patients with CNS disorders may be at increased risk of seizures and neurological complications in relationship to ULTRAVIST administration. Neurological complications are more frequent in cerebral angiography and related procedures. Caution should be exercised in situations in which there may be a reduced seizure threshold, such as a previous history of seizures, intrathecal administration, alcoholism, drug addiction and the use of certain concomitant medication. Factors such as brain tumours and cerebrovascular ischaemia, which increase blood-brain barrier permeability, facilitate the passage of the contrast medium into cerebral tissue, possibly leading to CNS reactions.

**Hydration**

Adequate hydration must be assured before and after intravascular and intrathecal ULTRAVIST administration in order to minimise the risk of contrast media-induced nephrotoxicity (see also Precautions, Renal Impairment). This applies especially to patients with multiple myeloma, diabetes mellitus, polyuria, oliguria, hyperuricemia, as well as to newborns, infants, small children and elderly patients.

**Anxiety**

Pronounced states of excitement, anxiety and pain may increase the risk of side effects or intensify contrast medium-related reactions. Care should be taken to minimise the state of anxiety in such patients.

**Pretesting**

Sensitivity testing using a small test dose of contrast medium is not recommended as it has no predictive value. Furthermore, sensitivity testing itself has occasionally led to serious and even fatal hypersensitivity reactions.

**Cardiovascular Disease**

Patients with significant cardiac disease or severe coronary artery disease are at an increased risk of developing clinically relevant haemodynamic changes and arrhythmia.

In patients with valvular disease and pulmonary hypertension, contrast medium administration may lead to pronounced haemodynamic changes. Reactions involving ischaemic ECG changes and major arrhythmia are more common in older patients and in those with pre-existing cardiac disease.

Patients with congestive heart failure receiving concurrent diuretic therapy may have relative intravascular volume depletion, which may affect the renal response to the contrast agent osmotic load. Such patients should be observed for several hours following the procedure to detect delayed haemodynamic renal function disturbances.

Intravascular injection of ULTRAVIST may precipitate pulmonary oedema in patients with heart failure.

**Thromboembolic Events**

Serious, rarely fatal, thromboembolic events causing myocardial infarction and stroke have been reported during angiographic procedures with both non-ionic and ionic contrast media. Exercise care when performing venography in patients with suspected thrombosis, phlebitis, severe ischaemic disease, local infection, venous thrombosis or a totally obstructed venous
system. Avoid angiography whenever possible in patients with homocystinuria because of the risk of inducing thrombosis and embolism.

A property of non-ionic contrast media is the low interference with normal physiological functions. As a consequence of this, non-ionic contrast media have less anticoagulant activity *in vitro* than ionic media. Numerous factors in addition to the contrast medium, including length of procedure, number of injections, catheter and syringe material, underlying disease state, and concomitant medication may contribute to the development of thromboembolic events. Therefore, when performing vascular catheterisation procedure one should be aware of this and pay meticulous attention to the angiographic technique and flush the catheter frequently with physiological saline (if possible with the addition of heparin) and minimise the length of the procedure so as to minimise the risk of procedure-related thrombosis and embolism. Clotting may occur when blood remains in contact with syringes containing iodinated contrast agents.

**Renal Impairment**

In patients with impaired renal function, the plasma half-life of iopromide is prolonged according to the reduced glomerular filtration rate. Therefore, caution must be exercised in patients with severely impaired renal function, combined renal and hepatic disease, combined renal and cardiac disease, or anuria, particularly when large doses are administered.

In the case of severe renal insufficiency the coexistence of severe hepatic dysfunction can seriously delay contrast medium excretion. Haemodialysis should be used only if clinically indicated.

Contrast media-induced nephrotoxicity, presenting as a transient impairment of renal function, may occur after intravascular administration of ULTRAVIST. Acute renal failure may occur in some cases.

Risk factors include, for example:

- pre-existing renal insufficiency
- dehydration
- diabetes mellitus
- multiple myeloma / paraproteinemia
- gout
- age over 70 years
- concurrent administration of nephrotoxic drugs
- repetitive and/or large doses of ULTRAVIST

Adequate hydration must be ensured in all patients who receive ULTRAVIST administration. Patients on dialysis, if without residual renal function, may receive ULTRAVIST for radiological procedures as iodinated contrast media are cleared by the dialysis process.

