SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

XENETIX 250

XENETIX 300

XENETIX 350

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

XENETIX 250

Per 100 mL of solution:

Iobitridol ..... 54.84 g (548.4 mg/ml)

corresponding quantity of iodine..... 25 g (250 mg/ml)

- Iodine content per mL: 250 mg
- Viscosity at 20 °C : 6 mPa.s
- Viscosity at 37 °C : 4 mPa.s
- Osmolality: 585 mOsm / kg H_2O
- Iodine quantity per 50 mL bottle: 12.5 g
- Iodine quantity per 100 mL bottle: 25 g
- Iodine quantity per 200 mL bottle: 50 g
- Iodine quantity per 500 mL bottle: 125 g

XENETIX 300

Per 100 mL of solution:

Iobitridol ..... 65.81 g (658.1 mg/mL)

corresponding quantity of iodine..... 30 g (300 mg/mL)

- Iodine content per mL: 300 mg
- Viscosity at 20°C: 11 mPa.s
- Viscosity at 37°C: 6 mPa.s
- Osmolality: 695 mOsm/kg H_2O
- Iodine quantity per 20 mL bottle: 6 g
- Iodine quantity per 50 mL bottle: 15 g
- Iodine quantity per 60 mL bottle: 18 g
- Iodine quantity per 75 mL bottle: 22.5 g
- Iodine quantity per 100 mL bottle: 30 g
- Iodine quantity per 150 mL bottle: 45 g
- Iodine quantity per 200 mL bottle: 60 g
- Iodine quantity per 500 mL bottle: 150 g

XENETIX 350

Per 100 mL of solution:

Iobitridol ..... 76.78 g (767.8 mg/mL)

corresponding quantity of iodine..... 35 g (350 mg/mL)

- Iodine content per mL: 350 mg
- Viscosity at 20°C: 21 mPa.s
- Viscosity at 37°C: 10 mPa.s
- Osmolality: 915 mOsm/kg H2O
- Iodine quantity per 20 mL bottle: 7 g
- Iodine quantity per 50 mL bottle: 17.5 g
- Iodine quantity per 60 mL bottle: 21 g
- Iodine quantity per 75 mL bottle: 26.25 g
- Iodine quantity per 100 mL bottle: 35 g
- Iodine quantity per 150 mL bottle: 52.5 g
- Iodine quantity per 200 mL bottle: 70 g
- Iodine quantity per 500 mL bottle: 175 g

Excipient with known effect: sodium (up to 3.5 mg per 100 mL).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

This medicinal product is for diagnostic use only.

Xenetix 250

Contrast agent to be used for adults and children undergoing:

- phlebography / venography/chest CT-scan
- intra-arterial digital subtraction angiography

Xenetix 300, Xenetix 350

Contrast agent to be used for adults and children undergoing:

- Intravenous urography
- brain or whole body CT scan
- intravenous digital subtraction angiography
- arteriography
- angiocardiography

4.2. Posology and method of administration

The doses must be adapted to the examination and the areas to be opacified, and to the subject's weight and renal function, particularly in children.

Recommended mean dosages:

Xenetix 250

Indications	Mean dose mL/kg	Total volume (min–max) mL
Phlebography/ Venography	2.6	150-220
Thoracic CT	2.0	95-170
Intra-arterial digital subtraction angiography	3.1	75-360

Xenetix 300

Indications	Mean dose mL/kg	Total volume (min-max) mL
Intravenous urography: • rapid intravenous injection • slow intravenous injection	 1.2 1.6	 50-100 100
• Computed tomography (CT) Head • Whole body	1.4 1.9	 20-100 20-150
Digital subtraction angiography by Intravenous route	1.7	40-270
Arteriography • Cerebral • Legs	 1.8 2.8	 42-210 85-300
Angiocardiography	1.1	70-125

Xenetix 350

Indications	Mean dose mL/kg	Total volume (min-max) mL
Intravenous urography	1.0	50-100
• Computed tomography (CT)Head • Whole-body	1.0 1. 8	40-100 90-180
Digital subtraction angiography by intravenous route	2.1	95-250
Arteriography • peripheral • legs	2.2 1.8	105-205 80-190

• abdominal	3.6	155-330
Angiocardiography • adults • children	 1.9 4.6	 65-270 10-130

Method of administration

XENETIX 250 mg is for use by intravascular route and as a single-dose for the 50, 10, 200 and 500 mL pack sizes.

