GASTROGRAFIN
Gastrografin Solution

Composition
100 ml Gastrografin contain 10 g sodium amidotrizoate and 66 g meglumine amidotrizoate (sodium diatrizoate and meglumine diatrizoate) in aqueous solution.

Pharmacodynamic/Pharmacokinetic properties

Pharmacodynamic properties
The contrast-giving substance of Gastrografin is a salt of the amido(dia-)trizoic acid in which the X-ray absorbing iodine is present in stable chemical bond. The physico-chemical characteristics of Gastrografin listed below are:

Iodine concentration (mg/ml)	370
Osmolality (osm/kg H_2O) at 37 °C	2.15
Viscosity (mPa·s) at 20 °C at 37 °C	 18.5 8.9
Density (g/ml) at 20 °C at 37 °C	 1.427 1.417
pH-value	6.0-7.0

Pharmacokinetic properties
Absorption of amidotrizoic acid, the radiopaque agent of Gastrografin, following oral administration is only 3 %. Even in the absence of perforation a higher absorption was observed in some patients demonstrated by opacification of the renal calyces and ureters.

If a perforation of the gastrointestinal tract is present, Gastrografin finds its way into the abdominal cavity or the surrounding tissue, where it is absorbed and finally excreted via the kidneys.

Indications
Gastrografin is a contrast medium for the radiological examination of the gastrointestinal tract. It can be administered orally and as an enema and is primarily indicated in cases in which the use of barium sulfate is unsatisfactory, undesirable or contraindicated.

Among these are:
Threatening perforation (peptic ulcer, diverticulum), after resection of the stomach or the intestine (danger of perforation or leak), suspected partial or complete stenosis, acute haemorrhage, other acute conditions which are likely to require surgery, megacolon, visualization of a foreign body or tumour before endoscopy , visualization of a gastrointestinal fistula.

In addition to these conditions Gastrografin can generally be used for the same purposes as barium sulfate.

In combination with barium sulfate, Gastrografin has considerably improved routine investigation of the gastrointestinal tract both from a diagnostic and from an organizational point of view- the latter by speeding up the examination. It is unsuitable only for the diagnosis of enteritis.

Further indications:

a) Early diagnosis of a radiologically undetectable perforation or anastomotic defect in the oesophagus and/or gastrointestinal tract
b) Treatment of meconium ileus
c) Computerized tomography in the abdominal region. The danger of false diagnoses is significantly reduced if the intestine is opacified with Gastrografin, especially for differential diagnoses in the minor pelvis. Gastrografin facilitates delimitation of the intestine from neighbouring organs and permits an assessment of changes in the shape of the pancreas

Dosage and method of administration

General information

Because of the additives (flavorings and a wetting agent), Gastrografin must not be used intravascularly.

Because of its high osmotic pressure and the tendency to absorption from the intestine, Gastrografin should not be administered to newborns, infants and young children in doses higher than those recommended. In newborns and infants low osmolar contrast media can often be used more safely than the high osmolar Gastrografin.

Dosage for oral use

The dosage is dependent on the type of examination and the age of the patient.

Adults

In adult patients and children of 10 years of age and over, 60 ml is sufficient for visualization of the stomach; for a follow-through examination of the gastrointestinal tract a maximum of 100 ml may be required. For elderly and cachectic patients a dilution with an equal volume of water is recommended.

For the early diagnosis of a perforation or anastomosis in the oesophagus and/or gastrointestinal tract, the patient should drink 100 ml Gastrografin. If the suspected lesion cannot be clearly identified in the X-ray film, a chemical reaction can be employed for further clarification. After 30 - 60 minutes (later, if the defect is suspected of being in the distal gut), a urine specimen should be taken and 5 ml mixed with 5 drops of concentrated hydrochloric acid.

The contrast medium which has undergone renal excretion will appear within 2 hours as a typical crystal formation in the precipitate.

Children

In children up to 10 years of age, 15 - 30 ml is generally sufficient. This dose can be diluted with twice its volume of water. For infants and young children it is recommended that the contrast medium be diluted with 3 times its volume of water.

Computerized tomography (CT)

The examination can be made after the administration of 1 - 1.5 l of an approx. 3 % Gastrografin solution (30 ml Gastrografin/1 l water).

Dosage for rectal use

Adults

For adult patients the contrast medium should be diluted with 3 - 4 times its volume of water. In general, unlike a barium-sulfate enema, not more than 500 ml of this Gastrografin dilution is required.