**Pheochromocytoma**

Administration of radiopaque materials to patients with known or suspected of having pheochromocytoma should be performed with extreme caution. If, in the opinion of the physician, the possible benefits of such a procedure outweigh the considered risks, the procedure may be performed; however, the amount of radiopaque medium injected should be kept to an absolute minimum. The blood pressure should be assessed throughout the procedure, and measures for treatment of a hypertensive crisis should be available. These patients should be monitored very closely during contrast enhanced procedures. Premedication with alpha-receptor blockers is recommended.
Intravascular Use

Patients with Autoimmune Disorders
Cases of severe vasculitis or Stevens-Johnson-like syndrome have been reported in patients with pre-existing autoimmune disorders.

Myasthenia Gravis
The administration of iodinated Ultravist may aggravate the symptoms of myasthenia gravis.

Cerebral Angiography
Use caution in patients with extreme senility, advanced atherosclerosis or severe hypotension; the procedure may be hazardous in subarachnoid haemorrhage and in migraine (because of ischaemic complications).

Peripheral Angiography
Pulsation should be present in the artery to be injected; in thromboangitis obliterans (Buerger's Disease) or ischaemia associated with ascending infection, angiography should be performed with extreme caution, if at all.

Intrathecal Use
Care is needed in patients with a seizure history due to an increased risk for seizures in relationship to intrathecal ULTRAVIST administration. Preparedness for institution of anti-convulsive measures is recommended.

The majority of adverse events after myelography occur some hours after administration. During this period observation is advisable.

Patients with a history of epilepsy and receiving anticonvulsant therapy should be maintained on anticonvulsant therapy when receiving the contrast medium intrathecally.

ULTRAVIST injection is not indicated for use in thoracic, cervical or total columnar myelography, nor for cerebral ventriculography and cisternography as there are insufficient data to support its use in these indications.

The safety and effectiveness of ULTRAVIST have not been established in children for intrathecal use.

Carcinogenicity, Mutagenicity and Impairment of Fertility
Long term animal studies have not been performed to evaluate carcinogenic potential or effects on fertility. Iopromide was not genotoxic in a series of studies for gene mutations (Ames test) and chromosomal damage (in vivo mouse micronucleus assay and in an in vivo mouse dominant lethal assay).

Use in Pregnancy
Category B2
Adequate and well-controlled studies in pregnant women have not been conducted. Embryotoxicity including teratogenicity studies have been performed in rats and rabbits at doses up to 3.7 g I/kg body weight. These studies did not indicate an increased risk of adverse effects to the fetus following the intended diagnostic use in humans.

Therefore, before administration to women during pregnancy, the benefit to the patient should be carefully weighed against the possible risk to the fetus. ULTRAVIST should be used only if, in the judgement of the clinician, its use is deemed essential to the welfare of the patient. Generally, radiography of the abdomen is considered to be contraindicated during pregnancy.
Use in Lactation
The safety of ULTRAVIST for nursed infants has not been investigated. Contrast media are poorly excreted in human breast milk. Harm to the nursed infant is not likely to occur (see also Precautions, Thyroid Dysfunction).

Paediatric Use
Paediatric patients at higher risk of experiencing an adverse reaction during and after administration of any contrast agent may include those with asthma, sensitivity to medication and/or allergens, cyanotic and acyanotic heart disease, congestive heart failure, or a serum creatinine greater than 1.5 mg/dL. The injection rates in small vascular beds, and the relationship of the dose by volume or concentration in small paediatric patients have not been established. Caution should be exercised in selecting the dose.

Interactions with Other Medicines

Metformin
In patients with acute kidney failure, or severe chronic kidney disease, metformin elimination can be reduced leading to accumulation and the development of lactic acidosis. As the application of ULTRAVIST can lead to renal impairment or an aggravation of renal impairment, patients treated with metformin may be at an increased risk of developing lactic acidosis, especially those with prior renal impairment (see Precautions, Renal impairment).

Neuroleptics and Antidepressants
Concomitant use of neuroleptics and antidepressants may reduce the seizure threshold, thus increasing the risk of a contrast medium related reaction.

