Product Monograph

Gastrografin
(meglumine and sodium diatrizoate oral solution)

Radiopaque Contrast Agent

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NAME OF DRUG
Gastrografin
(Diatrizoate Meglumine and Diatrizoate Sodium Solution, USP)

THERAPEUTIC CLASSIFICATION
Radiopaque Contrast Agent

ACTION AND CLINICAL PHARMACOLOGY
Diatrizoate meglumine and diatrizoate sodium are sparingly absorbed from the intact gastrointestinal tract, and therefore permit gastrointestinal opacification and delineation after oral or rectal administration. Oral administration is used for radiographic evaluation of the esophagus, stomach and proximal small intestine. Rectal administration is used for examination of the colon; however, visualisation of the distal small bowel is generally unsatisfactory, since the hypertonicity of the medium causes intraluminal diffusion of water and subsequent dilution of the medium.

Diatrizoate meglumine and diatrizoate sodium exert a mild laxative effect attributable to their high osmolarity.

Enough absorption from the gastrointestinal tract to permit incidental visualisation of the urinary tract has been reported; this should be considered when thyroid testing is being contemplated, since iodine-mediated thyrotropic effects may occur.

INDICATIONS AND CLINICAL USE
Gastrografin (diatrizoate meglumine and diatrizoate sodium solution) is indicated for radiographic examination of the gastrointestinal tract, particularly in cases in which barium suspensions would be potentially risky. Gastrografin is also used for examinations for foreign bodies in the pharynx and esophagus and disorders of the swallowing mechanism.

CONTRAINDICATIONS
Gastrografin (diatrizoate meglumine and diatrizoate sodium solution) is contraindicated in patients with severe debility and hypersensitivity to salts of diatrizoic acid. It is contraindicated for intravenous and intramuscular use.

WARNINGS
A 1 in 4.6 dilution of Gastrografin (diatrizoate meglumine and diatrizoate sodium solution) yields an approximately isotonic 16.5% diatrizoate salts solution; less dilute solutions are hypertonic and may lead to intraluminal movement of fluid with resulting hypovolemia. In young or debilitated children and in elderly cachectic persons, the loss of plasma fluid may be sufficient to cause a shock-like state. See DOSAGE AND ADMINISTRATION for recommended dilutions that must be used for infants and young children (under 10 kg) and for dehydrated or debilitated patients. Electrolyte disturbances must be corrected prior to using hypertonic solutions. In debilitated patients and in patients with electrolyte imbalances, postprocedural monitoring of hydration, serum osmolarity,
electrolytes and clinical status is essential. In pediatric or severely debilitated patients, the
maintenance of an open intravenous fluid line for rehydration may be advisable should hypotension
or shock supervene.

The possibility of accidental aspiration into the trachea or into a tracheosophageal fistula following
ingestion or instillation could result in serious pulmonary complications (e.g. pulmonary edema or
pneumonitis) even though the medium may be promptly expectorated. Bronchial entry of any orally
administered contrast medium causes a copious osmotic effusion. Therefore, pulmonary entry by
aspiration and use in patients with esophagotracheal fistula should be avoided.

**Thyroid Dysfunction**
Gastrografin, like all other iodinated contrast media, may induce changes in thyroid function in some
patients. Transient hyperthyroidism or hypothyroidism has been reported following iodinated
contrast media administration to adult and pediatric patients. Decreased levels of thyroxine (T4) and
triiodothyronine (T3) and increased level of TSH were reported after exposure to ICM in infants,
especially preterm infants, which remained for up to a few weeks or even more than a month (see
ADVERSE REACTIONS). Some patients were treated for hypothyroidism. (See WARNINGS AND
PRECAUTIONS - Special Populations - Pediatrics - Infants)"

**PRECAUTIONS**

**General**
A history of sensitivity to iodine per se or to contrast media other than salts of diatrizoic acid, is not
an absolute contraindication to the use of Gastrografin, but calls for extreme caution in
administration.

A history of bronchial asthma or allergy or a family history of allergy warrants special attention and
may predict the likelihood of an allergic reaction, although neither the severity nor type of reaction
in the individual case may be predicted.

Rectal administration of undiluted Gastrografin (diatrizoate meglumine and diatrizoate sodium
solution) in any patient, particularly with large doses and/or in those with overdistension, has been
reported to be associated with mucosal irritation.

Cases of hyperthyroidism have been reported with the use of oral contrast media. Some of these
patients reportedly had multinodal goiters which may have been responsible for the increased
hormone synthesis in response to excess iodine. Administration of an intravascular iodinated
radiopaque diagnostic agent to a hyperthyroid patient precipitated thyroid storm: a similar situation
could follow administration of oral preparations of iodides. Therefore, caution should be exercised
when administering enteral gastrointestinal radiopaque agents to hyperthyroid and euthyroid
goiterous patients.
Consideration should be given to the potential for precipitation of water-soluble contrast agents under conditions that may promote hyperacidity (i.e. fasting, emotional upset, or stress). Harmful effects directly attributable to precipitate formation have not been reported. However, the possibility of interpreting the precipitate radiologically as an anatomical abnormality (i.e. ulceration of the stomach or small intestine) or injury, should be kept in mind.