Children

For children over 5 years of age, the contrast medium should be diluted with 4 - 5 times its volume of water; for children up to 5 years of age a dilution with 5 times its volume of water is recommended.

Therapy of meconium ileus

Gastrografin can be given by enema for non-operative treatment of an uncomplicated meconium ileus. Advantage is taken of the high osmotic pressure of the contrast medium: the surrounding tissue is forced to release considerable amounts of fluid, which then flows into the gut and dissolves the hardened meconium.

Dosage for Gastrografin in combination with barium sulfate

Adults

In adult patients, addition of approximately 30 ml Gastrografin to the usual dose of barium sulfate has been shown to be most satisfactory.

Children

In children from 5 - 10 years of age, 10 ml Gastrografin may be added to the necessary amount of barium sulfate, in patients up to 5 years of age, addition of 2 - 5 ml Gastrografin to 100 ml barium sulfate suspension has proved of value.

If necessary (in cases of pylorospasm or pyloric stenosis), the portion of Gastrografin in the suspension may be further increased. This does not affect the contrast.

Exposures

Exposures of the stomach are taken in the usual way whether Gastrografin is used alone or in combination with barium sulfate.

The time taken for emptying of the stomach is the same as for barium sulfate whereas that for filling of the intestine is shorter. When Gastrografin alone is used, the contrast medium has generally reached the rectum after 2 hours, while the Gastrografin/barium sulfate mixture may take up to 3 hours and, in individual cases, longer.

The most favourable time for taking exposures of the colon is indicated by the urge to defaecate which all patients experience.

Contraindications

Gastrografin must not be administered undiluted in patients with low plasma volume, as for example in newborns, infants, children and in dehydrated patients, since hypovolemic complications can be particularly serious in these patients.

Gastrografin must not be administered undiluted in patients with suspected possibility of aspiration or broncho-esophageal fistula, since hyperosmolarity may cause acute pulmonary edema, chemical pneumonia, respiratory collapse and death.

Manifest hyperthyroidism.

Special warnings and special precautions for use

The following risks mentioned are higher in intravascular administration of iodinated contrast media, however, they are also relevant for the enteral use of Gastrografin.

- Hypersensitivity

Particularly careful risk-benefit assessment is required in patients with known hypersensitivity to Gastrografin or any of its ingredients due to an increased risk for anaphylactoid/hypersensitivity reactions.

Patients with hypersensitivity or a previous reaction to iodinated contrast media are at increased risk of experiencing a severe reaction. However, such reactions are irregular and unpredictable in nature.

In patients with an allergic disposition, known hypersensitivity to iodinated contrast media or a history of asthma, premedication with antihistamines and/or glucocorticoids may be considered.

Patients with bronchial asthma are at particular risk of experiencing bronchospasms or hypersensitivity reactions.

As with other contrast agents, Gastrografin can be associated with anaphylactoid/ hypersensitivity or other idiosynchratic reactions, characterized by cardiovascular, respiratory or cutaneous manifestations, and ranging to severe reactions including shock.

Delayed reactions may occur (hours later or up to several days) (see “Undesirable effects”).

Nausea, vomiting, mild angioedema, conjunctivitis, coughing, pruritus, rhinitis, sneezing and urticaria have been reported. These reactions, which can occur irrespective of the amount administered and the mode of administration, may be the first signs of an incipient state of shock.

If hypersensitivity reactions occur (see “Undesirable effects”), administration of the contrast medium must be discontinued immediately and- if necessary-specific therapy instituted via a venous access.

Medication for the treatment of hypersensitivity reactions as well as preparedness for institution of emergency measures are necessary.

The risk of anaphylactoid/hypersensitivity reactions is higher in case of:

- any history of allergic disorders
- history of bronchial asthma
- a previous anaphylactoid/hypersensitivity reaction to iodinated contrast media

Particularly careful risk-benefit assessment is required in patients with a previous anaphylactoid/hypersensitivity reaction to any other iodinated contrast medium because of an increased risk of anaphylactoid/hypersensitivity reactions in these patients.

Patients taking beta blockers who experience such reactions may be resistant to treatment with beta agonists.

Patients with cardiovascular disorders are more susceptible to serious or even fatal outcomes of severe anaphylactoid/hypersensitivity reactions.

• Thyroid dysfunction

Particularly careful risk-benefit assessment is required in patients with known or suspected hyperthyroidism or goiter, as iodinated contrast media may interfere with thyroid function, aggravate or induce hyperthyroidism and thyreotoxic crisis.