XENETIX 300 mg is for use by intravascular route and as a single-dose for the 20, 50, 60, 100, 150, 200 and 500 mL pack sizes.

XENETIX 350 mg is for use by intravascular route and as a single-dose for the 20, 50, 60, 100, 150, 200 and 500 mL pack sizes.

The solution for injection should be visually inspected before use. Only clear solutions free from visible particles should be used.

Before any use, the rubber stopper should be disinfected with an antiseptic solution after removing the plastic protective disc.

The manufacturers' instructions for the medical devices used must be scrupulously followed.

Instructions for manual single-dose use:

The solution should be drawn up through the stopper using a syringe and sterile single-use needles. Take the amount of product necessary for the examination and inject it immediately. Any unused remaining contrast product should be discarded after the examination.

Instructions for use in multiple patients with containers of 100 mL and over:

The contrast product should be administered using an automatic injector approved for multiple use.

The vial stopper should only be pierced once.

The connection between the injector and the patient (patient line) should be changed after each patient.

The connection tubing and all disposable elements of the injection system must be discarded in accordance with the manufacturer's instructions of the injection device.

The manufacturer's instructions for the device must be followed.

24 hours after first opening, any unused contrast product present in the vial must be discarded.

4.3. Contraindications

- Hypersensitivity to iobitridol or to any of the excipients listed in section 6.1.
- History of a major immediate reaction or delayed cutaneous reaction (see section 4.4 and 4.8) to a XENETIX injection. In the absence of specific studies, iobitridol is not indicated for myelography.
- Manifest thyrotoxicosis.

4.4. Special warnings and precautions for use

- Regardless of the route of administration and dose, there is a risk of allergy.
- The risk of intolerance is not clear when it comes to medicinal products administered locally for the opacification of body cavities:

a) Administration by certain routes (articular, biliary, intrathecal, intrauterine, etc.) leads to fairly significant systemic passage: systemic effects may be observed.

b) Oral or rectal administration normally results in very limited systemic diffusion; if the digestive mucosa is normal, no more than 5% of the administered dose is found in the urine, the remainder being eliminated in the faeces. However, in the event of damage to the mucosa, absorption is increased; it is total and rapid in the event of perforation, with passage into the peritoneal cavity, and the drug is eliminated in the urine. The potential occurrence of dose-dependent systemic effects is therefore dependent on the condition of the digestive mucosa.

c) By contrast, immunoallergic mechanism is non-dose-dependent and may be observed in any patient, regardless of the route of administration.

The frequency and intensity of adverse reactions therefore differ between the following two groups:

- Medicinal products administered by the vascular route and certain local routes
- Medicinal products administered by the digestive route and absorbed very little under normal conditions.

4.4.1. General information applicable to all iodinated contrast agents

4.4.1.1 Warnings

In the absence of specific studies, myelography is not an indication for XENETIX.

All iodinated contrast agents may cause minor or major reactions that can be life-threatening. These reactions can occur immediately (within 60 minutes) or be delayed (within 7 days). They are often unpredictable.

The risk of major reactions means that emergency resuscitation equipment must be immediately available.

Several mechanisms have been discussed:

- Direct toxicity to the vascular endothelium and tissue proteins.
- Pharmacological action modifying the concentration of certain endogenous factors (histamine, complement components, inflammatory mediators) is more common with hyperosmolar products.
- XENETIX contrast agent-dependent immediate IgE allergy (anaphylaxis)
- Allergic reactions of cellular mechanism (delayed skin reactions)

Patients who have experienced a reaction with a previous administration of an iodinated contrast agent have an increased risk of a new reaction in the event of re-administration of the same or possibly another iodinated contrast agent and are therefore considered to be at risk.

