SUMMARY OF PRODUCT CHARACTERISITCS

1. NAME OF THE MEDICINAL PRODUCT

TELEBRIX GASTRO (300 mg I/mL),

solution for oral or rectal administration

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

For 100 mL of solution:

Meglumine ioxitalamate ..... 66.03 g

Equivalent to iodine ..... 30 g

- Iodine content per mL: 300 mg
- Iodine mass per 50 mL vial: 15 g
- Iodine mass per 100 mL bottle: 30 g

Excipient with known effect: ethanol (alcohol) (0.48 to 0.52 mL for 100 mL of solution)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for oral or rectal administration

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Contrast medium for use in adults and children by oral or rectal administration for:

Conventional X-ray and computed tomographic (CT) examinations of the gastrointestinal tract, gastroduodenal radiography, opaque enema examinations, especially in cases in which barium products are contraindicated.

4.2. Posology and method of administration

Posology

The doses must be adapted to the examination and the regions to be investigated, as well as to the age and body weight of the subject, particularly in children.

Indications	Average dose	Total volume (min.-max.) mL
Conventional Radiography ORAL ROUTE Adults Children RECTAL ROUTE Adults Children	 200 mL of product diluted with 250 mL water 40 mL of product diluted with 10 mL water 400 mL of product diluted with 400 mL water 30 mL to 150 mL of undiluted product	 < 500 < 100 < 1500 < 200
Computed tomography	50 mL diluted with 950 mL water	< 1300

Special populations

Elderly patients

TELEBRIX GASTRO should be administered with caution (see section 4.4), in well-hydrated patients at the minimum effective dose.

Paediatric population

As with all other hyperosmolar contrast media, the use of this preparation should be carefully considered in neonates, infants, and children. The administered dose should be reduced to the minimum.

Patients with renal impairment

In patients with serious renal failure or diabetes (see section 4.4), the minimum effective dose of TELEBRIX GASTRO must be administered carefully to well hydrated patients.

4.3. Contraindications

This medicinal product must not be injected.

- Hypersensitivity to ioxitalamic acid or to any of the excipients listed in section 6.1.
- History of major immediate or delayed skin reaction (see section 4.8) to TELEBRIX GASTRO administration
- If a broncho-oesophageal fistula or a risk of aspiration is suspected, hyperosmolar monomeric ionic contrast agents are contraindicated because of the risk of intra-alveolar oedema
- Manifest thyrotoxicosis

4.4. Special warnings and precautions for use

- Allergic reaction is possible regardless of the administration route and dose.
- The intolerance risk is not univocal in the case of medicinal products administered locally for opacification of bodily cavities:

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

b) Administration by oral or rectal route generally leads to very limited systemic diffusion; if the gastro-intestinal mucosa is normal, only 5% maximum of the dose administered is found in the urine, the remainder being eliminated in the faeces. However, if the gastro-intestinal mucosa is altered, absorption is increased; it becomes total and rapid in the event of perforation, with passage into the cavity of the peritoneum. The medicinal product is then eliminated in the urine. The occurrence of any dose-dependent systemic effects therefore depends on the condition of the gastro-intestinal mucosa.

c) The immuno-allergic mechanism is however not dose-dependent and always likely to be observed, regardless of the administration route.

With respect to the prevalence and the intensity of adverse effects, the following therefore are antagonists:
- Medicinal products administered by vascular route and by certain local routes
- Medicinal products administered by intestinal route and little absorbed under normal conditions

4.4.1. Special warnings

4.4.1.1. Hypersenstivity

Any iodinated contrast medium may cause minor or major reactions that may be life-threatening. They may be immediate (less than 60 minutes) or delayed (up to 7 days). They are often unpredictable.

The risk of major reaction requires the immediate availability of the means necessary for emergency resuscitation.

