



ULTRAVIST® 300 / 370

Solution for injection/Infusion

Important information, please read carefully!

Composition

Ultravist 300: 1 ml contains 623 mg iopromide (equivalent to 300 mg iodine)
Ultravist 370: 1 ml contains 769 mg iopromide (equivalent to 370 mg iodine)

Pharmaceutical Form

Solution for injection/infusion.

Pharmacological Properties

Pharmacodynamic properties

Pharmacotherapeutic group: Watersoluble, nephrotropic, low osmolar X-ray contrast media
ATC code: V08AB05

The contrast-giving substance in the Ultravist formulations 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.

Injection of iopromide opacifies those vessels or body cavities in the path of flow of the contrast agent, permitting radiographic visualization of the internal structures until significant dilution occurs.

Pharmacokinetic properties

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 ($\leq 0.3\%$ 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 metabolized.

Elimination

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 fecal 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 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. C_{max} , AUC) or are dose independent (e.g. V_{ss} , $t_{1/2}$).

Characteristics in special patient populations

Elderly population (aged 65 years and above)

Middle-aged patients (49 - 64 years) and elderly patients (65 - 70 years), without significantly impaired renal function, had total plasma clearances between 74 and 114 ml/min (middle aged group, mean 102 ml/min) and between 72 and 110 ml/min (elderly group, mean 89 ml/min), which is only marginally lower than those in young healthy subjects (88 to 138 ml/min, mean 106 ml/min). The individual elimination half-lives were between 1.9 - 2.9 hours and 1.5 - 2.7 hours, respectively. Compared to the range of 1.4 to 2.1 h in young healthy volunteers, terminal half-lives are similar. The minor differences correspond to the physiologically reduced glomerular filtration rate with age.

Pediatric population

Pharmacokinetics of iopromide have not been investigated in the pediatric population (see section 'Dosage and method of administration').

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 ($80 \geq CLCR > 30$ 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 hemodialysis. 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 metabolized and only about 2% of dose are excreted in feces.

Preclinical safety data

Preclinical data reveal no evidence of risk for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and reproduction toxicity.

• Systemic toxicity

Experimental systemic tolerance studies following repeated daily intravenous and repeated weekly intrathecal administration produced no findings which object to a diagnostic administration of Ultravist to humans.

- **Genotoxic potential, tumorigenicity**

Studies into genotoxic effects (gene-, chromosomal- and genome mutation tests) in vivo and in vitro gave no indication of a mutagenic potential of Ultravist.

Due to the absence of genotoxic effects and taking into account the metabolic stability, pharmacokinetics and the absence of indications of toxic effects on fast-growing tissues as well as the fact that Ultravist was only administered once, there is no evident risk of a tumorigenic effect on humans.

- **Local tolerance and contact-sensitizing potential**

Local tolerance studies following single as well as repeated intravenous administration and single intraarterial, intramuscular, paravenous, intraperitoneal, intrathecal and conjunctival administration indicated that no or only slight adverse local effects are to be expected in blood vessels, paravenous tissue, subarachnoidal space or on the human mucosa.

Studies into contact-sensitizing effect, gave no indication of a sensitizing potential.

Indication

This medicinal product is for diagnostic use only.

Ultravist 300:

Contrast enhancement in computerized tomography (CT), digital subtraction angiography (DSA), intravenous urography, phlebography of the extremities, venography, arteriography, visualization of body cavities (e.g. arthrography, hysterosalpingography, fistulography) with the exception of myelography, ventriculography, cisternography.

Ultravist 370:

Contrast enhancement in computerized tomography (CT), digital subtraction angiography (DSA), intravenous urography, arteriography and especially angiocardiology, visualization of body cavities (e.g. arthrography, fistulography) with the exception of myelography, ventriculography, cisternography.

Dosage and method of administration

- **General information**

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

For additional instructions see section 'Instructions for use/handling'.