Use in Children
See WARNINGS and PRECAUTIONS, General.
Local injury to colonic mucosa, particularly in the presence of underlying disease which interferes with intestinal viability, has been reported in cases where recommended doses and dilutions (see DOSAGE AND ADMINISTRATION) were not used; when extemporaneous dosage is elected, the polysorbate 80 level in the dose may be a contributing factor to injury.

Infants
Decreased levels of thyroxine (T4) and triiodothyronine (T3) and increased level of TSH were reported after exposure to ICM in infants, especially preterm infants, which remained for up to a few weeks or more than a month (see ADVERSE REACTIONS). Hypothyroidism in infants may be harmful for growth and development, including mental development and may require treatment. Thyroid function in infants exposed to ICM should therefore be evaluated and monitored until thyroid function is normalized.

Nursing Mothers
Diatrizoate meglumine is excreted in breast milk following intravascular administration.

Because small amounts of enteral gastrointestinal radiopaque agents may be absorbed following oral or rectal administration, caution should be exercised when they are administered to a nursing woman.

Pregnancy
The safety of the preparation for use during pregnancy has not been established; therefore, it should only be used when its use is deemed essential to the welfare of the patient.

When administered intravenously, diatrizoate salts cross the placenta and are evenly distributed in fetal tissues. No teratogenic effects attributable to diatrizoate meglumine or diatrizoate sodium have been observed in teratology studies performed in animals. There are, however, no adequate and well-controlled studies in pregnant women. Because small amounts of these agents may be absorbed, and animal teratology studies are not always predictive of human response, these agents should be used during pregnancy only when clearly needed.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals have not been performed to evaluate carcinogenic or mutagenic potential, or possible impairment of fertility in males or females.

Laboratory Tests
In general, any test which might be affected by contrast media should be performed prior to administration of the contrast medium.
Thyroid Function Tests:
The results of protein bound iodine and radioactive iodine uptake studies, which depend on iodine estimations, will not accurately reflect thyroid function for six months, and possibly as long as one year, following the administration of diagnostic enteral radiopaque media.

Therefore, if thyroid function tests are indicated they should be performed prior to the administration of any iodinated agent if possible. However, thyroid function tests can be evaluated after use of these agents by using (T₃) resin uptake and total or free thyroxine (T₄) assays which are not dependent on iodine estimations.

Pancreatic Tests:
Small quantities of contrast medium in the intestinal tract may cause false low trypsin values when determined spectrophotometrically. Therefore, duodenal instillation should not precede pancreatic function tests involving spectrophotometric trypsin assays.

ADVERSE REACTIONS
Most adverse reactions to enteral diagnostic radiopaque agents are mild and transitory. Occasionally some degree of diarrhea may be encountered due to the osmotic activity of the preparation when it is used as an enema. Nausea, vomiting and/or diarrhea, urticaria with erythema, hypoxia, acute dyspnea, tachyarrhythmia and anaphylaxis have occurred following ingestion of the contrast medium, particularly when high concentrations or large volumes are administered.

Oral administration in children may cause a decrease in circulating plasma volume due to osmosis when the contrast agent passes through the stomach and small intestine. In the very young child (weighing less than 10 kg) and the debilitated child, the loss of plasma fluid may be sufficient to cause a shock like state which, if left untreated, could be life threatening. This hazard can be avoided by dilution of the contrast medium with water before administration, and by the adequate hydration of the child before and after the procedure. The same considerations may possibly apply in elderly cachectic individuals as well.

It should be kept in mind that serious or anaphylactoid reactions that may occur with intravascular administration of radiopaque contrast agents are theoretically possible following administration by other routes.

Endocrine Disorders
Thyroid function tests indicative of hypothyroidism or transient thyroid suppression have been uncommonly reported following iodinated contrast media administration to adult and pediatric patients, including infants. Some patients were treated for hypothyroidism.

Treatment Of Adverse Reactions To Contrast Media
If, in spite of uneventful history taking, one or more of the following symptoms reveals the occurrence of an anaphylactoid reaction, i.e. respiratory difficulty (with laryngeal edema, pulmonary edema or asthma), shock, total vascular collapse, or cardiac arrest (with atonia and
fibrillation), immediate therapeutic measures must be taken. Heart and respiratory functions must be maintained, and allergic phenomena should be treated concomitantly by the injection of epinephrine USP 1:1000, 0.3 to 0.5 mL subcutaneously, repeated every 10 to 15 minutes until a definite permanent response or toxicity (tachycardia, excitability) occurs. Cardiac arrest may be treated by the injection of 0.2 mL epinephrine USP 1:1000, diluted by 10 mL physiological saline, into the left ventricle. Cardiac compression and defibrillation should be carried out whenever indicated. Acidosis should be combatted by injections of 3.75 g of sodium bicarbonate repeated every 5 minutes.

