SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Urografin 370 mg Iodine/ml solution for injection/infusion.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL Urografin contains 0.1 g sodium amidotrizoate and 0.66 g meglumine amidotrizoate (sodium diatrizoate and meglumine diatrizoate) in aqueous solution, equivalent to 370 mg iodine.

Excipients with known effect:
1 mL solution for injection contains 3.62 mg sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection/infusion.
Clear, colourless to pale yellow solution.

The physical and chemical characteristics of Urografin are as follows:

Osmolality (mOsm/kg H_2O) at 37ºC	2100
Viscosity (mPa·s) at 20ºC at 37ºC	 18.5 8.9
Density (g/mL) at 20ºC at 37ºC	 1.418 1.411
pH	6.0-7.0

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Urografin is indicated in adults for:

- intravenous urography
- angiographic examinations such as aortography, angiocardiography and coronary arteriography
- arthrography
- intraoperative cholangiography
- endoscopic retrograde cholangiopancreatography (ERCP)

- sialography
- fistulography
- hysterosalpingography
- galactography

Urografin is indicated in the paediatric population from 0 to 18 years for:

- intravenous urography

4.2 Posology and method of administration

Urografin must be used only under medical supervision and must be administered by trained healthcare professionals with technical experience in the performance of radiological techniques using meglumine amidotrizoate.

Posology

For intravenous and intraarterial routes of administration, the dose may vary depending on the age, body weight, cardiac output and general condition of the patient.

Sufficient time must be left between separate injections for the diffusion or intravascular movement of interstitial fluid in the body to permit normalisation of the increase in serum osmolality. In adequately hydrated patients, a period of 10-15 minutes is required to achieve this. In the case of special situations in adults where it is necessary to exceed a total dose of 300 to 350 mL, fluid and possibly electrolyte replacement will be necessary.

Adults:

Indication	Recommended dose	Route of administration
Intravenous urography by injection	20-50 mL The dose is 20 mL Urografin. The diagnostic yield increases considerably if the dose of Urografin is increased to 50 mL. For special indications, the dose may be increased further if considered necessary.	Intravenous
Intravenous urography by infusion	100 mL	Intravenous
Aortography	50-70 mL Angiographic examinations require a particularly high concentration of iodine.	Intraarterial

Indication	Recommended dose	Route of administration

	The dosage depends on the clinical situation, the diagnostic technique to be performed and the nature and volume of the vascular region to be studied.	
Angiocardiography	0.7-3.5 mL/kg b.w. Angiographic examinations require a particularly high iodine concentration. The dosage depends on the clinical situation, the diagnostic technique to be performed and the nature and volume of vascular region to be studied.	Intraarterial
Coronary arteriography	4-8 mL Angiographic examinations require a particularly high iodine concentration. The dosage depends on the clinical situation, the diagnostic technique to be performed and the nature and volume of vascular region to be studied.	Intraarterial
Arthrography	5-20 mL	Intraarticular
Intraoperative cholangiography	10-20 mL The dose generally depends on the clinical situation and the size of the structure to be studied.	Intracholangiopancreatic
Endoscopic retrograde cholangiopancreatography (ERCP)	The dose generally depends on the clinical situation and the size of the structure to be studied.	Intracholangiopancreatic
Sialography	0.5-2 mL	Intraglandular
Fistulography	The dose generally depends on the clinical situation and the size of the structure to be studied.	Not applicable
Hysterosalpingography	10-20 mL	Intrauterine
Galactography	0.5-2 mL	Intramammary

Paediatric population:

Indication	**Recommended dose**	**Route of administration**

Intravenous urography by injection	Up to 1 year: 7-10 mL 1 to 2 years: 10-12 mL 2 to 6 years: 12-15 mL 6 to 12 years: 15-20 mL Over 12 years: adult dose. The reduced physiological concentrating ability of the still immature nephron of infantile kidneys means that relatively high doses of Urografin need to be administered.	Intravenous
Intravenous Urografin by infusion	Over 12 years: adult dose	Intravenous

Intravenous urography

- *Intravenous urography by injection*
  The injection rate is generally 20 mL/min. If 100 mL or more is administered to patients with heart failure, an injection time of at least 20-30 minutes is recommended.

