SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Gastrografin 370 mg Iodine/ml oral and rectal solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

100 ml of oral and rectal solution contain 10 g of sodium amidotrizoate and 66 g of meglumine amidotrizoate (sodium diatrizoate and meglumine diatrizoate) in aqueous solution, equivalent to 37 g of iodine.

Excipients with known effect: 100 ml of oral and rectal solution contain 374.00 mg of sodium (see section 4.4).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral and rectal solution.
Solution almost colourless to yellowish.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic and therapeutic use.

Diagnostic use

Gastrografin is a contrast medium for the radiological examination of the gastrointestinal tract. It is mainly indicated when the use of barium sulphate is unsatisfactory, undesirable or contraindicated. These indications include:

- Early diagnosis of a perforation or anastomotic defect, radiologically undetectable, in the oesophagus and/or gastrointestinal tract, as well as acute perforations (peptic ulcer, diverticulum) and after gastric or intestinal resection (danger of perforation or leakage).
- Suspicion of partial or complete stenosis.
- Acute hemorrhage.
- Other acute conditions likely to require surgery such as small bowel obstruction and colon obstruction.
- Megacolon.
- Visualization of a foreign body or tumor prior to endoscopy.
- Visualization of a gastrointestinal fistula.
- Gastrografin is used with barium sulfate to accelerate gastrointestinal transit. In addition, Gastrografin can be used for the same indications as barium sulfate with the exception of visualization of mucosal conditions. Given the insufficient coating obtained with Gastrografin, barium sulfate should be used for single or double contrast techniques.
- Gastrografin is used for computed tomography (CT) to provide opacification of the entire upper gastrointestinal tract (esophagus, stomach, or small intestine) and lower gastrointestinal tract (large intestine and rectum) as a diagnostic aid for pathologies in these organs.

Therapeutic use
Treatment of uncomplicated meconial ileus.

4.2 Posology and method of administration

Gastrografin should be used only under medical supervision and should be administered by trained healthcare professionals with technical experience in performing radiological techniques with meglumine amidotrizoate.

Posology

The dose may vary depending on the age of the patient, the suspected/known pathology, the diagnostic technique to be performed, the route of administration of the contrast and the region studied.

X-ray examination

Target organ	Route of administration	Dosage/Preparation/Dilution	Concentration	Age
Esophagus	Oral	15-30 ml diluted with 3 times its volume of water	25% solution	Newborns and Infants
		15-30 ml diluted with 2 times its volume of water	33% solution	Children up to 10 years
		60 ml Undiluted	Undiluted	Adults and children from 10 years old
Stomach	Oral	15-30 ml diluted with 3 times its volume of water	25% solution	Newborns and Infants
		15-30 ml diluted with 2 times its volume of water	33% solution	Children up to 10 years
		60 ml Undiluted	Undiluted	Adults and children from 10 years old
Dynamic examination of the gastrointestinal tract	Oral	15-30 ml diluted with 3 times its volume of water	25% solution	Newborns and Infants
		15-30 ml diluted with 2 times its volume of water	33% solution	Children up to 10 years
		Maximum 100 ml Undiluted	Undiluted	Adults and children from 10 years old
Large intestin	Rectal	Up to 500 ml dilution Diluted with 5 times its volume of water	25% solution	Newborns and Infants
		Up to 500 ml dilution Diluted with 4- 5 times its volume of water	33% solution	Children up to 10 years
		Up to 500 ml dilution Diluted with 3-4 times its volume of water	Undiluted	Adults and children from 10

				years old

Tomografía computarizada (TC)

Depending on the area to be studied of the gastrointestinal tract, the oral or rectal route is used. The exploration can be performed after administration of 0.5-1.5 liters of Gastrografin solution at approximately 3% concentration (30 ml of Gastrografin in 1 liter of water).