Beta-blockers
Patients who experience hypersensitivity reactions while taking a beta-blocker may be resistant to treatment effects of beta agonists (see also Precautions, Hypersensitivity Reactions).

Patients on beta-blockers may be unresponsive to the usual doses of adrenalin used to treat allergic reactions. Because of the risk of hypersensitivity reactions, use caution when administering iodinated contrast agents to patients taking beta-blockers.

Interleukin-2
Previous treatment (up to several weeks) with Interleukin-2 is associated with an increased risk for delayed reactions to ULTRAVIST.

Effects on Laboratory Tests

Radioisotopes
Diagnosis and treatment of thyroid disorders with thyrotropic radioisotopes may be impeded for up to several weeks after administration of ULTRAVIST due to reduced radioisotope uptake.

Effects on Ability to Drive and Use Machines
As a precaution because of the risk of delayed adverse reactions, driving or operating machinery should be avoided for the first 24 hours after intrathecal as well as after intravascular administration of contrast media.
Adverse Effects

Summary of the Safety Profile

The overall safety profile of ULTRAVIST is based on data obtained in pre-marketing studies in more than 3900 patients and post-marketing studies in more than 74,000 patients, as well as data from spontaneous reporting and the literature.

The most frequently observed adverse drug reactions (≥ 4%) in patients receiving ULTRAVIST are headache, nausea and vasodilatation.

The most serious adverse drug reactions in patients receiving ULTRAVIST are anaphylactoid shock, respiratory arrest, bronchospasm, laryngeal oedema, pharyngeal oedema, asthma, coma, cerebral infarction, stroke, brain oedema, convulsion, arrhythmia, cardiac arrest, myocardial ischemia, myocardial infarction, cardiac failure, bradycardia, cyanosis, hypotension, shock, dyspnoea, pulmonary oedema, respiratory insufficiency and aspiration.

Tabulated List of Adverse Reactions

The adverse drug reactions observed with ULTRAVIST are represented in the table below. They are classified according to System Organ Class (MedDRA version 13.0). The most appropriate MedDRA term is used to describe a certain reaction and its synonyms and related conditions. Adverse drug reactions from clinical trials are classified according to their frequencies. Frequency groupings are defined according to the following convention:

- Common (≥ 1/100 to < 1/10)
- Uncommon (≥ 1/1,000 to < 1/100)
- Rare (≥ 1/10,000 to < 1/1,000)

Table 1: Adverse drug reactions (ADRs) reported in clinical trials

<table>
<thead>
<tr>
<th>System organ class</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system disorders</td>
<td>Hypersensitivity / anaphylactoid reactions (anaphylactoid shock*, respiratory arrest*, bronchospasm*, laryngeal* / pharyngeal* / face oedema, tongue oedema, laryngeal / pharyngeal spasm, asthma*, conjunctivitis, lacrimation, sneezing, cough, mucosal oedema, rhinitis, hoarseness, throat irritation, urticaria, pruritus, angioedema)</td>
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<tr>
<td>Psychiatric disorders</td>
<td>Anxiety</td>
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<tr>
<td>Nervous system disorders</td>
<td>Dizziness</td>
<td>Vasovagal reactions</td>
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<tr>
<td></td>
<td>Headache</td>
<td>Confusional state</td>
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<td></td>
<td>Dysgeusia</td>
<td>Restlessness</td>
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<td></td>
<td></td>
<td>Paraesthesia / hypoesthesia</td>
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<td></td>
<td></td>
<td>Somnolence</td>
<td></td>
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<tr>
<td>Eye disorders</td>
<td>Blurred / disturbed vision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>System organ class</td>
<td>Common</td>
<td>Uncommon</td>
<td>Rare</td>
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<tr>
<td>--------------------------------------------------------</td>
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<td>--------------------------------------------</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>Chest pain / discomfort</td>
<td>Arrhythmia*</td>
<td>Cardiac arrest*</td>
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<td></td>
<td></td>
<td>Myocardial ischaemia*</td>
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<td></td>
<td></td>
<td>Palpitations</td>
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<tr>
<td>Vascular disorders</td>
<td>Hypertension</td>
<td>Hypotension*</td>
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<tr>
<td></td>
<td>Vasodilatation</td>
<td></td>
<td></td>
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<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
<td>Dyspnoea*</td>
<td></td>
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<tr>
<td>Gastrointestinal disorders</td>
<td>Vomiting</td>
<td>Abdominal pain</td>
<td></td>
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<tr>
<td></td>
<td>Nausea</td>
<td></td>
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<tr>
<td>General disorders and administration site conditions</td>
<td>Pain</td>
<td></td>
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<tr>
<td></td>
<td>Injection site reactions</td>
<td></td>
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<tr>
<td></td>
<td>(various kinds, e.g. pain,</td>
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<td></td>
<td>warmth, oedema, inflammation</td>
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<td></td>
<td>and soft tissue injury in case of</td>
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<td></td>
<td>extravasation)</td>
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<tr>
<td></td>
<td>Feeling hot</td>
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</tr>
</tbody>
</table>