The patient should attend for examination fasting but adequately hydrated. Disorders of the water and electrolyte balance must be corrected. This applies in particular to patients who are predisposed to such disturbances.

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 the 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 p.m. Moreover, it can 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.

Experience shows that pronounced states of excitement, anxiety and pain can be the cause of side effects or intensify contrast medium-related reactions. They can be counteracted by calm management of the patient and the use of suitable drugs.

Experience shows that contrast medium is tolerated better if it is warmed to body temperature.

Intravascular administration of contrast media should, if possible, be done with the patient lying down. After the administration, the patient should be kept under observation for at least 30 minutes, since experience shows that the majority of all severe incidents occur within this time.

A property of non-ionic contrast media is the extremely low interference with normal physiological functions. As a consequence of this non-ionic contrast media have less anticoagulant activity in vitro than ionic media. Therefore, the

period of contact between blood and contrast media in syringes and catheters should be kept as short as possible and meticulous attention should be paid to the angiographic technique and frequent catheter flushing with physiological saline solution (if necessary with heparin added) so as to minimize the risk of procedure-related thrombosis and embolism.

In addition, the following applies to use of the 500 ml and 1000 ml bottles:

The contrast medium must be administered by means of an automatic injector. The tube from the injector to the patient (patient's tube) must be changed after every examination because it is contaminated with blood. Any contrast medium solution left over in the bottle, the connecting tubes and all disposable parts of the injector system must be discarded at the end of the examination day. Any additional instructions from the respective equipment manufacturer must also be adhered to.

• **Intravenous urography**

Dosage

Adults

The dose should not be less than 1 ml Ultravist 300 (0.8 ml Ultravist 370)/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, e.g. with the use of Ultravist 300:

Neonatus : 1.2 g l/kg body weight, corresponding to 4.0 ml/kg body weight
Babies : 1.0 g l/kg body weight, corresponding to about 3.0 ml/kg body weight
Small children : 0.5 g l/kg body weight, corresponding to about 1.5 ml/kg body weight

Filming times

When the above dosage guidelines are observed and Ultravist 300/370 is injected over 1 to 2 minutes, the renal parenchyma is usually highly opacified 3 to 5 minutes and the renal pelvis with the urinary tract 8 to 15 minutes after the start of administration. The earlier time should be chosen for younger patients and the later time for older patients. In babies and young children it is advisable to take the first film as early as about 2 minutes after the administration of the contrast medium.

Insufficient contrast can necessitate later films.

• **Computerized tomography (CT)**

Cranial CT

The following dosages are recommended for cranial CT:

Ultravist 300: 1.0 - max. 2.0 ml/kg body weight

Ultravist 370: 1.0 - max. 1.5 ml/kg body weight

Whole-body CT

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. The infusion should be preferred for slow scanners and the injection as a bolus for fast scanners.

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.

Suggested dosages:

Cerebral angiography

Aortic arch angiography	50-80ml	Ultravist 300
Retrograde carotid angiography	30-40 ml	Ultravist 300
Selective angiography	6-15 ml	Ultravist 300

- Thoracic aortography 50-80 ml Ultravist 300
- Abdominal aortography 40-60 ml Ultravist 300
- Angiography of the extremities
 - Upper extremities:
 - Arteriography 8-12 ml Ultravist 300
 - Venography 15-30 ml Ultravist 300
 - Lower extremities:
 - Arteriography 20-30 ml Ultravist 300
 - Venography 30-60 ml Ultravist 300
- Angiocardiography
 - Selective, in the individual cardiac cavities: 40-60 ml Ultravist 370
- Coronarangiography 5- 8 ml Ultravist 370

• **Intravenous Digital subtraction angiography (DSA)**

Basing on experience with ionic contrast media, the iv 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 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.

• **Intraarterial digital subtraction angiography**

Intraarterial digital subtraction angiography requires smaller volumes and lower iodine concentrations than the intravenous technique. The more selective the angiography is, the lower the dose of contrast medium can be. This method is therefore recommended for patients with impaired renal function. The values used in conventional angiography for bolus concentration, bolus volume and flow rate can be reduced for intraarterial DSA.

