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PROFESSIONAL INFORMATION

PATIENT INFORMATION LEAFLET

PROFESSIONAL INFORMATION: GASTROGRAFIN AQUEOUS SOLUTION

Bayer (Pty) Ltd	**Date of revision of text: 02 September 2018**

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

GASTROGRAFIN®
Aqueous solution

COMPOSITION

GASTROGRAFIN contains a mixture of sodium amidotrizoate and meglumine amidotrizoate in a proportion of 10:66 (amidotrizoic acid or diatrizoic acid: 3,5-bis-acetamido-2,4,6-triiodobenzoic acid).

1 ml GASTROGRAFIN contains sodium amidotrizoate 100,00 mg and meglumine amidotrizoate 660,00 mg (sodium diatrizoate and meglumine diatrizoate) in aqueous solution plus flavourings and a wetting agent.

Iodine concentration	370 mg/ml
Iodine content per bottle of 100 ml	37 g
Contrast medium concentration	760 mg/ml
Contrast medium content per bottle of 100 ml	76 g
Viscosity (mPa.s or cP)	
at 20 °C	18,5
at 37 °C	8,9
Osmotic pressure at 37 °C	
(MPa)	5,58
(atm)	55,1
Osmolality at 37 °C (osm/kg H_2O)	2,15

The excipients are: disodium edetate, polysorbate 80, purified water, saccharin sodium, sodium hydroxide, star anise oil.

PHARMACOLOGICAL CLASSIFICATION

A 28 Contrast media

PHARMACOLOGICAL ACTION

Pharmacodynamic properties:

The contrast-giving substance of GASTROGRAFIN is a salt of amido(dia-)trizoic acid in which the X-ray absorbing iodine is present in stable chemical bond.

Pharmacokinetic properties:

Following oral administration only about 3 % of the amidotrizoic acid is absorbed from the stomach and intestines. This portion, and also any contrast medium that might have reached the abdominal cavity or surrounding tissue through perforations in the gastro-intestinal tract, are eliminated mainly via the kidneys.

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INDICATIONS

GASTROGRAFIN is designed for investigation for the gastrointestinal tract. It can be used either orally or as an enema. Follow-through examinations with barium can often be improved by combining it with GASTROGRAFIN. GASTROGRAFIN may be of particular value in the following instances:

- Suspected partial or complete stenosis.
- Acute haemorrhage.
- Threatening perforation (peptic ulcer, diverticulum).
- Other acute conditions which are likely to require surgery.
- After resection of the stomach or intestine (danger of perforation or leak).
- Megacolon.
- Visualisation of a foreign body or tumour before endoscopy.
- Visualisation of a gastrointestinal fistula.
- Before endoscopy.
- Early diagnosis of a radiologically undetectable perforation or anastomotic defect in the oesophagus.
- The treatment of uncomplicated meconium ileus.
- Computerised tomography in the abdominal region.

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 hypovolaemic complications can be particularly serious in these patients.

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

Not to be administered to patients who are hypersensitive to iodine or to any constituents of GASTROGRAFIN.

Pregnancy and lactation, as safety has not been established.

WARNINGS AND SPECIAL PRECAUTIONS

Fatal reactions (allergy-like hypersensitivity reactions ranging to severe reactions including shock) have been associated with the administration of water-soluble contrast media, such as GASTROGRAFIN. It is therefore of the utmost importance that a course of action be carefully planned in advance for the treatment of serious reactions, and that adequate and appropriate facilities and personnel be readily available in case of a severe reaction. Patients should be observed for a possible severe reaction during and for at least 30 to 60 minutes after administration.

The following risks are relevant for the enteral use of GASTROGRAFIN.

Hypersensitivity:

Particularly careful risk-benefit assessment is required in patients with a known hypersensitivity due to an increased risk for anaphylactoid/hypersensitivity reactions.

GASTROGRAFIN can be associated with anaphylactoid/hypersensitivity or other idiosynchratic reactions, characterised 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 Side Effects).

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.

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 increased thyroid activity or goiter, as iodinated contrast media may interfere with thyroid function, aggravate or induce hyperthyroidism and thyrotoxic crisis.

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

In neonates, especially 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.

Barium sulphate:

If GASTROGRAFIN is used together with barium sulphate preparations, attention must be drawn to the Contraindications, Warnings and Special Precautions and possible Side Effects relevant to the preparation.

Gastrointestinal:

Because of its high osmotic pressure and minimal tendency to absorption from the intestine, GASTROGRAFIN should not be administered to babies and young children in higher doses than those recommended.
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.
Disturbances of water and electrolyte balance must be corrected before the examination.
Because of the additives (flavourings and a wetting agent), GASTROGRAFIN must not be used intravascular.

Following the administration of GASTROGRAFIN, the capacity of the thyroid tissue to take up radioisotopes for diagnosing disorders of the thyroid is reduced for up to 2 weeks and even longer in individual cases.