* life-threatening and/or fatal cases have been reported

**Adverse drug reactions from Post-Marketing Spontaneous Reports**

**Endocrine disorders**
Thyrotoxic crisis, thyroid disorder

**Nervous system disorders**
Coma*, cerebral ischaemia / infarction*, stroke*, brain oedema # *, convulsion*, transient cortical blindness*, loss of consciousness, agitation, amnesia, tremor, speech disorders, paresis / paralysis

**Ear and labyrinth disorders**
Hearing disorders

**Cardiac disorders**
Myocardial infarction*, cardiac failure*, bradycardia*, tachycardia, cyanosis*

**Vascular disorders**
Shock*, thromboembolic events*, vasospasm#

**Respiratory, thoracic and mediastinal disorders**
Pulmonary oedema*, respiratory insufficiency*, aspiration*

**Gastrointestinal disorders**
Dysphagia, salivary gland enlargement, diarrhoea
Skin and subcutaneous tissue disorders
Bullous conditions (e.g. Stevens-Johnson’s or Lyell syndrome), rash, erythema, hyperhydrosis

Musculoskeletal, connective tissue and bone disorders
Compartment syndrome in case of extravasation

Renal and urinary disorders
Renal impairment, acute renal failure

General disorders and administration site conditions
Malaise, chills, pallor, pain, warmth, oedema, inflammation

Investigations
Body temperature fluctuation
* life-threatening and/or fatal cases have been reported
^ intravascular use only

In addition to the adverse drug reactions (ADRs) listed above, the following ADRs have been reported with:

Intrathecal use: Chemical meningitis and meningism at an unknown frequency.

Use for ERCP: Elevation of pancreatic enzyme levels and pancreatitis at an unknown frequency.

The majority of the reactions after myelography or use in body cavities occur some hours after the administration.

Description of Selected Adverse Reactions
Based on experience with other non-ionic contrast media, the following undesirable effects, in addition to the undesirable effects listed above, may occur with intrathecal use:
Psychosis, neuralgia, paraplegia, aseptic meningitis, back pain, pain in extremities, micturition disorder, EEG abnormal.

Dosage and Administration

General Information
In the case of abdominal angiography and urography, the diagnostic yield is increased if the bowels are emptied of faecal matter and gas. On the two days prior to examination patients should, therefore, avoid flatulent food, in particular peas, beans and lentils, salads, fruit, dark and fresh bread and all kinds of uncooked vegetables. On the day before the examination patients should refrain from eating after 6 pm. It may also be appropriate to administer a laxative in the evening.

In babies and young children, however, prolonged fasting and the administration of a laxative before the examination are contraindicated.

Newborns (< 1 month) and Infants (1 month - 2 years)
Young infants (age < 1 year) and especially newborns are susceptible to electrolyte imbalance and haemodynamic alterations. Care should be taken regarding the dose of
contrast medium to be given, the technical performance of the radiological procedure and the patient status.

**Patients with Renal Impairment**

Since iopromide is excreted almost exclusively in an unchanged form via the kidneys, the elimination of iopromide is prolonged in patients with renal impairment. In order to reduce the risk of additional contrast media-induced renal impairment in patients with pre-existing renal impairment, the minimum possible dose should be used in these patients (see also Precautions and Pharmacokinetics).

**Visual Inspection**

Contrast media such as ULTRAVIST should be visually inspected prior to use and must not be used in the presence of particulate matter (including crystals) or if the solution is discoloured or the container defective in any way. As ULTRAVIST is a highly concentrated solution, crystallisation (evident as a milky-cloudy appearance and/or sediment or floating crystals) may occur very rarely.