Target organ	**Route of administration**	**Dosage/Preparation/Dilution**	**Concentration**	**Dosage**
Esophagus	Oral	9 to 15 ml Gastrografin diluted with 0.3 to 0.5 litres of water	3% solution	Patients should drink 300 to 500 ml of this solution.
Stomach	Oral	9 to 15 ml Gastrografin diluted with 0.3 to 0.5 litres of water	3% solution	Patients should drink 300 to 500 ml of this solution.
Small intestine	Oral	9 to 15 ml Gastrografin diluted with 0.3 to 0.5 litres of water	3% solution	Patients should drink 300 to 500 ml of this solution.
Distal GI Tract / Complete Intestine	Oral*	30 ml Gastrografin diluted with 1 litre of water, or 45 ml Gastrografin in 1.5 litres of water	3% solution	Up to 1500 ml of prepared solution can be administered
Large intestine/ Rectum	Rectal	15 ml of Gastrografin in 0.5 litres of water	3% solution	Up to 500 ml of prepared solution can be administered

*Oral/rectal administration may be combined.

In the case of pediatrics, volumes must be adjusted. In the table below are specified the maximum volumes to administer from the dilution of Gastrografin with water.

	Oral		**Enema/rectal**	
Age	**Gastrografin**	**Water**	**Gastrografin**	**Water**
6 months	3 ml	100 ml	1 ml	50 ml
2 years	6 ml	200 ml	2 ml	100 ml
5 years	9 ml	300 ml	3 ml	150 ml
10 years	15 ml	500 ml	4 ml	200 ml
> 10 years	15 – 30 ml	500 – 1000 ml	500 ml	1500 – 2000 ml

Treatment of uncomplicated meconial ileus

Rectal dose Gastrografin may be administered to newborn infants in the form of an enema for the non-surgical treatment of uncomplicated meconial ileus. The high osmotic pressure of the contrast medium is exploited: the adjacent tissue is forced to release considerable amounts of fluid, which then flows into the intestines and dissolves the thick meconium.

Gastrografin should be diluted 3-4 times its volume in water. Normally a dosage of 2 to 5 ml of the diluted solution is required but in other cases more is required. The solution should be administered under fluoroscopic control.

Gastrografin associated with barium sulfate

Age	Gastrografin	Barium sulfate
From 0 to 5 years	2 – 5 ml	100 ml
From 5 to 10 years	10 ml	100 ml
From 11 to 18 years	30 ml	Usual dose according to the organ to be studied
Adults	30 ml	Usual dose according to the organ to be studied

The proportion of Gastrografin may be increased further if necessary (in cases of pyloric spasm or pyloric stenosis).

Cachectic and elderly patients

X-ray examination: The adult dose diluted with an equal volume of water is recommended.

Method of administration

For the early diagnosis of a perforation or anastomosis in the esophagus and/or gastrointestinal tract, the patient should ingest up to 100 ml of Gastrografin. If the suspicious lesion cannot be clearly identified by X-ray, the following test may be used as a diagnostic aid. After 30-60 minutes (later, if the lesion is suspected to be located in the distal bowel), a urine sample should be taken, mixing 5 ml with 5 drops of concentrated hydrochloric acid. Contrast that has undergone renal excretion will appear within 2 hours as a typical crystal formation in the precipitate.

For the treatment of uncomplicated meconial ileus, an irrigator and a soft rubber catheter are recommended. The return of the contrast agent is prevented by means of an adhesive tape with which the buttocks are squeezed. A Foley catheter should not be used. The introduction will be done slowly and under constant radiological control. The application is considered finished as soon as Gastrografin passes into the small intestine. In order to be able to compensate for excessive fluid loss, an intravenous plasma infusion must be prepared before application begins. If, one hour after the catheter has been removed, the contrast medium has not been evacuated again, it must be ensured radiologically that the intestine has not expanded excessively. If indications requiring immediate operation such as intestinal volvulus, gangrene, perforation, peritonitis and atresia are required, this method should not be used.

For patient preparation, see section 4.4.

Image Acquisition
The time required for gastric emptying is the same as for barium sulfate, while the time required for filling the intestine is less. When Gastrografin alone is used, the contrast medium usually reaches the rectum after 2 hours, while the association Gastrografin/Barium Sulfate may take up to 3 hours and, in isolated cases, even longer.

The most favorable time to perform radiological exposures of the colon is indicated by the sensation of need to defecate experienced by all patients.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in Section 6.1.
Hypersensitivity to iodine contrast media.
Clinical hyperthyroidism.