- *Intravenous urography by infusion*

  Adults and adolescents

  In general, the infusion time must not be less than 5 minutes or much higher than 10 minutes. For patients with heart failure, an infusion time of 20-30 minutes is necessary.

Compression is contraindicated in neonates and children up to 2 years of age, and is not advisable either during infusion of large quantities of contrast medium in children, adolescents and adults. This is because, if drainage is obstructed, the increase in diuresis can lead to rupture of the fornix as a result of the increase in pressure. However, compression may be applied about 10 minutes after the end of infusion to distinguish organic filling defects from functional ones.

Angiographic examinations

The 76% solution is suitable for angiographic examinations that require a particularly high iodine concentration, e.g. aortography, angiocardiography and coronary arteriography. The dosage depends on the clinical situation, the diagnostic technique to be performed and the nature and volume of the vascular region to be studied.

Additional information in special populations

Renal insufficiency / Heart failure

In patients with marked cardiovascular or renal insufficiency, and in those in a deteriorated general condition, the dose of contrast medium to be administered must be as low as possible. In these patients, it is recommended that renal function be monitored for at least 3 days after the examination.

Elderly patients (population over 65 years of age):

No clinical studies have been performed with Urografin in the elderly. It is not recommended to adjust the

dose compared with younger adults, as the iodine concentrations required for diagnostic imaging are not age-dependent, as with other iodinated contrast agents.

Patients with hepatic insufficiency:
For patients with hepatic insufficiency, an additional dose adjustment is not considered necessary.

Method of administration

For single use only. Do not use the same container for several patients.

Routes of administration: intravenous, intraarterial, intraarticular, intracholangiopancreatic, intraglandular, intramammary and intrauterine.

Administration by the intraarterial and intravenous route:

Wherever possible, intravascular administration of the contrast medium must be performed with the patient recumbent. After the injection, the patient must remain under observation for at least half an hour, as experience has shown that the majority of adverse reactions arise during this period.

Angiographic examinations
Intraarterial route of administration for the indications: aortography, angiocardiography and coronary arteriography.

Administration in other body cavities

During arthrography, hysterosalpingography and in particular endoscopic retrograde cholangiopancreatography (ERCP), the injections of contrast medium must be performed under fluoroscopy guidance.

Image acquisition

Intravenous urography by injection
The renal parenchyma is visualised better when radiography is performed immediately after completion of administration of the contrast medium.

For visualisation of the renal pelvis and the urinary tract, the first X-ray is performed 3-5 minutes and the second 10-12 minutes after administration of the contrast medium. Within these ranges, the time closest to the injection must be chosen for younger patients and the furthest time for older patients.

In neonates, infants and young children, it is recommended that the first X-ray be performed as early as approximately 2 minutes after administration of the contrast medium.

If the quantity of contrast medium is insufficient, further X-rays may be required.

Intravenous urography by infusion
The first X-ray must be performed towards the end of the infusion. Further X-rays may be performed during the following 20 minutes, or later in case of excretion abnormalities.

Other indications for intravenous urography
The details of the image acquisition technique depend on the examination technology used. Users must follow the device specifications of the examination equipment used.

Dietary recommendations

In the case of urography, the diagnostic yield increases if the intestine does not contain gas or faecal matter. Therefore, for 2 days before the examination, patients must avoid flatulent foods, especially peas, beans and lentils, salad, fruit, bread and all types of raw vegetables. The day before the examination, patients must not eat any food from 6 o'clock in the evening. It may also be appropriate to administer a laxative at night. However, in neonates, infants and small children, prolonged fasting and the administration of a laxative before the examination are contraindicated.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Manifest hyperthyroidism.
- Decompensated heart failure.
- Hysterosalpingography must not be performed during pregnancy or in the presence of acute inflammatory processes in the pelvic cavity.
- ERCP is contraindicated in cases of acute pancreatitis.