**Warming Prior to Use**

Contrast media such as ULTRAVIST which are warmed to body temperature before administration maybe be better tolerated and can be injected more easily because of reduced viscosity.

**Intravascular Administration**

After the administration, the patient should be observed for at least 30 minutes, since the majority of reactions occur within this time.

The dosage should be adapted to age, weight, cardiac output, general condition of the patient, clinical question and examination technique, and the region to be investigated.

The dosages given below are recommendations only and represent common doses for an average normal adult weighing 70 kg. Doses are given for single injections or per kilogram (kg) body weight (BW) as indicated below.

Generally, doses of up to 1.5 g iodine per kg body weight are well tolerated (corresponding to 3 - 5 mL ULTRAVIST 300/kg body weight).

**Recommended Doses for Single Injections**

**Intravenous Urography**

The physiologically poor concentrating ability of the still immature nephron of infantile kidneys demands relatively high doses of contrast medium.
The following dosages are recommended:

**Newborns**
(< 1 month)
- 1.2 g I/kg body weight 5.0 mL/kg BW ULTRAVIST 240
- 4.0 mL/kg BW ULTRAVIST 300
- 3.2 mL/kg BW ULTRAVIST 370

**Infants**
(1 month - 2 years)
- 1.0 g I/kg body weight 4.2 mL/kg BW ULTRAVIST 240
- 3.0 mL/kg BW ULTRAVIST 300
- 2.7 mL/kg BW ULTRAVIST 370

**Children**
(2 - 11 years)
- 0.5 g I/kg body weight 2.1 mL/kg BW ULTRAVIST 240
- 1.5 mL/kg BW ULTRAVIST 300
- 1.4 mL/kg BW ULTRAVIST 370

**Adolescents and Adults**
- 0.3 g I/kg body weight 1.3 mL/kg BW ULTRAVIST 240
- 1.0 mL/kg BW ULTRAVIST 300
- 0.8 mL/kg BW ULTRAVIST 370

Increasing the dose in adults is possible if this is considered necessary in special indications.

**Filming Times**
When the above dosage guidelines are observed and ULTRAVIST 300/370 is injected over 1 to 2 minutes (3 - 5 minutes in the case of ULTRAVIST 240), the renal parenchyma is usually highly opacified 3 to 5 minutes (5 - 10 minutes for ULTRAVIST 240) and the renal pelvis with the urinary tract 8 to 15 minutes (12 - 20 minutes for ULTRAVIST 240) after the start of administration. The earlier time should be chosen for younger patients and the later time for older patients.

Normally, it is advisable to take the first film as early as 2 - 3 minutes after administration of the contrast medium. In newborns, infants and patients with impaired renal function later films may improve visualisation of the urinary tract.

**Computerised Tomography (CT)**
Whenever possible, ULTRAVIST should be injected as an i.v bolus, preferably using a power injector. Only for slow scanners about half of the total dosage should be administered as a bolus and the rest within 2 - 6 minutes to guarantee a relatively constant - though not maximum - blood level.

Spiral CT in single and especially in multi-slice technique allows the rapid acquisition of a volume of data during a single breath-hold. To optimise the effect of the i.v. administered bolus (80 - 150 mL ULTRAVIST 300) in the region of interest (peak, time and duration enhancement), the use of an automatic power injector and bolus tracking is strongly recommended.

**Whole-Body CT**
In whole-body computerised tomography, the necessary doses of contrast medium and the rates of administration depend on the organs under investigation, the diagnostic problem and in particular, the different scan and image reconstruction times of the scanners in use.

**Cranial CT**
The following adult dosages are recommended for cranial CT:

- ULTRAVIST 240: 1.5 - 2.5 mL/kg BW
- ULTRAVIST 300: 1.0 - 2.0 mL/kg BW
- ULTRAVIST 370: 1.0 - 1.5 mL/kg BW
Paediatric Contrast Enhanced CT (CECT, head and body)

ULTRAVIST 300 mg I/mL is indicated for intravenous administration for CECT of the head and body. Paediatric dosing is suggested proportional to body weight. The suggested dose is 1 - 2 mL/kg. Total dose for the procedure should not usually exceed 3 mL/kg.

