

PRODUCT INFORMATION

ULTRAVIST®

NAME OF THE MEDICINE

Proprietary name:

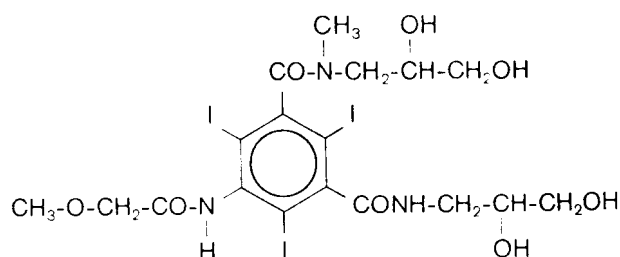
ULTRAVIST 150, ULTRAVIST 240, ULTRAVIST 300, ULTRAVIST 370

Non-proprietary name:

iopromide

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

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



Molecular Weight: 791.12
CAS No.: 73334-07-3
Chemical Formula: C₁₈H₂₄I₃N₃O₈

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, dilute hydrochloric acid (10%) (for pH adjustment) in water for injections.

The iodine concentrations (mg I/mL) available have the following physicochemical properties:

Property	ULTRAVIST 150 150 mg I/mL	ULTRAVIST 240 240 mg I/mL	ULTRAVIST 300 300 mg I/mL	ULTRAVIST 370 370 mg I/mL
Viscosity (mPa.s or cP) at 20°C	2.3	4.9	8.9	22.0
at 37°C	1.5	2.8	4.7	10.0
Osmolality at 37°C (osm/kg H ₂ O)	0.33	0.48	0.59	0.77
Osmolarity at 37°C (osm/L solution)	0.28	0.36	0.43	0.49
Osmotic pressure				
Density (g/mL) 20°C	1.164	1.262	1.330	1.409
Density (g/mL) 37°C	1.157	1.255	1.322	1.399

Solutions of ULTRAVIST injection 150 mg I/mL, 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

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 very low (about 1%). There is no indication that iopromide crosses the intact blood-brain-barrier. A small amount crossed the placental barrier in animal studies ($\leq 0.3\%$ of the dose were found in rabbit foetuses).

Following intravenous administration (infusion over 15 minutes), maximum serum concentrations of total iodine following a low dose of about 15 g iodine (118 mmol) were about 1.39 ± 0.242 g/L (10.9 ± 1.90 mmol/L) and following a high dose of 80 g iodine (630 mmol), were about 7.06 ± 1.13 g/L (55.6 ± 8.89 mmol/L), at 15 min after start of infusion.

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 concentrations of total iodine following a mean dose of about 7.3 g iodine (57.4 ± 22.8 mmol) were about $85.2 \mu\text{mol/L}$ 4 hours after administration of ULTRAVIST 300. This value is about factor 40 lower than the maximum serum concentrations reached after the respective intravenous dose. During the same time period, free serum iodine levels rose to about $5.42 \mu\text{mol/L}$.

Metabolism

Iopromide is not metabolised.

Excretion

The terminal elimination half-life of iopromide in patients with normal kidney function is approximately 2 hours, irrespective of the dose.

In the dose range tested, the mean total clearance of iopromide following intravenous administration of a low (15 g iodine) and a high (80 g iodine) dose amounts to mean values between 109.5 ± 11.0 mL/min and 103 ± 13.3 mL/min, respectively. Total clearance is very similar to the renal clearance of 104 ± 12.7 mL/min (low dose) and 100 ± 17.8 mL/min (high dose). 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 are excreted within 3 hours after intravenous administration via urine. In the mean $\geq 93\%$ of dose were 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 $78 \pm 15\%$ 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. C_{max} , AUC) or are dose independent (e.g. V_{ss} , $t_{1/2}$).

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 ($80 > \text{CL}_{\text{CR}} > 30$ mL/min/1.73 m²) and to 18.1 mL/min/1.73 m² (CV = 30%) in severely impaired patients not depending on dialysis ($\text{CL}_{\text{CR}} = 30 - 10$ mL/min/1.73 m²).

The mean terminal half-life is 6.1 hours (CV = 43%) in mildly and moderately impaired patients ($80 \geq \text{CL}_{\text{CR}} > 30$ mL/min/1.73 m²) and 11.6 hours (CV = 49%) in severely impaired patients not depending on dialysis ($\text{CL}_{\text{CR}} = 30 - 10$ 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

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

INDICATIONS

ULTRAVIST is indicated for all angiographic and urographic examinations and for contrast enhancement in computerised tomography.

ULTRAVIST 240 is additionally indicated for lumbar myelography in adults.