Urografin must not be used for myelography, ventriculography or cisternography as neurotoxic symptoms (pain, convulsions and coma, frequently with a fatal outcome) are likely to arise in these examinations.

4.4 Special warnings and precautions for use

For all indications

The following warnings and precautions apply to any method of administration, although the risks indicated are greater in the case of intravascular administration.

- Hypersensitivity reactions

Occasionally, allergy-like hypersensitivity reactions have been observed in patients after the use of X-ray contrast media such as Urografin (see section 4.8). These reactions generally manifest as non-serious respiratory or cutaneous symptoms, such as slight respiratory difficulty, reddening of the skin (erythema), urticaria, pruritus or facial oedema. Serious adverse reactions such as angioedema, subglottal oedema, bronchospasm and allergic shock are possible. These reactions generally arise during the first hour after administration of the contrast medium. However, delayed reactions (after hours or days) may arise on rare occasions.

Patients with hypersensitivity or previous reactions to iodinated contrast media are at greater risk of having a severe reaction.

Before any contrast medium is injected, the patient must be questioned as to whether he/she has a history of allergies, e.g. allergy to shellfish, allergic rhinitis (hay fever) or hives, sensitivity to iodine or X-ray media and bronchial asthma, as the incidence of adverse reactions to contrast media is higher in patients with these disorders. Prior treatment with antihistamines and/or glucocorticoids may be considered.

Patients with bronchial asthma are particularly at risk of experiencing bronchospasms or a hypersensitivity reaction.

Hypersensitivity reactions may be aggravated in patients under treatment with beta-blockers, especially in patients with bronchial asthma. It must also be borne in mind that patients being treated with beta-blockers may be refractory to standard treatment for hypersensitivity reactions with beta agonists.

If hypersensitivity reactions occur (see section 4.8), administration of the contrast medium must be stopped immediately and, if necessary, specific intravenous treatment initiated. It is therefore advisable to use a permanent flexible cannula for intravenous administration of the contrast medium. To be able to take immediate action in an emergency, appropriate drugs, an endotracheal tube and an artificial respirator must be readily available.

- Thyroid dysfunction

It is necessary to carry out a careful benefit/risk assessment, especially in patients with diagnosed or suspected

hyperthyroidism or goitre, as iodinated contrast media can interfere with thyroid function, or aggravate or induce hyperthyroidism and thyroid storm.

Thyroid function in patients with known or suspected hyperthyroidism must be assessed prior to administration of Urografin and/or preventive thyrostatic drugs.

Monitoring of thyroid function is recommended in neonates, especially if premature, who have been exposed to Urografin either through the mother during pregnancy or after birth, as excessive exposure to iodine can cause hypothyroidism, possibly requiring treatment.

- Cardiovascular disease

There is greater risk of serious reactions arising in individuals with severe heart disease, and especially those with heart failure and coronary artery disease.

- Elderly patients

Underlying neurological disorders or vascular disease that are frequently observed in elderly patients increase the risk of adverse reactions to iodinated contrast media.

- Patients in a very poor state of health

The need for the examination must be assessed very carefully in these patients.

- Hydration

Adequate hydration of the patient must be ensured before and after administration of the contrast medium. This is especially important in patients with multiple myeloma, diabetes mellitus with nephropathy, polyuria, oliguria or hyperuricaemia, and also in neonates, infants, small children and elderly patients. Abnormalities in the fluid/electrolyte balance must be corrected before the examination.

- Neonates (< 1 month) and infants (1 month to 2 years)

Infants of under 1 year of age and in particular neonates are prone to developing electrolyte disorders and haemodynamic abnormalities. Special attention should be paid with regard to the dose of the contrast medium to be administered, to the technical performance of the radiological procedure and to the patient's condition.

- Anxiety

Pronounced states of excitement, anxiety and pain can increase the risk of adverse reactions or intensify contrast media-related reactions. A sedative may be administered to these patients.