Conventional Angiography

The dosage should be adapted to age, weight, cardiac output and general condition of the patient, the clinical question, examination technique and the nature and volume of the vascular region to be investigated.

Aortic arch angiography 50 – 80 mL ULTRAVIST 300
Retrograde carotid angiography 30 – 40 mL ULTRAVIST 300
Selective angiography 6 – 15 mL ULTRAVIST 300
Thoracic aortography 50 – 80 mL ULTRAVIST 300 or 370
Abdominal aortography 40 – 60 mL ULTRAVIST 300

Arteriography:
Upper extremities 8 – 12 mL ULTRAVIST 300
Lower extremities 20 – 30 mL ULTRAVIST 300

Angiocardiography:
Cardiac ventricles 40 – 60 mL ULTRAVIST 370
Intracoronary 5 – 8 mL ULTRAVIST 370

Venography:
Upper extremities 50 – 60 mL ULTRAVIST 240
or 15 – 30 mL ULTRAVIST 300
Lower extremities 50 – 80 mL ULTRAVIST 240
or 30 – 60 mL ULTRAVIST 300

Paediatric Angiocardiography

ULTRAVIST 370 mg I/mL is indicated for intra-arterial and intra-cardiac administration in the radiographic contrast evaluation of the heart cavities and of the major arteries. Paediatric dosing is suggested proportional to body weight. The suggested dose is 1 - 3 mL/kg. Total dose for the procedure should not usually exceed 5 mL/kg.

Digital Subtraction Angiography (DSA)

Intravenous DSA

The i.v. injection of 30 – 60 mL ULTRAVIST 300 or 370 as a bolus (flow rate: 8 - 12 mL/second into the cubital vein; 10 - 20 mL/second into the vena cava) is only recommended for high-contrast demonstrations of the great vessels, of the pulmonary arteries and of the arteries of the neck, head, kidneys and extremities.

The period of time for which the contrast medium is in contact with the wall of the veins can be reduced by injecting 20 to 40 mL isotonic sodium chloride solution as a bolus immediately afterwards.

Adults: 30 - 60 mL ULTRAVIST 300/370

Intra-arterial DSA

The dosages and concentrations used in conventional angiography can be reduced for intra-arterial DSA.
For high-contrast demonstration of the arteries e.g. in the regions of the head, neck and extremities, several injections of 10 - 40 mL of diluted ULTRAVIST of a strength equivalent to 150 mg iodine per mL - depending on the size of the vessels - are usually given directly or via a catheter.

Higher doses of contrast medium (about 200 mL of diluted ULTRAVIST of a strength equivalent to 150 mg iodine per mL) may be necessary in some cases to demonstrate the vessels of the lower extremity e.g. if both legs are to be examined.

**Intrathecal Use**

**Adults**

The dosage may vary depending on the clinical problem, examination technique and the region to be investigated. Generally, a dose of 3 g iodine should not be exceeded in one examination.

If equipment is available which shows all necessary projections to be filmed without the patient having to move and with which the instillation can be performed under fluoroscopic control, then often lower volumes are sufficient.

Recommended dose for single examinations:

**Myelography**

ULTRAVIST 240: Up to 12.5 mL for myelography

Generally, a dose of 3 g iodine should not be exceeded for one examination.

Please note: The more the patient moves or exerts himself after the administration of ULTRAVIST, the quicker the contrast medium will mix with the fluid of other regions of no interest. As a consequence, the contrast density decreases more quickly than usual.

After the examination the contrast medium should be directed to the lumbar region. This is achieved by placing the patient in an upright sitting position or by elevating the head of the bed by 15° for at least 6 hours. Thereafter, the patient should rest for about 18 hours to minimise any discomfort caused by leakage of cerebrospinal fluid. During this period observation for adverse reactions is advisable. Patients suspected of having a reduced seizure threshold must be kept under particularly careful observation for some hours.

Repeat Procedure: An interval of at least 48 hours should be allowed before repeat examination.

**Children**

The safety and effectiveness in children has not been established for intrathecal use of ULTRAVIST.

**Other Body Cavities**

During arthrography, hysterosalpingography and ERCP, injections of contrast medium should be monitored by fluoroscopy.