Iodinated contrast agents and the thyroid (see also Section 4.4.1.2.5.)

Prior to administration of iodinated contrast agents, it is important to ensure that the patient is not due to undergo a scintigraphic or biological examination of the thyroid or receive radioactive iodine for therapeutic purposes.

In fact, the administration, regardless of the route of iodinated contrast agents interferes with the hormonal doses and iodine uptake by the thyroid or thyroid cancer metastases until normalization of the ioduria.

Other warnings

Extravasation is an uncommon complication (0.04% to 0.9%) of intravenous injections of contrast agents. This occurs more frequently with high osmolar products; most of the injuries are minor, however severe injuries such as skin ulceration, tissue necrosis, or compartment syndrome may occur with any iodinated contrast agent. The risk and/or severity factors are patient-related (poor or fragile vascular conditions), and technique-related (use of a syringe driver, large volume). It is important to identify these factors, optimise the injection site and technique accordingly, and monitor the injection prior to, during and after the injection of XENETIX.

4.4.1.2. Precautions for use

4.4.1.2.1. Intolerance to iodinated contrast agents:

Prior to the examination:

- Identify at-risk subjects by asking specific questions about their history.

Corticosteroids and H1 antihistamines have been suggested as premedication in patients with the highest risk of intolerance reactions (those with known intolerance to an iodinated contrast agent). However, they do not prevent severe or fatal anaphylactic shock. During the examination, the following measures must be in place:

- medical surveillance
- in situ venous access

After the examination:

- After contrast agent administration, the patient must remain under observation for at least 30 minutes, as the majority of serious adverse reactions occur within this time frame.
- The patient must be informed of the potential for delayed reactions (up to 7 days) (see Section 4.8 Undesirable effects).

Severe cutaneous adverse reactions

Severe cutaneous adverse reactions (SCARs), such as drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, Stevens-Johnson syndrome (SJS), Lyell's syndrome (toxic epidermal necrolysis or TEN) and acute generalised exanthematous postulosis (AGEP), potentially life-threatening, have been reported in patients to whom Xenetix had been administered (see section 4.8, Undesirable effects). When initiating the treatment, patients must be informed of the signs and symptoms and monitored closely to detect serious adverse skin reactions. Xenetix should be discontinued immediately if a severe hypersensitivity reaction is suspected. In the event of a severe cutaneous adverse reaction in a patient taking Xenetix, Xenetix should never be re-administered to this patient (see Section 4.3).

4.4.1.2.2. Renal failure

Iodinated contrast agents may cause temporary changes in renal function or worsen pre-existing renal failure. Preventive measures are as follows:

- Identify at-risk patients, i.e., those with dehydration, renal insufficiency, diabetes, severe heart failure, monoclonal gammopathy (multiple myeloma, Waldenstrom's disease), history of renal failure after contrast agent administration; children below the age of one year and elderly subjects with atheroma.
- Hydrate as necessary using an appropriate quantity of saline solution.
- Avoid combinations with nephrotoxic medicinal products. If this combination is necessary, increase biological renal monitoring. The medicinal products concerned include aminosides, organoplatinum compounds, high dose methotrexate, pentamidine, foscarnet and certain antivirals (aciclovir, ganciclovir, valaciclovir, adefovir, cidofovir, tenofovir), vancomycin, amphotericin B, immunosuppressants such as ciclosporin, or tacrolimus and ifosfamide.
- Allow at least 48 hours between two radiological examinations with contrast agent injections or delay further examinations until renal function returns to baseline.
- Prevent lactic acidosis in diabetics treated with metformin, by monitoring serum creatinine levels. Normal renal function: administration of metformin is discontinued when the contrast agent is administered, for a period of at least 48 hours or until normal renal function is restored. Abnormal renal function: metformin is contraindicated. In an emergency: if the examination cannot be avoided, precautions must be taken: discontinuation of metformin, hydration, renal function monitoring and monitoring for signs of lactic acidosis.