- Warming the contrast medium prior to administration

Contrast media that are warmed to body temperature before administration are better tolerated and easier to administer due to their reduced viscosity. If a heater is used, only the estimated number of bottles to be used on the day of the examination must be heated to 37ºC. If Urografin is protected from sunlight, it may be kept at that temperature for longer periods without affecting the chemical purity of the product. However, this period must not exceed 3 months.

- Tests prior to administration of the contrast medium

Performing sensitisation tests using small doses of contrast medium is not recommended, as these do not have any predictive value. Moreover, occasionally sensitisation tests have themselves caused severe and even fatal hypersensitivity reactions.

<u>For intravascular administration</u>

- Renal insufficiency

Rarely, transient renal insufficiency may occur. Preventive measures against acute renal insufficiency after the administration of contrast media include:

Identification of high-risk patients (e.g. patients with a history of kidney disease, pre-existing renal insufficiency, prior renal insufficiency after administration of contrast media, diabetes mellitus with nephropathy, reduction in volume, multiple myeloma, age over 60 years, advanced vascular disease, paraproteinaemia, severe and chronic hypertension, gout or patients receiving high or repeated doses).
Ensure that at-risk patients are adequately hydrated before administration of the contrast medium, preferably by intravascular transfusion before and after the procedure and until the contrast medium has been eliminated by the kidneys.

Avoid additional renal overload in the form of nephrotoxic drugs, oral cholecystographic agents, artery clamping, renal artery angioplasty, major surgery, etc. until the contrast medium has been eliminated.

Delay any further examination with contrast medium until renal function is completely restored to pre-examination levels.

Contrast media may be administered for radiological examinations to patients on dialysis, as iodinated contrast media are eliminated in the dialysis process.

- Treatment with metformin

The use of intravascular X-ray contrast media excreted by the kidneys may give rise to transient impairment of renal function. This may cause lactic acidosis in patients who are taking biguanides.
As a precaution, the administration of biguanides must be suspended for the period between 48 hours before and at least 48 hours after administration of the contrast medium, being resumed only when normal renal function has been restored.

- Cardiovascular disease

In patients with valve disease and pulmonary hypertension, the administration of contrast media may give rise to significant haemodynamic changes. Reactions involving ischaemic changes in the ECG and significant arrhythmia are more common in elderly patients and those with pre-existing heart disease.

Intravascular injection of the contrast medium may precipitate the onset of pulmonary oedema in patients with heart failure.

- CNS disorders

Special attention must be paid to the intravascular administration of contrast media to patients with acute cerebral infarction, acute intracranial haemorrhage or other disorders that involve impairment of the blood-brain barrier, cerebral oedema or acute demyelination.

Intracranial tumours or metastases and a history of epilepsy may increase the incidence of convulsions after the administration of iodinated contrast media.

Neurological symptoms due to cerebrovascular disease, intracranial tumours or metastases and degenerative or inflammatory diseases may be exacerbated by the administration of contrast media.
Intraarterial injection of contrast media can cause vasospasm and the resulting cerebral ischaemic events.
Patients with symptomatic cerebrovascular disease, recent cerebrovascular accidents or frequent transient ischaemic episodes are at higher risk of suffering neurological complications.

- Severe impairment of hepatic function

The coexistence of severely impaired hepatic function and severe renal insufficiency can considerably delay excretion of the contrast medium and may render haemodialysis necessary.

- Multiple myeloma and paraproteinaemia

Multiple myeloma or paraproteinaemia may predispose to a deterioration in renal function after the administration of contrast media. It is essential to maintain adequate hydration.

- Phaeochromocytoma

Patients with phaeochromocytoma may develop a severe hypertensive crisis (sometimes uncontrollable) after intravascular administration of contrast media. Prior treatment with alpha-blockers (alpha-adrenoreceptor antagonists) is recommended.

- Patients with autoimmune disorders

Cases of severe vasculitis or Stevens-Johnson type syndrome have been reported in patients with prior autoimmune disorders.