Gastrografin should not be administered WITHOUT DILUTION in patients with low plasma volume, such as neonates, infants, children under 10 years of age and dehydrated patients.
Gastrografin should not be administered orally in patients at risk of aspiration or bronchoesophageal fistula.

4.4 Special warnings and precautions for use

Due to its high osmotic pressure and absorption in the intestine, it is contraindicated to administer Gastrografin WITHOUT DILUTION to newborns, infants, children under 10 years of age and dehydrated patients (see section 4.3).

Gastrografin should not be administered orally in patients at risk of aspiration or bronchoesophageal fistula, as hyperosmolarity can cause acute pulmonary edema, chemical pneumonia, respiratory collapse and death (see section 4.3).

Pre-cleansing the bowel improves diagnostic reliability.

- Hydration and hydroelectrolytic balance

Adequate hydration of the patient should be ensured before and after administration of the contrast especially in infants, young children and elderly patients.

Alterations in hydration and electrolyte balance should be corrected prior to administration of Gastrografin solution. Adequate hydration and electrolyte balance should be established and maintained in all patients, as Gastrografin hyperosmolarity may cause dehydration and electrolyte imbalance, especially in patients with multiple myeloma, diabetes mellitus, renal failure, polyuria, oligouria, hyperuricemia as well as in neonates, infants, young children and elderly patients. In dehydrated hypovolemic patients the hydroelectrolyte imbalance is compensated with fluid therapy.

To compensate for possible clinically relevant electrolyte losses during rectal administration, when necessary, Ringer lactate solution should be prepared for administration by intravenous infusion.

- Anxiety

Excitement, anxiety and intense pain may increase the risk of adverse reactions or intensify reactions related to contrast media. These patients may be given a sedative.

- Hypersensitivity Reactions

A risk-benefit assessment is necessary, especially in those patients with known hypersensitivity to Gastrografin or any of its components due to an increased risk of hypersensitivity/anaphilactic reactions.

As with other iodine contrast media, Gastrografin may be associated with hypersensitivity reactions or other idiosyncratic reactions, characterized by cardiovascular, respiratory or skin symptoms and extending to severe reactions including shock (see section 4.8).

After administration of the contrast medium the patient should be observed for at least 30 minutes, as most adverse reactions occur during this time. Delayed reactions (after hours or days) may occur (see section 4.8).

Allergic reactions cannot be foreseen individually due to their irregular appearance.

Before administering any contrast media, the patient should be questioned about possible allergic history (e.g., shellfish allergy, hay fever/seasonal acute allergic rhinitis, kidney beans), sensitivity to iodine or radiological contrast media, and bronchial asthma, as the reported incidence of adverse reactions to contrast media is higher in patients with these pathologies.

Patients with bronchial asthma have an elevated risk of suffering bronchospasm or a hypersensitivity reaction.

Nausea, vomiting, mild angioedema, conjunctivitis, cough, itching, rhinitis, sneezing and hives have been reported. These reactions, which may occur regardless of the amount administered and the route of administration, may be the first signs of shock.

If hypersensitivity reactions occur (see section 4.8), administration of the contrast medium should be immediately discontinued and, if necessary, specific intravenous treatment initiated. In order to be able to act immediately in an emergency, appropriate drugs, an endotracheal tube and an artificial respirator should be readily available.

- Thyroid dysfunction

It is necessary to perform a risk-benefit balance assessment in patients with suspected clinical hyperthyroidism, patients with subclinical hyperthyroidism or known or suspected goiter because, like any iodine contrast medium, Gastrografin can interfere with thyroid function, aggravate or induce hyperthyroidism and thyrotoxic crisis.

If iodinated contrast media is planned for these at-risk patient groups, thyroid function should be assessed prior to exploration and hyperthyroidism should be excluded.

In newborn infants, especially preterm infants, who have been exposed to Gastrografin, through the mother during pregnancy or during the neonatal period, thyroid function monitoring is recommended, as exposure to an excessive dose of iodine may cause hypothyroidism and may require treatment.