Several mechanisms have been reported:
- Direct toxicity affecting the vascular endothelium and tissue proteins.
- Pharmacological action altering the concentration of certain endogenous factors (histamine, complement fractions, inflammation mediators), more frequent with hyperosmolar products.
- Immediate IgE-type allergy dependent on the TELEBRIX GASTRO contrast medium(300 mg Iodine/mL), solution for oral or rectal administration (anaphylaxis)
- Cell-mediated allergic reactions (late onset cutaneous reactions)

Patients having previously suffered a reaction during administration of an iodinated contrast medium are at increased risk of experiencing a renewed reaction during administration of the same, or another iodinated contrast medium, and are therefore considered to be high risk subjects.

4.4.1.2. Iodinated contrast media and the thyroid (see 4.4.2.5. Precautions for use - Dysthyroidism)

Prior to administration of an iodinated contrast medium, it must be ensured that the patient is not to undergo a scintigraphic exploration of the thyroid, or administration of radioactive iodine treatment.

Administration of iodinated contrast media, regardless of the route, disturbs hormone assays and iodine fixation by the thyroid or thyroid cancer metastases until normalisation of urine iodine levels.

4.4.2. Precautions for use

4.4.2.1. Intolerance to iodinated contrast media:

Prior to the examination:
- Identify subjects at risk via specific questioning concerning history.

Corticosteroids and H1-antihistamines were suggested as premedication in patients at the highest risk of hypersensitivity reaction. However, they do not prevent serious or fatal anaphylactic shock to occur.

During the examination, the following must be ensured:

- Medical supervision.
- Maintenance of a venous access.
- necessary resuscitation equipment at hand.

After the examination:

- Further to administration of a contrast medium, the patient must remain under observation for at least 30 minutes, as most adverse effects occur within this time.
- The patient must be warned that late onset reactions may occur (up to 7 days later) (see section 4.8 – Undesirable effects).

4.4.2.2. Renal failure

Iodinated contrast media may temporarily alter renal function or aggravate existing renal failure. The preventive measures to be taken are as follows:

- Identify high risk patients: dehydrated subjects, patients with renal failure, diabetes, severe heart failure, monoclonal gammapathy (multiple myeloma, Waldenström's disease) recent myocardial infarction, intra-aortic balloon pump, low haematocrit, hyperuricaemia, or a history of renal failure following administration of iodinated contrast media, children under one year and atheromatous elderly subjects or with polymorbidity syndrome.
- Initiate appropriate hydration by fluid and sodium solution where required.
- Avoid combinations of nephrotoxic medicines (if such combinations are necessary, reinforce renal biological monitoring). The medicinal products in question are notably angiotensin-converting enzyme (ACE) inhibitors, aminoglycosides, organoplatins, high-dose methotrexate, pentamidine, foscarnet and certain antivirals (aciclovir, ganciclovir, valaciclovir, adefovir, cidofovir, and tenofovir), vancomycin, amphotericin B, non-steroidal anti-inflammatory drugs, diuretics, immunosuppressants such as ciclosporine or tacrolimus, ifosfamide.
- Since renal elimination is reduced in the presence of renal dysfunction, the interval between two X-ray examinations involving injection of an iodinated contrast medium must be as long as clinically acceptable, especially in risk patients. For these patients, allow for a 48- to 72-hour interval. In the event of renal failure following the first examination, any further examination should be deferred until after initial renal function has been restored.

Haemodialysis patients may receive iodinated contrast media as these products are dialysable. The haemodialysis department must first be consulted.

4.4.2.3. Liver failure

Special attention must be paid when a patient suffers both from liver failure and renal failure, as this situation increases the risk of contrast medium retention.

4.4.2.4. Asthma

Asthma must be stabilized prior to injection of an iodinated contrast medium.

Special attention must be paid in cases of asthma attacks occurring 8 days prior to the examination, due to the increased risk of bronchospasm.

4.4.2.5. Dysthyroidism

Following injection of an iodinated contrast medium, in particular in patients with goitre or with a history of dysthyroidism, the risk of hyperthyroidism or induction of hypothyroidism also exists. Hypothyroidism may also occur in newborns that have received, or whose mother has received an iodinated contrast medium. Their thyroid function should be therefore evaluated and monitored.