Additional information on special populations

Newborns (< 1 month) and infants (1 month -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.

Elderly population (aged 65 years and above)

In a clinical study, no differences in pharmacokinetics of iopromide were observed between elderly (aged 65 years and above) and younger patients. Therefore, no specific recommendation for a dosage adjustment is given for elderly patients beside those described in subsection 'Dosage regimen'.

Patients with hepatic impairment

Elimination of iopromide is not affected by impaired liver function as only about 2% of the dose is eliminated via feces and iopromide is not metabolized. No dosage adjustment is considered necessary in patients with hepatic impairment.

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 kidney injury in patients with pre-existing renal impairment, the minimum possible dose should be used in these patients (see also sections 'Special warnings and precautions for use' and 'Pharmacokinetic properties')

Contraindications

There are no absolute contraindications to the use of Ultravist.

Special warnings and precautions for use

For all indications

• Hypersensitivity reactions

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

Allergy-like reactions ranging from mild to severe reactions including shock are possible (see “Undesirable effects”). Most of these reactions occur within 30 minutes 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

Particularly careful risk/benefit judgement is required in patients with known hypersensitivity to Ultravist or any excipient of Ultravist, or with a previous hypersensitivity reaction to any other iodinated contrast medium due to an increased risk for hypersensitivity reactions (including severe reactions).

However, such reactions are irregular and unpredictable in nature.

Patients who experience such reactions while taking beta blocker may be resistant to treatment effects of beta agonists (see also “Interactions with other medicaments and other forms of interaction”).

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.

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.

• 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 and thyrotoxic crisis in these patients. Testing of thyroid function prior to Ultravist administration and/or preventive thyreostatic medication should be considered in patients with known or suspected hyperthyroidism.

[Thyroid functions tests indicative of hypothyroidism or transient thyroid suppression have been reported following iodinated contrast media administration to adult and pediatric patients. Evaluate the potential risk of hypothyroidism in patients with known or suspected thyroid diseases before use of iodinated contrast media.](#)

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 to have 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 and the use of certain concomitant medication.

Factors which increase blood-brain barrier permeability facilitate the passage of the contrast medium into cerebral tissue, possibly leading to CNS reactions.

• Hydration

Adequate hydration status must be assured in all patients before intravascular or intrathecal Ultravist administration (see also subsection ‘Acute Kidney Injury’). This applies especially to patients with multiple myeloma, diabetes mellitus, polyuria, oliguria, hyperuricemia, as well as to newborns, infants, small children and elderly patients.

Adequate hydration status must be assured in renally impaired patients. However, prophylactic IV hydration in patients with moderate renal impairment (eGFR 30-59 mL/min/1.73 m²) is not recommended as additional renal safety benefits have not been established. In patients with severe renal impairment (eGFR <30 mL/min/1.73 m²) and concomitant cardiac conditions, prophylactic IV hydration can lead to increased serious cardiac complications. Refer to subsection 'Acute Kidney Injury', 'Cardiovascular disease', 'Tabulated list of adverse 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.

- **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.

Intravascular use

Acute Kidney Injury

Post-contrast Acute Kidney Injury (PC-AKI), 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, e.g.:

- pre-existing renal insufficiency (see subsection 'Patient with renal impairment')
- dehydration (see subsection 'Hydration')
- diabetes mellitus
- multiple myeloma / paraproteinemia
- repetitive and/or large doses of Ultravist

Patients with moderate to severe (eGFR 44-30 mL/min/1.73 m²) or severe renal impairment (eGFR <30 mL/min/1.73 m²) are at increased risk of Post-Contrast Acute Kidney Injury (PC-AKI) with intra-arterial contrast administration and first pass renal exposure.

Patients with severe renal impairment (eGFR <30 mL/min/1.73 m²) are at increased risk of PC-AKI with intra-venous or intra-arterial contrast administration with second pass renal exposure (see subsection 'Hydration').