- Myasthenia gravis

The administration of iodinated contrast media can aggravate the symptoms of myasthenia gravis.

- Alcoholism

Acute or chronic alcoholism can increase the permeability of the blood-brain barrier. This facilitates the passage of the contrast medium into the brain tissue, which may lead to reactions in the CNS. Special caution must also be exercised in the case of alcoholics and drug addicts, due to the possibility that the seizure threshold may be lowered.

- Coagulation

Ionic iodinated contrast media inhibit blood coagulation, *in vitro,* more than non-ionic contrast media. However, healthcare personnel performing vascular catheterisation procedures must consider that, in addition to the contrast medium, numerous factors may contribute to the development of thromboembolic events, such as the duration of the procedure to be performed, the number of injections, the type of material of the catheter and syringe, the patient's underlying disease and concomitant medication. Consequently, all this must be taken into account when a vascular catheterisation procedure is performed. Particular attention must be paid to the angiographic technique used, the catheter must be irrigated frequently with physiological saline solution (adding heparin wherever possible), and the duration of the procedure must be minimised with a view to minimising the risk of thromboembolic events related to the diagnostic procedure performed.

It has been reported that using plastic syringes instead of glass syringes reduces, but does not eliminate, the possibility of coagulation phenomena occurring *in vitro*.

Caution is advised in patients with homocystinuria due to the risk of induction of thromboembolic events.

For administration in body cavities

All possibility of pregnancy must be ruled out before hysterosalpingography is performed.

Inflammation of the bile ducts or Fallopian tubes can increase the risk of reactions after cholangiography, ERCP or hysterosalpingography.

Warnings regarding excipients

This medicinal product contains 72.40-181.00 mg sodium per dose (20-50 ml), equivalent to 3.62-9.05% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

This medicinal product contains 362.00 mg sodium per dose (100 ml), equivalent to 18.1% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

Treatment with interleukin

The prevalence of delayed reactions to contrast media (e.g. fever, rash, flu-like symptoms, joint pain and pruritus) is higher in patients who have received treatment with interleukin.

Interference with diagnostic tests

After the administration of iodinated contrast media, the radioisotope uptake capacity of the thyroid, for the diagnosis of thyroid disorders, decreases for up to 2 weeks, and even more in particular cases.

4.6 Fertility, pregnancy and lactation

Pregnancy

Toxicological studies on reproduction with sodium or meglumine amidotrizoate did not indicate teratogenic or embryotoxic potential after inadvertent administration of Urografin during pregnancy.

It has not been sufficiently demonstrated that the use of contrast media in pregnant patients is safe. Given that any exposure to radiation must be avoided as much as possible during pregnancy, radiological examinations in pregnant women, with or without contrast media, must be performed only after a careful assessment of the benefits compared with the possible risks.

Breastfeeding

Renally eliminated contrast media such as Urografin are excreted in human milk only in very small amounts. Limited data suggest that the risk to breastfed infants after administration of salts of diatrizoic acid to the mother is low. Breastfeeding is probably safe.

4.7 Effects on ability to drive and use machines

As with all iodinated contrast media, in rare cases there is a possibility of delayed adverse reactions after the administration of contrast media, which may affect the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Intravascular administration

The adverse reactions associated with the intravascular administration of iodinated contrast media are usually of a mild-to-moderate nature and transitory in character. However, serious and potentially fatal reactions, and even death, have also been reported. The prevalence of adverse drug reactions in patients to whom ionic iodinated contrast media are administered is over 12%, compared with over 3% in patients to whom non-ionic contrast media are administered.

The most common adverse reactions recorded are nausea, vomiting, pain sensation and general sensation of heat.

Administration in body cavities

Adverse reactions following administration into body cavities are rare. Most occur several hours after administration, due to the slow absorption from the administration site and distribution through the body, mainly through controlled diffusion processes.

Regarding hysterosalpingography, cases of vasovagal reactions are uncommon.

Tabulated list of adverse reactions

The following table summarises the approximate incidences of reported adverse reactions to Urografin. The frequency groups are defined in accordance with the following convention: common (≥ 1/100), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000), very rare (< 1/10,000).