**Recommended Doses for Single Examinations**

The dosage may vary depending on the age, weight and general condition of the patient. It also depends on the clinical problem, examination technique and the region to be investigated. The dosages given below are recommendations only and represent average doses for a normal adult.

**Arthrography:** 5 - 15 mL ULTRAVIST 240/300/370

**Hysterosalpingography:** 10 - 25 mL ULTRAVIST 240

**ERCP:** Dosage depends generally on clinical question and size of structure to be imaged.
Other. Dosage depends generally on clinical question and size of structure to be imaged.

Instructions for Use/Handling
ULTRAVIST must not be mixed with any other medicinal products to avoid the risk of possible incompatibilities.
ULTRAVIST should be warmed to body temperature prior to use.
Avoid rapid dispersion of the medium.
Extreme caution during injection of a contrast medium is necessary to avoid extravasation. This is especially important in patients with severe arterial or venous disease.

Inspection
Contrast media such as ULTRAVIST should be visually inspected prior to use and must not be used in the presence of particulate matter (including crystals) or if the solution is discoloured or the container defective in any way. As ULTRAVIST is a highly concentrated solution, crystallisation (evident as a milky-cloudy appearance and/or sediment or floating crystals) may occur very rarely.

Single Dose Vials/Bottles
The contrast medium solution should not be drawn into the syringe, or the infusion bottle attached to the infusion set until immediately before the examination.
The rubber stopper should never be pierced more than once to prevent large amounts of microparticles from the stopper getting into the solution. The use of cannulas with a long tip and a maximum diameter of 18 G is recommended for piercing the stopper and drawing up the contrast medium (dedicated withdrawal cannulas with a lateral aperture e.g. Nocore - Admix cannulas, are particularly suitable).
Any contrast solution not used in one examination for a given patient is to be discarded. ULTRAVIST does not contain preservatives.
Unused ULTRAVIST in opened containers must be discarded ten hours after first opening the container.

Overdosage
Results from acute toxicity studies in animals do not indicate a risk of acute intoxication following use of ULTRAVIST.

Intravascular Overdose
Symptoms may include fluid and electrolyte imbalance, renal failure, cardiovascular and pulmonary complications.
In case of inadvertent intravascular overdosage it is recommended to monitor fluids, electrolytes and renal function. Treatment of overdose should be directed toward the support of vital functions.
ULTRAVIST is dialysable.

Intrathecal Overdose
Serious neurological complications may occur. Close monitoring is recommended in case of inadvertent intrathecal overdosage
Presentations and Storage Conditions

ULTRAVIST is registered in 3 strengths:

ULTRAVIST 240:  ULTRAVIST 300:  ULTRAVIST 370:
Vials of 10 mL  Vials of 20 mL  Vials of 30 mL
Bottles of 50 mL  Bottles of 50 mL  Bottles of 50 mL
Vials of 30 mL  Bottles of 75 mL  Bottles of 75 mL
Bottles of 100 mL  Bottles of 100 mL  Bottles of 100 mL
Bottles of 200 mL

Iodine and iopromide content are given below:

ULTRAVIST 240: Each mL of injection contains 499 mg iopromide, (equivalent to 240 mg iodine) with vials of 10 mL and bottles of 50 mL having iodine contents of 2.4 g and 12 g respectively, and having iopromide contents of 5 g and 25 g respectively.

ULTRAVIST 300: Each mL of injection contains 623 mg iopromide, (equivalent to 300 mg iodine) with vials of 20 mL and bottles of 50 mL, 75 mL and 100 mL having iodine contents of 6 g, 15 g, 22.5 g and 30 g respectively, and having iopromide contents of 12.5 g, 31.2 g, 46.7 g and 62.3 g, respectively.

ULTRAVIST 370: Each mL of injection contains 769 mg iopromide, (equivalent to 370 mg iodine) with vials of 30 mL and bottles of 50 mL, 75 mL, 100 mL, and 200 mL having iodine contents of 11.1 g, 18.5 g, 27.8 g, 37 g and 74 g respectively, and having iopromide contents of 23.1 g, 38.4 g, 57.7 g, 76.9 g, and 153.8 g respectively.

Not all presentations are marketed.

Store below 30°C.

Protect from light and secondary X-rays.

Medicine Classification

General Sales Medicine

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