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

- **Cardiovascular disease**

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

The intravascular injection of Ultravist may precipitate pulmonary edema in patients with heart failure.

- **Pheochromocytoma**

Patients with pheochromocytoma may be at an increased risk to develop a hypertensive crisis.

- **Myasthenia gravis**

The administration of Ultravist may aggravate the symptoms of myasthenia gravis.

- **Thromboembolic events**

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 catheterization 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 minimize the length of the procedure so as to minimize the risk of procedure-related thrombosis and embolism.

Undesirable effects

Name of Product/Active ingredient/Dosage form/Version/Date of approval
ULTRAVIST 300 & 370/Iopromide/Solution for injection/BEC 19581 & 19924 - CCDS #15&16/

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 edema, pharyngeal edema, asthma, coma, cerebral infarction, stroke, brain edema, convulsion, arrhythmia, cardiac arrest, myocardial ischemia, myocardial infarction, cardiac failure, bradycardia, cyanosis, hypotension, shock, dyspnea, pulmonary edema, 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 ($\geq 1/100$ to $< 1/10$),
 uncommon ($\geq 1/1,000$ to $< 1/100$),
 rare ($\geq 1/10,000$ to $< 1/1,000$).

The adverse drug reactions identified only during post-marketing surveillance, and for which a frequency could not be estimated, are listed under 'not known'.

Table 1: Adverse drug reactions (ADRs) reported in clinical trials or during post-marketing surveillance in patients treated with Ultravist

System organ class	Common	Uncommon	Rare	Not known
Immune system disorders		Hypersensitivity / anaphylactoid reactions (anaphylactoid shock ^{§) *} , respiratory arrest ^{§) *} , bronchospasm [*] , laryngeal ^{*)} / pharyngeal ^{*)} / face edema, tongue edema ^{§)} , laryngeal / pharyngeal spasm ^{§)} , asthma ^{§) *} , conjunctivitis ^{§)} , lacrimation ^{§)} , sneezing, cough, mucosal edema, rhinitis ^{§)} , hoarseness ^{§)} , throat irritation ^{§)} , urticaria, pruritus, angioedema)		
Endocrine disorders				Thyrotoxic crisis, Thyroid disorder
Psychiatric disorders			Anxiety	
Nervous system disorders	Dizziness, Headache, Dysgeusia	Vasovagal reactions, Confusional state, Restlessness, Paraesthesia / hypoaesthesia, Somnolence		Coma [*] , Cerebral ischaemia / infarction [*] , Stroke [*] , Brain edema ^{a) *} , Convulsion [*] , Transient cortical blindness ^{a)} , Loss of consciousness, Agitation, Amnesia, Tremor, Speech disorders, Paresis / paralysis

System organ class	Common	Uncommon	Rare	Not known
Eye disorders	Blurred / disturbed vision			
Ear and labyrinth disorders				Hearing disorders
Cardiac disorders	Chest pain / discomfort	Arrhythmia ^{*)}	Cardiac arrest ^{*)} , Myocardial ischemia ^{*)} , Palpitations	Myocardial infarction ^{*)} , Cardiac failure ^{*)} , Bradycardia ^{*)} , Tachycardia, Cyanosis ^{*)}
Vascular disorders	Hypertension Vasodilatation	Hypotension ^{*)}		Shock ^{*)} , Thromboembolic events ^{a)} Vasospasm ^{a)}
Respiratory, thoracic and mediastinal disorders		Dyspnea ^{*)}		Pulmonary edema ^{*)} , Respiratory insufficiency ^{*)} , Aspiration ^{*)}
Gastrointestinal disorders	Vomiting, Nausea	Abdominal pain		Dysphagia, Salivary gland enlargement, Diarrhoea
Skin and subcutaneous tissue disorders				Severe cutaneous reactions: Toxic epidermal necrolysis (TEN)/Lyell syndrome*, Stevens-Johnson syndrome (SJS)*. Drug reaction with eosinophilia and systemic symptoms (DRESS), Acute generalized exanthematous pustulosis (AGEP), 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	Pain, Injection site reactions (various kinds, e.g. pain, warmth ^{§)} , edema ^{§)} , inflammation ^{§)} and soft tissue injury ^{§)} in case of extravasation), Feeling hot	Edema		Malaise, Chills, Pallor
Investigations				Body temperature fluctuation