Table 1: Reported adverse reactions in patients treated with Urografin, during intravascular use and use in body cavities

System organ classes	Common	Uncommon	Rare	Very rare
Immune system disorders	Anaphylactoid/ hypersensitivity reactions (angioedema,	Hypotension[1], bronchospasm[1], laryngeal spasm[1], laryngeal oedema[1]	Type IV hypersensitivity reaction (delayed	

	conjunctivitis, cough, pruritus, rhinitis, sneezing and urticaria)		reactions to the contrast medium)	

General disorders and administration site conditions	Feeling hot, local pain[2,3,5], oedema[3,5]	Discomfort, chills, sweating		Inflammation[5], tissue necrosis[5]
Cardiac disorders		Transitory change in heart rate, transitory change in arterial pressure, change in rhythm or in cardiac function, cardiac arrest	Myocardial infarction	
Ear and labyrinth disorders		Hearing impairment[4]		
Eye disorders		Transitory blindness[4], photophobia[4,] visual disturbance[4]		
Gastrointestinal disorders	Nausea, vomiting	Abdominal pain	Swelling of the salivary glands, pancreatitis[8,9], necrotising pancreatitis[8,9]	
Investigations			Body temperature fluctuation, elevated amylase	
Nervous system disorders	Headache	Vasovagal reactions[7], dizziness[4], agitation[4], confusion[4], amnesia[4], speech disorders[4], convulsions[4], tremor[4], paresis/paralysis[4], coma[4], somnolence[4]	Cerebrovascular accident[6]	
Renal and urinary disorders			Renal function impairment, renal insufficiency	
Respiratory, thoracic and mediastinal disorders	Transitory changes in respiratory rate, dyspnoea, breathing difficulty, coughing		Respiratory arrest, pulmonary oedema	
Skin and subcutaneous tissue	Erythema		Mucocutaneous syndrome (e.g.	

disorders			Stevens-Johnson syndrome or toxic epidermal necrolysis / Lyell syndrome)	
Vascular disorders	Hot flush with vasodilation		Thrombophlebitis[5], venous thrombosis[5], embolism	

[1] In the context of anaphylactic/hypersensitivity reactions.

[2] Mainly associated with peripheral angiography.

[3] Associated with extravasation of contrast media, generally disappearing without sequelae.

[4] Transitory neurological symptoms and/or complications associated with procedures in which the contrast medium reaches the brain in high concentrations.

[5] Associated with the injection site.

[6] In isolated cases, fatal.

[7] Related to hysterosalpingography.

[8] Encountered rarely in relation to the use of body cavities.

[9] Post endoscopic retrograde cholangiopancreatography (CPRE).

Description of some adverse reactions

Intravascular administration

Anaphylactoid/hypersensitivity reactions (e.g. mild angioedema, conjunctivitis, cough, pruritus, rhinitis, sneezing and urticaria) may occur irrespectively of the quantity administered and the route of administration, and may be the first signs of an incipient state of shock. The administration of the contrast medium must be stopped immediately and, if necessary, specific intravenous treatment must be initiated (see section 4.4).

Severe anaphylactoid/hypersensitivity adverse reactions or cardiac disorders that require emergency treatment may arise in the form of a circulatory reaction accompanied by peripheral vasodilation and the resulting hypotension, reflex tachycardia, dyspnoea, agitation, confusion and cyanosis, which can lead to loss of consciousness.
On rare occasions, severe thromboembolic episodes have been reported which have led to stroke, in isolated cases fatal, and myocardial infarction.

Administration in body cavities

Systemic hypersensitivity is rare, usually mild, and generally occurs in the form of cutaneous reactions. However, the possibility of a severe hypersensitivity reaction cannot be fully ruled out (see section 4.8, subsection Summary of the safety profile – Intravascular administration, to obtain a complete text on the anaphylactoid reactions).