Haemodialysis patients can receive iodinated contrast agents, as these products are dialysable. Consult with the haemodialysis department prior to administration.

4.4.1.2.3. Hepatic failure

Particular attention is required when a patient presents with both hepatic and renal failure since, in this situation, the risk for retention of the contrast agent is increased.

Care should be taken in patients with renal or hepatic failure, diabetes or sickle cell disease.

Adequate hydration must be ensured in all patients before and after contrast agent administration and particularly in patients with renal failure or diabetes where it is important to maintain hydration to minimise deterioration in renal function.

4.4.1.2.4. Asthma

It is recommended that asthma be brought under control before injection of an iodinated contrast agent.

Due to an increased risk of bronchospasm, special caution must be taken in patients who have suffered an asthma attack within 8 days prior to the examination.

4.4.1.2.5. Disturbed thyroid function

Thyroid function tests indicative of hypothyroidism or transient thyroid suppression have been reported following iodinated contrast media administration to adult and paediatric patients, including infants. Some patients were treated for hypothyroidism. See also section on Paediatric population.

Paediatric population:

Thyroid Dysfunction in Pediatric Patients 0 to 3 Years of Age

Thyroid dysfunction characterized by hypothyroidism or transient thyroid suppression has been reported after both single exposure and multiple exposures to iodinated contrast media (ICM) in pediatric patients 0 to 3 years of age.

Younger age, very low birth weight, prematurity, underlying medical conditions affecting thyroid function, admission to neonatal or pediatric intensive care units, and congenital cardiac conditions are associated with an increased risk of hypothyroidism after ICM exposure. Pediatric patients with congenital cardiac conditions may be at the greatest risk given that they often require high doses of contrast during invasive cardiac procedures.

An underactive thyroid during early life may be harmful for cognitive and neurological development and may require thyroid hormone replacement therapy. After exposure to ICM, individualize thyroid function monitoring based on underlying risk factors, especially in term and preterm neonates.

4.4.1.2.6. Cardiovascular diseases (see Section 4.8 Undesirable effects)

In patients with cardiovascular disease (such as early or patent heart failure, coronaropathy, arterial pulmonary hypertension, valvular heart disease, cardiac arrhythmias), the risk of cardiovascular reactions is increased after administration of an iodinated contrast agent. Intravascularinjection of the iodinated contrast agent may cause lung oedema in patients with manifest or incipient heart failure, whereas administration in pulmonary arterial hypertension and heart valve disease may result in marked changes in haemodynamics. The frequency and degree of severity appear to be related to the severity of the cardiac disorders. In case of severe and chronic hypertension, the risk of renal injury secondary to the administration of the contrast agent and also due to the catheterization itself may be increased. Careful evaluation of the benefit/risk balance is necessary in these patients.

4.4.1.2.7. Central nervous system disorders

The benefit/risk balance must be evaluated in each case:

- Due to the risk of aggravation of neurological symptoms in patients with transient ischaemic attack, acute cerebral infarction, recent intracranial haemorrhage, cerebral oedema, or idiopathic or secondary (tumour, scar) epilepsy.
- In the case of intra-arterial use in alcoholics (acute or chronic alcoholism) and in people addicted to other substances.
- Encephalopathy has been reported with the use of iobitridol (see section 4.8). Contrast- induced encephalopathy may manifest with symptoms and signs of neurological dysfunction such as headache, visual disturbance, cortical blindness, confusion, seizures, loss of coordination, hemiparesis, aphasia, unconsciousness,

coma, and cerebral oedema. Symptoms usually occur within minutes to hours after administration of iobitridol and generally resolve within days.

- Factors which increase blood-brain barrier permeability facilitate the passage of the contrast medium into cerebral tissue, which can lead to central nervous system reactions, e.g. encephalopathy. If contrast encephalopathy is suspected, appropriate medical management should be initiated and iobitridol should not be readministered.