Hypersensitivity reactions can be aggravated in patients on beta-blockers.
The prevalence of delayed reactions (e.g. fever, rash, flu-like symptoms, joint pain and pruritus) to contrast media is higher in patients who have received interleukin.

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INTERACTIONS

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.

HUMAN REPRODUCTION

Safety in pregnancy and lactation has not been established.

Adequate and well-controlled studies in pregnant and lactating women have not been conducted.

DOSAGE AND DIRECTIONS FOR USE

Because of the additives (flavourings 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.

GASTROGRAFIN must not be mixed with other medicinal products except those mentioned in this section.

Oral administration:

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

In adult patients and children of 10 years of age and over, 60 ml is sufficient for visualisation 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.

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

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 to 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.

- Computerised tomography (CT)

The examination can be made after the administration of 0,5 to 1,5 l of approximately 3 % GASTROGRAFIN solution (30 ml GASTROGRAFIN/1 l water).

Rectal administration (including therapy of uncomplicated meconium ileus):

For adult patients the contrast medium should be diluted with 3 to 4 times its volume of water.
In general, unlike a barium sulphate enema, not more than 500 ml of this dilute GASTROGRAFIN solution is required.

For children over 5 years of age, the contrast medium should be diluted with 4 to 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.

In the presence of uncomplicated meconium ileus advantage is taken of the high osmotic pressure of GASTROGRAFIN: the surrounding tissue is forced to release considerable amounts of fluid, which then flows into the gut and dissolves the hardened meconium.

- **Technique for the treatment of uncomplicated meconium ileus**

GASTROGRAFIN can be given by enema to infants for non-operative treatment of uncomplicated meconium ileus in the absence of, e.g. volvulus, gangrene, perforation, peritonitis or atresia, all of which require immediate operation.

A large syringe and soft rubber catheter, No 8 French, are recommended. The buttocks can be taped tightly together to minimise leakage, but a balloon catheter should not be used. **The procedure must be carried out slowly and only under fluoroscopic control**. Injection should stop as soon as GASTROGRAFIN is seen to enter the ileum. Owing to its high osmolarity, GASTROGRAFIN may cause the loss of a large amount of fluid into the intestines. An intravenous drip must therefore be set up before the enema is given and a suitable parenteral fluid should be infused as required. If the GASTROGRAFIN is not expelled during the first hour after removal of the rectal catheter, an X-ray should be taken to ensure that overdistension of the bowel as a result of the high osmolarity of GASTROGRAFIN has not occurred.

GASTROGRAFIN and barium sulphate:

In adult patients, addition of approximately 30 ml GASTROGRAFIN to the usual dose of barium sulphate has proved most satisfactory.

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

If necessary (in cases of pylorospasm or pyloric stenosis), the portion of GASTROGRAFIN in the GASTROGRAFIN-barium sulphate suspension may be further increased, thereby lowering the viscosity of the suspension. 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 sulphate.

The time taken for emptying of the stomach is the same as for barium sulphate 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 sulphate 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.

The bottle should be securely closed after each withdrawal and the contents discarded within 72 hours of first opening the bottle.

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SIDE EFFECTS

Frequency of adverse reactions from spontaneous reports and literature:

Undesirable effects in association with the use of GASTROGRAFIN 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 diarrhoea are the most frequently recorded reactions.

System organ class	**Common (≥ 1/100)**	**Rare (< 1/1000)**
Immune system disorders		Anaphylactoid shock Anaphylactoid/hypersensitivity reaction
Endocrine disorders		Hyperthyroidism
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 Diarrhoea	Intestinal perforation Abdominal pain Oral mucosal blistering
Skin and subcutaneous tissue disorders		Toxic epidermal necrolysis Urticaria Rash Pruritus Erythema Facial oedema
General disorders and administration site conditions		Pyrexia Sweating

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 Warnings and Special Precautions).

Gastrointestinal disorders:

The hypertonic GASTROGRAFIN solution may give rise to diarrhoea, but this ceases as soon as the intestine has been emptied. An 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.

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Data from post-marketing experience:

Side effects derived from post-marketing reports:
Endocrine disorders: Hypothyroidism

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Based on the results of preclinical acute toxicological studies, there is no risk of acute intoxication with the use of GASTROGRAFIN. Disorders of water and electrolyte balance caused by overdose should be corrected. Treatment should be symptomatic and supportive.

IDENTIFICATION

A clear, colourless to faintly yellowish solution with a faint odour of anise oil.

PRESENTATION

Amber glass bottles of 100 ml with a high-density polyethylene cap.

STORAGE INSTRUCTIONS

Until required for use, the product must be stored in the original outer carton below 30 °C.
Protect from light, heat and secondary X-rays.
KEEP OUT OF REACH OF CHILDREN.
Contents should be discarded within 72 hours of first opening the bottle.

At temperatures below 7 °C GASTROGRAFIN tends to crystallise, 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.

REGISTRATION NUMBER

H/28/2842

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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