^{*)} life-threatening and/or fatal cases have been reported

^{a)} intravascular use only

^{§)} identified only during post-marketing surveillance (frequency not known)

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.

In addition to the ADRs listed above, the following ADRs have been reported with 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

Overdose

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 towards the support of vital functions.

Ultravist is dialyzable (see section 'Pharmacokinetic properties').

- Suggestions for the treatment of contrast medium incidents
Management of adverse event related to contrast media use is based on the hospital's management standard of drug poisoning.

Interaction with other medicinal products and other forms of interaction

Biguanides (metformin): In patients with acute kidney failure or severe chronic kidney disease biguanide 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 section 'Special warnings and precautions for use' – subsection 'Intravascular use' – 'Acute Kidney Injury').

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

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.

Pregnancy and lactation

Pregnancy

Adequate and well-controlled studies in pregnant women have not been conducted. It has not been sufficiently demonstrated that non-ionic contrast media are safe for use in pregnant patients. Since, wherever possible, radiation exposure should be avoided during pregnancy, the benefits of any X-ray examination, with or without contrast media, should be carefully weighed against the possible risk.

Animal studies do not indicate harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development following diagnostic application of iopromide in humans.

Lactation

Safety of Ultravist for nursing infants has not been investigated. Contrast media are poorly excreted in human breast milk. Harm to the nursing infant is not likely (see also section 'Special warnings and precautions for use' – subsection 'Thyroid dysfunction').

List of Excipients

Calcium disodium edetate
Hydrochloric acid (for pH adjustment)

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Tromethamine
Water for injections

Instructions for use / handling

Ultravist should be warmed to body temperature prior to use.

Visual inspection

Contrast media should be visually inspected prior to use and must not be used, if discolored, nor in the presence of particulate matter (including crystals) or defective containers. As Ultravist is a highly concentrated solution, crystallization (milky-cloudy appearance and/or sediment at bottom, or floating crystals) may occur very rarely.

Large volume containers

The following applies to the multiple withdrawal of contrast medium from containers of 200 ml or more:

The multiple withdrawal of contrast medium must be done utilizing a device approved for multiple use.

The rubber stopper of the bottle should never be pierced more than once to prevent large amounts of microparticles from the stopper getting into the solution.

The contrast medium must be administered by means of an automatic injector, or by other approved procedures which ensure sterility of the contrast medium.

The tube from the injector to the patient (patient's tube) must be replaced after every patient to avoid cross contamination.

The connecting tubes and all disposable parts of the injector system must be discarded when the infusion bottle is empty or ten hours after first opening the container

Instructions of the device manufacturer must be followed.

Unused Ultravist in opened containers must be discarded ten hours after first opening the container.

Presentation

Ultravist 300	
10 bottles @ 50 ml	Reg. No.: [REDACTED]
10 bottles @ 100 ml	Reg. No.: [REDACTED]
1 bottle @ 500 ml	Reg. No.: [REDACTED]

Ultravist 370	
10 bottles @ 50 ml	Reg. No.: [REDACTED]
10 bottles @ 100 ml	Reg. No.: [REDACTED]
1 bottle @ 500 ml	Reg. No.: [REDACTED]

Storage

Protect from light and ionizing radiation.
Do not store above 30°C.
Store all drugs properly and keep them out of reach of children.

Harus dengan resep dokter

Imported by:
PT. Bayer Indonesia,
Depok-Indonesia

Manufactured by:
Bayer AG,
Berlin-Germany