Asthma may be treated with intravenous aminophylline injection USP. Secondary treatments with anti-arrhythmics, antihistamines, corticosteroids and anticonvulsants should then be considered. Metaraminol bitartrate injection, USP or levarterenol bitartrate injection, USP should also be considered if hypotension is encountered.

**SYMPTOMS AND TREATMENT OF OVERDOSE**
See WARNINGS regarding potential hypovolemia, hypotension or shock. The maintenance of an open intravenous fluid line for rehydration may be advisable. See DOSAGE AND ADMINISTRATION for appropriate doses and dilutions. Treatment of an overdose should be directed toward the support of all vital functions, and prompt institution of symptomatic therapy.

**DOSAGE AND ADMINISTRATION**
This medium is not to be used for the preparation of solutions for parenteral administration.

The routine preparatory measures employed for barium studies are also appropriate for this agent. For pediatric and severely cachectic patients the maintenance of an intravenous fluid line may be advisable.

Oral adult doses may range from 30 to 90 mL depending on the nature of the examination and the size of the patient. Give by mouth, tube, nursing bottle, or by rectum. Infants and children up to 5 years of age, 30 mL; 5 to 10 years, 60 mL. Debilitated children, or infants weighing less than 10 kg require diluted doses: 1 part diatrizoate meglumine to 3 parts of water may be given. Elderly, cachectic patients, or infants and children may be given a 1:1 dilution, using water, carbonated beverages, milk or mineral oil as the diluent. As an enema, or for enterostomy instillations for adults, dilute 240 mL in 1000 mL of tap water. For rectal administration to children of 5 years of age or more, 90 mL of the contrast agent in 500 mL would be a suitable dilution. Under 5 years, a 1:5 dilution may be given.
PHARMACEUTICAL INFORMATION

Drug Substance:

Diatrizoate Meglumine:

Chemical Name:
1-deoxy-l(methylamino)-D-glucitol 3,5-diace–tami–do–2,4,6-triodo–benzo–ate

Molecular Formula:
C₁₈H₂₆I₃N₃O₉

Molecular Weight: 809.13

Diatrizoate Sodium:

Chemical Name:
monosodium 3,5-diace–tami–do–2,4,6-triodo–benzo–ate

Molecular Formula:
C₁₁H₈I₃N₂NaO₄

Molecular Weight: 635.90

Composition:
Each mL of Gastrografin (diatrizoate meglumine and diatrizoate sodium solution, USP) contains
660 mg diatrizoate meglumine and 100 mg diatrizoate sodium. pH has been adjusted with sodium hydroxide to 6.0 to 7.6. Each mL contains approximately 4.8 mg (0.21 mEq) sodium and 367 mg organically bound iodine. Non medicinal ingredients are: edetate sodium, flavour, polysorbate 80, purified water, saccharin sodium, simethicone and sodium citrate

**Stability and Storage Recommendations:**
Protect from light. Store at room temperature.

**AVAILABILITY OF DOSAGE FORMS**
An aqueous, palatable lemon-flavoured solution, providing 66% diatrizoate meglumine and 10% diatrizoate sodium. The solution contains 37% (11 g per 30 mL) firmly bound iodine. Alcohol- and sugar-free. Bottles of 30 and 120 mL.

**Pharmacology**

Single oral doses of 20mL of meglumine and sodium diatrizoates 76% were given to two dogs weighing 7.1 and 8.6 kg. There were no signs of toxic effects and urine samples collected at 1, 3, 6 and 24 hours after dosing showed traces of iodine excretion, that is, on the basis of the dose administered, of 0.4% in one dog and less than 0.4% in the other dog.

There was significant excretion of the medium through the urinary tract, with visualization of the kidneys and urinary bladder in 2 of 45 patients examined with meglumine and sodium diatrizoates. One of the two patients had undergone partial gastrectomy for an ulcer. In the other patient to whom oral meglumine and sodium diatrizoates were administered as an enema, opacification of the collecting system of both kidneys revealed marked left sided pyeloectasis and caluctasis, probably secondary to inflammation in the pelvis.

There was sufficient absorption of Gastrografin to give a pyelogram in 1 of 27 patients who had received the medium.

**Toxicology**

Gastrografin was administered orally to both mice and dogs. A dose of 10 mL per kg was not lethal to 10 mice during the 10 day observation period. After an oral dose of 10 mL/kg of Gastrografin in 10 mice all of the animals had diarrhea approximately 3 to 5 hours after dosing. All animals were normal the next day and all survived.