4.4.1.2.8. Phaeochromocytoma

Patients with phaeochromocytoma may develop a hypertensive crisis after intravascular administration of a contrast agent and require appropriate management prior to the examination.

4.4.1.2.9. Myasthenia gravis

Administration of a contrast agent may worsen the symptoms of myasthenia gravis.

4.4.1.2.10. Increased adverse reactions

Undesirable effects linked to iodinated contrast agent administration may be intensified in patients showing pronounced agitation, anxiety or pain. Appropriate management may be necessary, up to and including sedation.

4.4.1.2.11. Excipients

This medicinal product contains sodium. The sodium concentration is less than 1 mmol sodium per 100 mL i.e., it is essentially “sodium-free”.

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

4.5.1. Medicinal products

+ Metformin in diabetics (see Section 4.4 Precautions for use — Renal failure).

+ Radiopharmaceuticals (see Section 4.4 Warnings)

Iodinated contrast agents disrupt radioactive iodine uptake by thyroid tissue for several weeks, which may lead to impaired uptake in thyroid scintigraphy and decreased efficacy of iodine 131 treatment.
In patients due to undergo renal scintigraphy with injection of a radiopharmaceutical secreted by the renal tubules, it is preferable to carry out the scintigraphy before iodinated contrast agent injection.

+ Beta blockers

Vasoactive substances, angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists.
These medicinal products lead to a decrease in the efficacy of the cardiovascular compensatory mechanisms for blood pressure disorders: the doctor must be informed before the injection of iodinated contrast agent and have resuscitation equipment to hand available nearby.

+ Diuretics

Due to the risk of diuretic-induced dehydration, prior rehydration with fluids and electrolytes is necessary to limit the risk of acute renal failure.

+ Interleukin 2

There is a risk of increased reaction to contrast agents following recent treatment with interleukin 2 (intravenous route): rash or, more rarely, hypotension, oliguria, and even renal failure.

4.5.2. Other forms of interaction

High concentrations of iodinated contrast agent in plasma and urine may interfere with *in vitro* measurements of bilirubin, proteins and inorganic substances (iron, copper, calcium and phosphate); it is recommended not to perform these assays within 24 hours of the examination.

4.6. Fertility, pregnancy and lactation

Pregnancy

There are no or few data (fewer than 300 pregnancy outcomes) on the use of iobitridol in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of XENETIX during pregnancy.
Temporary iodine overload following administration of the product to the mother may lead to foetal dysthyroidism if the examination takes place after 14 weeks of pregnancy. However, in view of this reversibility of the effect and the expected benefit to the mother, isolated administration of an iodinated contrast agent is justifiable if the indication for the radiological examination in a pregnant woman has been carefully evaluated.

In neonates exposed to iobitridol in utero, it is recommended to monitor thyroid function (see section 4.4).

Lactation

Iodinated contrast agents are excreted in breast milk in very small amounts. Consequently, isolated administration to the mother involves a minor risk of adverse reactions in the infant. It is preferable to suspend breastfeeding for 24 hours after administration of the iodinated contrast agent.

Fertility

A study conducted on rats does not indicate any effects on reproductive function.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Undesirable effects

During clinical studies on 905 patients, 11% of patients experienced an adverse reaction related to administration of XENETIX (apart from feeling of warmth), the most common being pain, injection site pain, bad taste in the mouth and nausea.

Adverse reactions related to the use of XENETIX are generally mild to moderate, and transient.

The adverse reactions most commonly reported during administration of XENETIX since its marketing are a feeling of warmth, pain and oedema at the injection site.

Hypersensitivity reactions are usually immediate (during the injection or over the hour following the start of the injection) or sometimes delayed (one hour to several days after the injection), and then appear in the form of cutaneous adverse reactions.

Immediate reactions comprise one or more, successive or concomitant effects, usually including skin reactions, respiratory and/or cardiovascular disorders, which may be the first signs of shock, and can be fatal in rare cases.