- Severe cardiovascular pathology

Patients with cardiovascular alterations, especially those with heart failure and coronary artery disease, are more susceptible to severe hypersensitivity/anaphylaxis or even fatal reactions.
If these patients experience hypersensitivity reactions while taking beta-blockers, they may be refractory to beta-agonist treatment (see section 4.5).

- Very deteriorated state of health

The need for exploration must be carefully assessed.

- Combined use with barium sulphate

With regard to the use of Gastrografin in combination with barium sulfate, attention should be paid to contraindications, precautions and possible relevant side effects of barium sulfate.

- Gastrointestinal risks

In case of prolonged retention of Gastrografin in the gastrointestinal tract (e.g. obstruction, stasis), tissue damage, bleeding, necrosis and intestinal perforation may result.

- Interference with diagnostic tests

Iodized contrast media can interfere with thyroid function studies, as the thyroid's ability to fix iodine may be reduced for several weeks. The results of PBI and radioactive iodine uptake studies, which depend on the estimation of iodine, cannot accurately reflect thyroid function until 16 days after the administration of iodinated contrast media.

- Excipient Warnings

Gastrografin for oral use
This drug contains 224.40 to 374.00 mg of sodium per dose (60 - 100 ml), equivalent to 11.2-18.7% of the maximum daily intake of 2 g of sodium recommended by WHO for an adult.

Gastrografin in combination with barium sulphate
This drug contains 112.20 mg of sodium per dose (30 ml), equivalent to 5.6% of the maximum daily intake of 2 g of sodium recommended by WHO for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

Beta-blockers
Hypersensitivity reactions may be aggravated in patients being treated with beta-blockers, particularly in patients with bronchial asthma. In addition, it should be noted that beta-blocker patients may be refractory to standard treatment of hypersensitivity reactions with beta-receptor agonists.

Interleukin-2
The prevalence of delayed reactions to contrast media (e.g., fever, rash, flu-like symptoms, joint pain, and itching) is higher in patients treated with interleukin-2.

Diuretics
Due to the risk of dehydration caused by diuretics, saline rehydration is necessary before iodine contrast dye is administered to minimize the risk of acute renal failure.
Interference with diagnostic tests (see section 4.4.). Radiopharmaceuticals

Radiopharmaceuticals
The uptake capacity of radiopharmaceuticals, used in the diagnosis and treatment of thyroid pathologies, may decrease for several weeks after the administration of iodine contrast media.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data regarding the use of sodium amidotrizoate/meglumine in pregnant women. Animal studies do not suggest direct or indirect adverse effects in terms of reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Gastrografin during pregnancy.

The risk-benefit ratio should be assessed before iodine contrast is administered taking into account the sensitivity of the fetal thyroid to iodine, as acute overloading of iodine after iodine contrast is administered to the mother can lead to fetal thyroid dysfunction.

Breastfeeding

It is not known whether sodium amidotrizoate/meglumine or its metabolites pass into breast milk. After intravascular administration, salts of diatrizoic acid are excreted in breast milk.

Enteral absorption of Gastrografin is low. The decision on whether to continue or discontinue lactation or whether to continue or discontinue treatment with Gastrografin should be made taking into account the benefit of lactation to the infant and the benefit of administration of Gastrografin to the mother.

4.7 Effects on ability to drive and use machines

No studies have been conducted on the ability to drive or use machines.

4.8 Undesirable effects

Frequency of adverse reactions from spontaneous communications and bibliography:

Adverse reactions related to the use of iodized contrast media are generally mild to moderate in intensity and transient in nature. However, severe and life-threatening reactions and deaths have been reported.

The most frequently reported adverse reactions are vomiting, nausea and diarrhoea.

The following table lists the frequency and classification of adverse reactions by organs and systems.