CONTRAINDICATIONS

ULTRAVIST (iopromide) 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

For all indications

EVALUATE THE RISK BEFORE USE OF IOPROMIDE WHEN ANY OF THE FOLLOWING MEDICAL PROBLEMS EXIST:

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. To permit immediate countermeasures to be taken in emergencies, appropriate medicines, an endotracheal tube and respirator should be ready at hand.

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, premedication with a corticosteroid regimen may be considered

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.

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, especially 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 to have 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 acute cerebrovascular ischaemia, which increase blood-brain barrier permeability, facilitate the passage of the contrast medium into cerebral tissue, possibly leading to CNS reactions.

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 minimize the state of anxiety in such patients.

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.

The 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. Therefore, meticulous intravascular administration technique is necessary, particularly during angiographic procedures to minimise thromboembolic events.

Exercise care when performing venography in patients with suspected thrombosis, phlebitis, severe ischaemic disease, local infection, venous thrombosis or a totally obstructed venous system.

Clotting may occur when blood remains in contact with syringes containing iodinated contrast agents.

Avoid angiography whenever possible in patients with homocystinuria because of the risk of inducing thrombosis and embolism.

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.

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 / paraproteinaemia
- gout
- age over 70 years
- concurrent administration of nephrotoxic drugs
- repetitive and/or large doses of ULTRAVIST.

Patients on dialysis, if without residual renal function, may receive ULTRAVIST for radiological procedures as iodinated contrast media are cleared by the dialysis process.

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.

Hydration

Adequate hydration must be assured before and after intravascular and intrathecal ULTRAVIST administration in order to minimize the risk of contrast media-induced nephrotoxicity (see also subsection '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.

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.

Paediatrics

Paediatric patients at higher risk of experiencing an adverse reaction during and after administration of any contrast agent may include those with asthma, a 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.

Carcinogenicity, genotoxicity 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 l/kg bw. These studies did not indicate an increased risk of adverse effects to the foetus following the intended diagnostic use in humans.

Before administration to women during pregnancy, the benefit to the patient should be carefully weighed against the possible risk to the foetus. 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. See also PRECAUTIONS, subsection 'Thyroid dysfunction'.

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 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 this 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.

Children: the safety and effectiveness of ULTRAVIST have not been established in children for intrathecal use.

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

Because of the risk of delayed adverse reactions, as a precaution, driving or operating machinery should be avoided for the first 24 hours after intrathecal as well as after intravascular administration of contrast media.

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, subsection '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 (also see PRECAUTIONS).

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.

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 ($\geq 4\%$) 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 ischaemia, myocardial infarction, cardiac failure, bradycardia, cyanosis, hypotension, shock, dyspnoea, pulmonary oedema, respiratory insufficiency and aspiration.

Tabulated lists of adverse reactions

The adverse drug reactions observed with ULTRAVIST are represented in the tables 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 are classified according to their frequencies. Frequency groupings are defined according to the following convention:

Very common ($\geq 1/10$)
Common ($\geq 1/100$ to $< 1/10$)
Uncommon ($\geq 1/1,000$ to $< 1/100$)
Rare ($\geq 1/10,000$ to $< 1/1,000$)
Very rare ($< 1/10,000$)

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

System organ class	Common	Uncommon	Rare
Immune system disorders		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)	
Psychiatric disorders			Anxiety
Nervous system disorders	Dizziness Headache Dysgeusia	Vasovagal reactions Confusional state Restlessness Paraesthesia / hypoaesthesia Somnolence	
Eye disorders	Blurred / disturbed vision		
Cardiac disorders	Chest pain / discomfort	Arrhythmia*	Cardiac arrest* Myocardial ischaemia*
Vascular disorders	Hypertension Vasodilatation	Hypotension*	
Respiratory, thoracic and mediastinal disorders		Dyspnoea*	
Gastrointestinal disorders	Vomiting Nausea	Abdominal pain	
General disorders and administration site conditions	Pain Injection site reactions (various kinds, e.g. pain, warmth, oedema, inflammation and soft tissue injury in case of extravasation)		

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

Table 2: Adverse drug reactions reported in a post-marketing surveillance study

System organ class	Common	Uncommon	Rare
Cardiac disorders			Palpitations
General disorders and administration site conditions	Feeling hot	Oedema	

The above additional adverse drug reactions were reported in a post-marketing surveillance study conducted in over 74,000 patients from 25 countries.