Severe cardiac arrhythmias, including ventricular fibrillation have been very rarely reported in heart disease patients, and outside the context of a hypersensitivity reaction (see Section 4.4 Precaution for use).

The adverse reactions are listed in the table below by SOC (System Organ Class) and by frequency with the following guidelines: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10 000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data). The frequencies presented are from the data of an observational study on 352,255 patients.

System Organ Class	**Frequency: adverse reaction**
Immune system disorders	Rare: hypersensitivity Very rare: anaphylactic shock, anaphylactoid reaction, anaphylactic reaction
Endocrine disorders	Very rare: thyroid disorders Not known: transient neonatal hypothyroidism, hypothyroidism***
Nervous system disorders	Rare: presyncope (vasovagal reaction), tremor*, paresthesia* Very rare: coma*, convulsions*, confusion*, visual disorders*, amnesia*, photophobia*, transient blindness*, drowsiness *, agitation*, headache Not known: dizziness**, Contrast encephalopathy****
Ear and labyrinth disorders	Rare: dizziness Very rare: hearing disorders
Cardiac disorders	Rare: tachycardia, bradycardia

	Very rare: cardiac arrest, myocardial infarction (more frequent after intracoronary injection), arrhythmia, ventricular fibrillation, angina pectoris, Torsades de Pointes, coronary arteriospasm
Vascular disorders	Rare: hypotension (low blood pressure), hypertension Very rare: circulatory collapse Not known: cyanosis**
Respiratory, thoracic and mediastinal disorders	Rare: dyspnoea, cough, throat tightness, sneezing Very rare: respiratory arrest, pulmonary oedema, bronchospasm, laryngospasm, laryngeal oedema
Gastrointestinal disorders	Uncommon: nausea Rare: vomiting Very rare: abdominal pain
Skin and subcutaneous tissue disorders	Rare: angioneurotic oedema, urticaria (localised or extensive), erythema, pruritus Very rare: Acute Generalized Exanthematous Pustulosis, Stevens-Johnson syndrome, toxic epidermal necrolysis, eczema, maculopapular rash (all as delayed hypersensitivity reactions) (see Section 4.4) Not known: systemic drug hypersensitivity syndrome with eosinophilia (DRESS) and systemic symptoms (see Section 4.4).
Renal and urinary tract disorders	Very rare: acute renal failure, anuria
General disorders and administration site conditions	Uncommon: feeling of warmth Rare: facial oedema, malaise, chills, injection site pain Very rare: injection site necrosis following extravasation, injection site oedema, injection site inflammation following extravasation
Investigations	Very rare: serum creatinine increase

*Examinations during which the iodinated contrast agent concentration in arterial blood is high.

**Effect most often reported in the context of a hypersensitivity reaction.

***Transient hypothyroidism has been reported in younger children after exposure to iodine-based contrast agents (see Section 4.4)

****Contrast encephalopathy may manifest with symptoms and signs described in section 4.4

As described in Section 4.4, compartment syndrome may be observed after extravasation.

The following adverse reactions were reported for other water-soluble iodinated contrast agents:

System Organ Class	Frequency: adverse reaction
Nervous system disorders	Paralysis, paresis, speech disorders
Psychiatric disorders	Hallucinations
Gastrointestinal disorders	Acute pancreatitis (following ERP), abdominal pain, diarrhoea, parotid gland enlargement, excessive saliva secretion, bad taste in the mouth
Skin and subcutaneous tissue disorders	Erythema multiforme
Vascular disorders	Thrombophlebitis
Investigations	Abnormal electroencephalogram, serum amylase increase

Cardiovascular collapse of variable severity may occur immediately with no warning signs or may complicate the cardiovascular symptoms mentioned in the above table.

Abdominal pain associated with diarrhoea, not reported for XENETIX, is linked mainly to administration via the oral or rectal route.

Local pain and oedema may occur at the injection site without extravasation of the injected product and are benign and transient.

During intra-arterial administration, the sensation of injection site pain depends on the osmolality of the product injected.