System organ class	Common (≥1/100 to <1/10)	Uncommon (≥1/10000 to <1/1000)	Not known
Immune system disorders		Hypersensitivity / anaphylactoid reaction Anaphylactoid shock	
Endocrine disorders		Thyrotoxic crisis in patients with clinical hyperthyroidism	Hypothyroidism
Metabolism and nutrition disorders		Fluid and electrolyte imbalance	

Nervous system disorders		Disturbances in consciousness, headache, dizziness	
Cardiac disorders		Cardiac arrest, tachycardia	
Vascular disorders		Shock, Hypotension	
Respiratory, thoracic and mediastinal disorders		Bronchospasm, dyspnoea, medication aspiration, pulmonary oedema following aspiration, aspiration pneumonia	
Gastrointestinal disorders	Vomiting, Nausea, Diarrhea	Intestinal perforation, abdominal pain, Blistering of the oral mucosa	
Skin and subcutaneous tissue disorders		Toxic epidermal necrolysis, urticaria, rash, pruritus, erythema, oedema face	
General disorders and administration site conditions		Pyrexia, sweating	

Immune system disorders, anaphylactoid reaction / hypersensitivity
Systemic hypersensitivity reactions are rare, generally mild, and manifest mainly as skin reactions. It should be noted that these reactions may appear immediately after administration until a few days later.
However, the possibility of a severe hypersensitivity reaction cannot be completely excluded (see section 4.4).

Gastrointestinal disorders
The hypertonic solution of Gastrografin, both diluted and undiluted, can cause diarrhea, but it stops as soon as the intestine empties. Existing enteritis or colitis may be temporarily exacerbated. In case of intestinal obstruction, rectal application of Gastrografin may produce erosions, bleeding and intestinal necrosis.

Notification 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. Healthcare professionals are asked to report any suspected adverse reactions via the Spanish Pharmacovigilance System for Medicines for Human Use: https://www.notificaram.es

4.9 Overdose

The alterations of the hydroelectrolytic equilibrium produced by overdosing must be corrected by parenteral means.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: contrast media for X-rays, iodine, high osmolarity, hydrosoluble and nephropic, ATC code: V08A A.

The compound that provides the contrast is a salt of amido(dia-)trizalic acid, in which the iodine that absorbs the X-rays is present through stable chemical bonds. The physical-chemical characteristics of Gastrografin are as follows:

Iodine concentration (mg/ml)	370
Osmolality (osm/kg H2O) at 37ºC	2.15
Viscosity (mPa-s) at 20ºC at 37ºC	 18.5 8.9
Density (g/ml) at 20ºC at 37ºC	 1.427 1.417
pH	6.0 – 7.0

For the non-surgical treatment of uncomplicated meconial ileus, the high osmotic pressure of the contrast medium administered in the form of an enema is used. The surrounding tissue is forced to release considerable amounts of fluid, which flows through the intestine and dissolves the hardened meconium.

5.2 Pharmacokinetic properties

Absorption of amidotivoic acid after oral administration is only 3%. In some patients, even in the absence of perforation, absorption is greater as demonstrated by the opacification of the renal calyxes and ureters.

In case of perforation of the gastrointestinal tract, Gastrografin penetrates into the abdominal cavity or surrounding tissue, where it is absorbed and finally excreted via the kidney.

5.3 Preclinical safety data

Data from non-clinical studies do not show special risks to humans according to conventional studies of systemic toxicity, genotoxicity, reproductive toxicity, local tolerance and potential contact sensitization.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate
Sodium saccharin
Polysorbate 80 (E433)

Star anise essence
Sodium hydroxide
Purified water

6.2 Incompatibilities

This medication should not be mixed with other medications except those listed in Section 6.6.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 30 °C. Protect from light and X-rays

6.5 Nature and contents of container

Screw bottles of 100 ml, amber, glass type III.
Pilfer proof closure: high density polyethylene, PE-HD, colored, with sealing disk, low density polyethylene, PE-LD, natural

6.6 Special precautions for disposal <and other handling>

In case of crystallization of the contrast medium due to storage in refrigerated places, it can be dissolved again by agitation and gentle heating to body temperature. This alteration is not detrimental to the effectiveness and stability of the preparation.

Contrast medium not used within 24 hours after the first opening of the container must be discarded.

Disposal of the unused medicine and all materials that have been in contact with it should be carried out in accordance with local regulations.

For indications on how to perform dilutions and the possibility of using Gastrografin in combination with barium sulphate, see section 4.2.

7. MANUFACTURED BY:

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