Adverse drug reactions from post-marketing spontaneous reports

Endocrine disorders

Thyrotoxic crisis, Thyroid disorder

Nervous system disorders

Coma*, Cerebral ischaemia / infarction*, Stroke*, Brain oedema^a *, Convulsion*, Transient cortical blindness^a, 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^a, Vasospasm^a

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^a

Renal and urinary disorders

Renal impairment^a, Acute renal failure^a

General disorders and administration site conditions

Malaise, Chills, Pallor

Investigations

Body temperature fluctuation

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

^a 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 may occur with intrathecal use in addition to the undesirable effects listed above: Psychosis, neuralgia, paraplegia, aseptic meningitis, back pain, pain in extremities, micturition disorder, EEG abnormal.

DOSAGE AND ADMINISTRATION

Administration Technique

- Contrast media should be visually inspected prior to use and must not be used, if discoloured, nor in the presence of particulate matter (including crystals) or defective containers. As ULTRAVIST is a highly concentrated solution, crystallisation (milky-cloudy appearance and/or sediment at the bottom, or floating crystals) may occur very rarely.
- 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.)
- Do not mix with other medicines (i.e. such as agents for the prophylactic treatment of hypersensitivity reactions).
- Avoid immediate repeat myelography with ULTRAVIST.
- Each vial or bottle should be used in one patient on one occasion only and any residue should be discarded. ULTRAVIST contains no preservatives.

- Vials/bottles containing contrast medium solutions are not intended for the withdrawal of multiple doses. The rubber stopper should never be pierced more than once. The use of cannulas with a long tip and a diameter of maximally 18 G is recommended for piercing the stopper and drawing up the contrast medium (dedicated withdrawal cannulas with a side hole eg. Nocore-Admix cannulas, are particularly suitable).

General Information

Newborns (< 1 month) and infants (1 month to 2 years)

Young infants (age < 1 year) and especially newborns are susceptible to electrolyte imbalance and hemodynamic 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 PHARMACOLOGY, subsection 'Pharmacokinetics').

Warming prior to use

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

Dosage for intravascular use

Dosage should be adapted to age weight, clinical question and examination technique.

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.

Intravenous urography

Adults

The dose should be 300 mg I/kg body weight (1 mL ULTRAVIST-300, 0.8 mL ULTRAVIST-370, 1.3 mL ULTRAVIST 240/kg body weight) if the clinical problem also requires adequate filling of the ureters. Increasing the dose is possible if this is considered necessary in special indications.

Children

The physiologically poor concentrating ability of the still immature nephron of infantile kidneys demands relatively high doses of contrast medium.

Newborns (< 1 month):	1.2 g l/kg body weight	= 5.0 mL/kg body weight ULTRAVIST 240 = 4.0 mL/kg body weight ULTRAVIST 300 = 3.2 mL/kg body weight ULTRAVIST 370
Infants (1 month to 2 years):	1.0 g l/kg body weight	= 4.2 mL/kg body weight ULTRAVIST 240 = 3.0 mL/kg body weight ULTRAVIST 300 = 2.7 mL/kg body weight ULTRAVIST 370
Children (2 to 11 years):	0.5 g l/kg body weight	= 2.1 mL/kg body weight ULTRAVIST 240 = 1.5 mL/kg body weight ULTRAVIST 300 = 1.4 mL/kg body weight ULTRAVIST 370

Filming times:

When the above dosage guidelines are observed and ULTRAVIST 300/370 is injected over one to two minutes (3-5 minutes in the case of ULTRAVIST 240), the renal parenchyma is usually highly opacified three to five 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 neonates, infants and patients with impaired renal function later films may improve visualisation of the urinary tract.

Insufficient contrast necessitates late films.

Computerized 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 but 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 dose (80 – 150 mL ULTRAVIST 300) in the region of interest (peak, time and duration of enhancement), the use of an automatic power injector and bolus tracking is strongly recommended.

Whole-body CT

ULTRAVIST 300 0.5 – 1.5 mL/kg body weight

In whole-body computerized 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 dosages are recommended for cranial CT:

ULTRAVIST 300: up to 1.0 – 2.0 mL/kg body weight

ULTRAVIST 370: up to 1.0 – 1.5 mL/kg body weight

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 depends on the age, weight, cardiac output and general condition of the patient, the clinical problem, examination technique and the nature and volume of the vascular region to be investigated.

		ULTRAVIST
Cerebral angiography		
Aortic arch angiography	50 – 80 mL	300
Retrograde carotid angiography	30 – 40 mL	300
Selective angiography	6 – 15 mL	300
Thoracic aortography	50 – 80 mL	300
Abdominal aortography	40 – 60 mL	300
Angiography of the extremities		
Upper extremities		
Arteriography	8 – 12 mL	300
Venography	50 – 60 mL	240
	15 – 30 mL	300
Lower extremities		
Arteriography	20 – 30 mL	300
Venography	50 – 80 mL	240
	30 – 60 mL	300
Angiocardiography		
Selective, in the individual cardiac cavities:	40 – 60 mL	370
Coronarangiography	5 – 8 mL	370

Paediatric angiocardiology

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.