Testing of thyroid function prior to Gastrografin administration and/or preventive thyreostatic medication may be considered in patients with known or suspected hyperthyroidism.

In neonates, specially preterm infants, who have been exposed to Gastrografin, 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.

• Very poor state of health

The need for examination merits particularly careful consideration in patients with a very poor general state of health.

• Barium sulfate

If Gastrografin is used together with barium sulfate preparations, attention must be drawn to the contraindications, warnings and possible side effects relevant to this preparation.

• Gastrointestinal

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

• Hydration

Adequate hydration and electrolyte balance should be established and maintained in the patients, since the hyperosmolarity of Gastrografin may cause dehydration and electrolyte imbalance.

Interaction with other medicaments

Hypersensitivity reactions can be aggravated in patients on beta-blockers, particularly in people with bronchial asthma.

Patients who experience such reactions while taking beta blockers may be resistant to treatment of anaphylactoid/hypersensitivity reactions with beta agonists.

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

• Interference with diagnostic tests

Radioisotopes: Diagnosis and treatment of thyroid disorders with thyrotropic radioisotopes may be impeded for up to several weeks after administration of iodinated contrast agents due to reduced radioisotope uptake.

Pregnancy and lactation

Reproduction-toxicological studies with intravenous administration of meglumine- or sodium amidotrizoate gave no indication of a teratogenic or other embryotoxic potential. Due to the low resorption from the gastrointestinal tract (see systemic tolerance studies) no risk to

either the pregnancy or the fetus is to be expected following an inadvertent administration of Gastrografin during pregnancy.

It has not yet been demonstrated that Gastrografin is safe for use in pregnant patients.

Caution should be exercised when using Gastrografin in pregnant women.

Since, where possible, radiation stress should in any case be avoided during pregnancy, the benefits of any X-ray examination - whether with or without contrast material - should for this reason alone be carefully weighed against the possible risk.

It is not known whether Gastrografin enters the breast milk. Limited data suggest that the risk to suckling newborns or infants of administering salts of diatrizoic acid to its mother is low.

Undesirable effects
Frequency of adverse reactions from spontaneous reports and literature:

Undesirable effects in association with the use of iodinated contrast media are usually mild to moderate and transient in nature. However, severe and life-threatening reactions as well as deaths have been reported.

Vomiting, nausea and diarrhea are the most frequently recorded reactions.

The table below reports adverse reactions by MedDRA system organ classes (MedDRA SOCs).

System Organ Class	**Common (≥ 1/100)**	**Rare (< 1/1,000)**	**Not Known**
Immune system disorders		Anaphylactoid shock, Anaphylactoid/hypersensitivity reaction	
Endocrine disorders		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, Dyspnea, medication aspiration, pulmonary edema following aspiration, aspiration pneumonia	
Gastrointestinal disorders	Vomiting, nausea, diarrhea	Intestinal perforation, abdominal pain, oral mucosal blistering	
Skin and subcutaneous tissue disorders		Toxic epidermal necrolysis, urticaria, rash, pruritus, erythema, edema face	
General disorders and administration site conditions		Pyrexia, sweating	

The most appropriate MedDRA term is used to describe a certain reaction and its synonyms and related conditions.

Immune system disorders, anaphylactoid reaction/hypersensitivity:

Systemic hypersensitivity is rare, mostly mild and occurs generally in the form of skin reactions. However, the possibility of a severe hypersensitivity reaction cannot be entirely excluded (see"Special warnings").

Gastrointestinal disorders:

The hypertonic Gastrografin solution may give rise to diarrhea, but this ceases as soon as the intestine has been emptied. Existing enteritis or colitis may be temporarily exacerbated. In case of obstruction the prolonged contact with bowel mucosa can lead to erosions and to bowel necrosis.

Overdose and treatment
Disorders of water and electrolyte balance caused by overdose should be corrected.

Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned in the section “Dosage”.

Storage conditions
Store at or below 30ºC. The product does not require any special temperature storage conditions. Advice for handling : “Protect from light”

Instructions for use/handling
At temperatures below 7 °C Gastrografin tends to crystallize, but this can be reversed by gently warming and shaking the bottle. This phenomenon has no effect on the effectiveness or stability of the preparation.

Unused Gastrografin in opened containers must be stored at or below 30ºC and discarded within 72 hours after first opening of the container.

Presentation
Screw bottles of 100 ml

Shelf –life
24 months

Name and address of manufacturing
Berlimed SA, Spain
Poligono Ind Santa Rosa
28806 Alcala De Henares Madrid
Spain

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