Paediatric population

The undesirable effects of Xenetix in children are similar to the reactions reported in adults. Their frequency cannot be estimated from the available data.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/ and emailed to the Registration Holder's Patient Safety Unit at:
drugsafety@neopharmgroup.com

4.9. Overdose

In the event of very high doses, fluid and electrolyte loss must be compensated by appropriate rehydration. Renal function must be monitored for at least three days. Haemodialysis may be carried out if necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: IODINATED CONTRAST AGENT; ATC code: V08AB11

XENETIX 250 is a urographic and angiographic water-soluble nonionic contrast agent with an osmolality of 585 mOsm/kg.

XENETIX 300 is a urographic and angiographic water-soluble nonionic contrast agent with an osmolality of 695 mOsm/kg.

XENETIX 350 is a urographic and angiographic water-soluble nonionic contrast agent with an osmolality of 915 mOsm/kg.

The iobitridol molecule exhibits a stable and balanced hydrophilic character.
The evaluation of overall safety with respect to the hemodynamic, cardiovascular, bronchopulmonary, renal, neurological, vascular and rheological systems has shown that the safety profile of iobitridol is the same as that of other non-ionic water-soluble tri-iodinated lowosmolality contrast media, particularly in cardiovascular or neurological terms, or comparable to that of a reference solution.

5.2. Pharmacokinetic properties

Injected via the vascular route, iobitridol is distributed in the intravascular compartment and the interstitial space. In humans, the elimination half-life is 1.8 hours, the distribution volume is 200 mL/kg and the total clearance is 93 mL/min on average. Binding to plasma proteins is low (< 2%). It is mainly eliminated by the kidneys (glomerular filtration without reabsorption or tubular secretion at) in unchanged form.
The osmotic diuresis induced by XENETIX is related to the osmolality and the volume injected.

In the event of renal insufficiency, elimination is mainly by biliary route. The substance is dialysable.

5.3. Preclinical safety data

Toxicology studies using the intravenous route did not reveal any adverse effects except under conditions that differ considerably from those used clinically (doses, repetitions). In the case of iobitridol, as with all tri-iodinated, non-ionic and water-soluble contrast agents administered in single large-volume doses (25- 50 mL/kg), these effects manifest as transient signs of hypothermia, respiratory depression or dose-dependent histological signs in the target organs (liver, kidneys), such as hepatocellular vacuolisation, andtubular ectasia.
Repeated dose administration in dogs for 28 days at high doses (8 ml/kg) resulted in granular and vacuolar degeneration, which was reversible after discontinuation of treatment.
Local irritation may be observed in the event of perivascular infiltration.

The substance was not found to be mutagenic under the test conditions used. Animal studies have shown no toxic effects on fertility, reproductive performance and embryofoetal development.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Trometamol hydrochloride, trometamol, Sodium calcium edetate, hydrochloric acid or sodium hydroxide, water for injection.

6.2. Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3. Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4. Special precautions for storage

Store protected from light at a temperature below 30°C.

6.5. Nature and content of container

XENETIX 250
50 mL, 100 mL, 200 mL or 500 mL glass bottles with chlorobutyl rubber stoppers.

XENETIX 300, XENETIX 350
20 mL, 50 mL, 60 mL, 100 mL, 150 mL, 200 mL or 500 mL glass bottles with chlorobutyl rubber stoppers.

Not all pack sizes may be marketed.

6.6. Instructions for disposal and handling

No special requirements for disposal.

7. MANUFACTURER

Lab. Guerbet, France.
BP 57400, F-95943 ROISSY CdG, CEDEX, France.

8. MARKETING AUTHORISATION NUMBERS :

XENETIX 250 , 105-07-28746
XENETIX 300 , 105-07-28747
XENETIX 350 , 105-07-28748

9. REGISTRATION HOLDER

Promedico Ltd.
Hashiloach 6, POB 3340, Petach-Tikva, Israel.

Revised in August 2025.

Xenetix SPC vr 03A