Intravenous Digital Subtraction Angiography (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 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 flushing with 20 to 40 mL isotonic sodium chloride solution as a bolus immediately afterwards.

Intraarterial Digital Subtraction Angiography (DSA)

Intraarterial digital subtraction angiography requires small volumes and lower iodine concentrations than the intravenous technique. The more selective the angiography is, the lower the dose of contrast medium can be. The values used in conventional angiography for bolus concentration, bolus volume can be reduced for intraarterial DSA.

Dosage for intrathecal use

The dosage may vary depending on the clinical problem, examination technique and the region to be investigated.

If equipment is available which allows films in all necessary projections 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

Up to 12.5 mL ULTRAVIST 240

The maximum dose of 12.5 mL ULTRAVIST 240 corresponds to a total iodine dose of 3 g and should not be exceeded.

Please note: The more the patient moves or exerts themselves after the administration, 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 minimize 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.

INCOMPATIBILITIES

ULTRAVIST must not be mixed with any other medicinal products to avoid the risk of possible incompatibilities.

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 overdose, 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 overdose.

In cases of overdose, it is advisable to contact the Poisons Information Centre (131126) for recommendations on the management and treatment of overdose.

PRESENTATION AND STORAGE CONDITIONS

Injection solutions of ULTRAVIST (iopromide) are registered in 4 strengths. Iodine and iopromide content are given below:

ULTRAVIST 150: Each mL of injection contains 312 mg iopromide (equivalent to 150 mg iodine). Bottles of 50 mL, 100 mL and 200 mL have an iodine content of 7.5 g, 15 g and 30 g, respectively and an iopromide content of 15.6 g, 31.2 g and 62.4 g, respectively.

ULTRAVIST 240: Each mL of injection contains 499 mg iopromide (equivalent to 240 mg iodine). Vials of 10 mL and bottles of 50 mL and 100 mL have an iodine

content of 2.4 g, 12 g and 24 g, respectively and an iopromide content of 5 g, 25 g and 49.9 g, respectively.

ULTRAVIST 300: Each mL of injection contains 623 mg iopromide (equivalent to 300 mg iodine). Vials of 10 mL and 20 mL, and bottles of 50 mL, 75 mL, 100 mL and 150 mL have an iodine content of 3 g, 6 g, 15 g, 22.5 g, 30 g and 45 g, respectively and an iopromide content of 6.2 g, 12.5 g, 31.2 g, 46.7 g, 62.3 g and 93.5 g, respectively.

ULTRAVIST 370: Each mL of injection contains 769 mg iopromide (equivalent to 370 mg iodine). Vials of 20 mL and 30 mL, and bottles of 50 mL, 75 mL, 100 mL, 150 mL and 200 mL have an iodine content of 7.4 g, 11.1 g, 18.5 g, 27.8 g, 37 g, 55.5 g and 74 g, respectively and an iopromide content of 15.4 g, 23.1 g, 38.5 g, 57.7 g, 76.9 g, 115.4 g and 153.8 g, respectively.

The registered presentations of ULTRAVIST are:

ULTRAVIST 150:	ULTRAVIST 300:	ULTRAVIST 370:
10 glass bottles of 50 mL	10 glass vials of 10 mL	10 glass vials of 20 mL
10 glass bottles of 100 mL	10 glass vials of 20 mL	10 glass vials of 30 mL
1 glass bottle of 200 mL	10 glass bottles of 50 mL	10 glass bottles of 50 mL
	10 glass bottles of 75 mL	10 glass bottles of 75 mL
ULTRAVIST 240:	10 glass bottles of 100 mL	10 glass bottles of 100 mL
10 glass vials of 10 mL	1 glass bottle of 150 mL	1 glass bottle of 150 mL
10 glass bottles of 50 mL		1 glass bottle of 200 mL
10 glass bottles of 100 mL		

Not all presentations are marketed.

Store below 30°C. Protect from light and secondary X-rays.

NAME AND ADDRESS OF THE SPONSOR

Bayer Australia Ltd
ABN 22 000 138 714
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Pymble NSW 2073

POISONS SCHEDULE OF THE MEDICINE

Not scheduled.

Date of first inclusion in the Australian Register of Therapeutic Goods (the ARTG)

12 September 1991

Date of most recent amendment

29 August 2013