A certain increase in amylase levels after endoscopic retrograde cholangiopancreatography (ERCP) is common. It has been shown that acinar opacification after ERCP is associated with a greater risk of post-ERCP pancreatitis. On rare occasions, cases of necrotising pancreatitis have been descripted.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

4.9 Overdose

In the event of an accidental intravascular overdose in humans, compensation for the water and electrolyte

loss is necessary by means of infusion. Renal function must be monitored for at least 3 days after the performance of the test.

If necessary, haemodialysis may be used to eliminate most of the contrast medium from the patient's body.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Watersoluble, nephrotropic, high osmolar iodinated X-ray contrast media, ATC code: V08AA.
The compound that provides the contrast is a salt of amido(dia-)trizoic acid in which the iodine which absorbs the X-rays is present by means of stable chemical bonds.

5.2 Pharmacokinetic properties

Distribution
Plasma protein binding following intravenous injection is less than 10%.

After a bolus intravenous injection of 1 mL Urografin per kg body weight, a concentration of 2-3 g iodine/litre plasma can be expected after 5 minutes. During a period of 3 hours, the plasma level falls relatively rapidly during the first 30 minutes, and subsequently with a half-life of 1-2 hours.

Amidotrizoic acid does not penetrate red blood cells. It is distributed very rapidly in the extracellular space after intravascular administration, but does not cross the intact blood-brain barrier and is excreted in breast milk only in minimal quantities.

Metabolism and elimination
At diagnostic doses, amidotrizoic acid undergoes glomerular filtration. Approximately 15% of the dose is eliminated in urine in a chemically unchanged form within 30 minutes of the injection, and more than 50% within 3 hours; no metabolites could be demonstrated.

The kinetics observed in the distribution and elimination of Urografin are not dose-related within the clinically relevant range. This means that if the dose is doubled or halved, the blood levels and an eliminated quantity of contrast medium in grams per unit of time obtained that are double or half.

However, given the increased osmotic diuresis that occurs with a double dose, the urinary concentration of the contrast medium does not increase to the same degree.

In the presence of impaired renal function, amidotrizoate can also be eliminated extrarenally via the liver, although at a distinctly reduced rate. Renal contrast media can be removed from the body easily by means of extracorporeal haemodialysis. Regardless of the injection site, complete elimination after a short period of time is certain, including from the tissues.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of systemic toxicity, genotoxicity, local tolerance and potential contact sensitisation.

6 . PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium calcium edetate

Water for injection

6.2 Incompatibilities

This medicinal product must not be mixed with others in order to avoid the risk of possible incompatibilities.

6.3 Shelf life

Before opening the container for the first time: 5 years.
After opening the container for the first time and without extracting the contrast medium: 24 hours.

6.4 Special precautions for storage

Store in the original package in order to protect from light and ionising radiation.
Do not store above 30 ºC.
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Ampoule: colorless, glass type I

Presentations
20 mL ampoules.

6.6 Special precautions for disposal and other handling

Inspection
Urografin is supplied ready for use as a clear, colourless to pale yellow solution.

Contrast media must not be used if there are significant changes in colour, if particles in suspension appear or if the container is defective.

Handling
The contrast medium must not be drawn into the syringe, nor must the bottle be connected to the infusion equipment, until immediately before the examination.

The rubber stopper must not be pierced more than once, to prevent large quantities of microparticles being transferred from the stopper to the solution. The use of needles with a long bevel and a maximum diameter of 18 G is recommended for piercing the stopper and drawing up the contrast medium (special withdrawal spikes with a side opening are particularly suitable).

For single use. Do not use the same container for several patients.

Contrast medium not used in an examination must be discarded.

Any unused medicinal product and all the materials that have been in contact with it should be disposed of in accordance with local requirements.

7. MANUFACTURED BY:

Berlimed S.A ,
Poligono Industrial Santa Rosa,
Calle Francisco Alonso 7,
28806 Alcala de Henares
Madrid
Spain

8. MARKETING AUTHORISATION HOLDER

1953

9. DATE OF REVISION OF THE TEXT

15/01/2026