Four dogs fasted for 18 hours were given single oral doses of 7.5 mL Gastrografin/kg. Other than a slight emesis in one dog, 30 minutes after dosage, no adverse signs were noted. After a 5 hour observation period, the dogs were sacrificed and their gastrointestinal tracts examined grossly. No significant gross pathological changes were revealed.
READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

Gastrografin®
Diatrizoate meglumine and diatrizoate sodium oral solution

Read this carefully before you start taking Gastrografin® and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about Gastrografin®.

What is Gastrografin® used for?
To assist in radiographic (X-Ray) examination of:

- the digestive tract.
- the throat and the esophagus (passageway between the mouth and the stomach).

How does Gastrografin® work?
Gastrografin is absorbed by your digestive track and makes it appear darker in X-Ray examinations. This helps your doctor make a diagnosis.

What are the ingredients in Gastrografin®?
Medicinal ingredients: Diatrizoate meglumine and diatrizoate sodium.
Non-medicinal ingredients: edetate sodium, flavour, polysorbate 80, purified water, saccharin sodium, simethicone, sodium citrate and sodium hydroxide.

Gastrografin® comes in the following dosage forms:
Gastrografin is supplied in bottles of 30 and 120 mL containing 66% diatrizoate meglumine and 10% diatrizoate sodium.

Do not use Gastrografin® if:
- you have history of allergy to Gastrografin or salts of diatrozic acid. See the section “What are the ingredients in Gastrografin?” to see all the ingredients.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Gastrografin®. Talk about any health conditions or problems you may have, including if you:

- are pregnant or planning to become pregnant. If there is a need to use Gastrografin during your pregnancy, your doctor will discuss the benefits and risks of giving it to you.
- are breastfeeding or planning to breastfeed. Gastrografin may be passed on through breast milk. Talk to your doctor about the best way to feed your baby if you take Gastrografin.
- suffer from an abnormal passage between the esophagus and the trachea.
- are allergic, or have had allergic reaction to iodine or any other contrast agent.
• have a family history of allergy or asthma.
• suffer from a condition where your thyroid gland is enlarged (goiter).

**Other warnings you should know about:**
Gastrografin should not be administered into a blood vessel or a muscle.

Products like Gastrografin that contain iodine, may change thyroid activity in some patients, both in adults and infants. This may cause:
• hypothyroidism (i.e. too little thyroid hormones in the blood); or
• hyperthyroidism (i.e. too much thyroid hormones in the blood)

Gastrografin may cause hypothyroidism in infants, especially infants born too soon that:
• can continue for several weeks to a month after treatment
• can harm growth and development
• can harm mental growth
• may require treatment
• can cause symptoms such as:
  - fatigue, shortness of breath, low heart rate
  - reduced appetite, feeling cold, weight gain
  - muscle stiffness

Contact your doctor if these symptoms happen to you or your infant.

**Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.**

**The following may interact with Gastrografin®:**
No drugs are known to interact with Gastrografin.

Gastrografin may affect the results tests to measure the thyroid gland function. Gastrografin may also affect the results of tests for the pancreas. Tell your doctor if you have any of these tests scheduled.

**How to take Gastrografin®:**
Gastrografin® will be given to you by a healthcare professional who is experienced in the use of contrast media. Gastrografin can be given by the mouth (oral) or by the rectum. Gastrografin should not be used as an injection.

**Usual dose:**
Your healthcare professional will decide on the dose that is right for you. The dose depends on the type of examination and your weight.
**Overdose:**
If you think you have taken too much Gastrografin®, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

**What are possible side effects from using Gastrografin®?**
These are not all the possible side effects you may feel when taking Gastrografin®. If you experience any side effects not listed here, contact your healthcare professional.

Common side effects with Gastrografin include nausea, vomiting, allergy, and diarrhea.

### Serious side effects and what to do about them

<table>
<thead>
<tr>
<th>Symptom / effect</th>
<th>Talk to your healthcare professional</th>
<th>Stop taking drug and get immediate medical help</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Only if severe</td>
<td>In all cases</td>
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<tr>
<td><strong>RARE</strong></td>
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<tr>
<td>Severe allergic reactions, with symptoms such as trouble breathing, increase heart rate, or rashes</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Diarrhea or vomiting in children</td>
<td>X</td>
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</tbody>
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If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

**Reporting Side Effects**
You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or

- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

**Storage:**
Store at room temperature. Protect from light.

Keep out of reach and sight of children.
If you want more information about Gastrografin®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php); the manufacturer’s website http://www.braccoimaging.com, or by calling 1-800-465-5820.

This leaflet was prepared by Bracco Imaging Canada

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