4.4.2.6. Severe cardiovascular disease

In the event of existing or early stage heart failure, coronary artery disease, pulmonary arterial hypertension or valvular heart disease, the risk of pulmonary oedema, myocardial ischemia and arrhythmia or severe hemodynamic disorders is increased following administration of an iodinated contrast medium.

4.4.2.7. Central nervous system disorders

The benefit/risk ratio must be estimated on a case per case basis due to the risk of worsening of neurological symptoms in patients presenting with transient ischemic attack, acute cerebral infarction, recent intracranial haemorrhage, cerebral oedema, idiopathic or secondary epilepsy (tumour, scar).

4.4.2.8. Myasthenia

Administration of a contrast medium may worsen myasthenia symptoms.

4.4.2.9. Enhanced side effects

Side effects related to administration of iodinated contrast media may be enhanced by pronounced states of excitation, anxiety and pain. Appropriate treatment, and possibly sedation, may be necessary

4.4.2.10 Warnings concerning excipients

This medicinal product contains low amounts of ethanol (alcohol), up to 0.52 mL for 100 mL.

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

4.5.1. Medicinal products

+ **Radiopharmaceuticals (see also section 4.4. Special warnings)**

A risk of hyperthyroidism or induction of hypothyroidism exists in at-risk patients.

Iodinated contrast media disturb radioactive iodine uptake by thyroid tissue during several weeks, and this may lead to poor fixation in the thyroid scintigraphy and reduced effectiveness of iodine 131 treatment.

Where renal scintigraphy performed by injection of renal tubular secreted radiopharmaceuticals is planned, it is recommended to carry out this procedure prior to injection of the iodinated contrast medium.

+ **Beta-blockers, vasoactive substances, angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists**

These medicinal products lead to a reduction in the effectiveness of cardiovascular compensation mechanisms in blood pressure disorders.
Hypersensitivity reactions may be aggravated in patients taking beta-blockers, particularly in the presence of bronchial asthma. These patients may be refractory to standard treatment for hypersensitivity reactions with beta-agonists.
The doctor must be informed if the patient is taking such treatment prior to injection of the iodinated contrast medium and dispose of the necessary resuscitation means.

+ **Diuretics**

Due to the risk of dehydration induced by diuretics, fluid and electrolyte rehydration is initially necessary for minimising the risk of acute renal failure.

+ **Interleukin 2**

Enhanced reaction to contrast media during treatment with interleukin 2 (intravenous route) may occur: rash, congestive flush, erythema, fever or flu-like symptoms, or more rarely hypotension, oliguria or even renal failure.

+ **Potentially nephrotoxic agents (see section 4.4.2.2. Precautions for use - Renal failure)**

+ **Fibrinolytic agents**

It has been demonstrated that, *in vitro*, contrast media perturb the effects of fibrinolytic agents in a dose-dependent manner. Given this enzyme inhibition, which varies between fibrinolytic agents, iodinated contrast media should not be administered concomitantly.

4.5.2. Other forms of interaction

High concentrations of iodinated contrast media in plasma and urine may interfere with in vitro bilirubin, protein and inorganic substance assay (iron, copper, calcium and phosphate); it is therefore recommended to not perform assay of these substances during the 24 hours following the procedure.

4.6. Pregnancy and lactation

Pregnancy

Given that exposure to radiation should generally be avoided during pregnancy, whether a contrast agent is used or not, the benefit of a radiological examination must be carefully assessed.

Embryotoxicity

Studies conducted in animals have not shown any teratogenic effects.

In the absence of teratogenic effects in animals, no malformation in humans is expected. To date, the substances causing malformations in humans have been found to be teratogenic in animals in well conducted studies in two species.

Foetotoxicity

Occasional iodine overload following administration of the medium in the mother may lead to foetal dysthyroidism if the examination is carried out after 14 weeks' amenorrhea. However, reversibility of this effect and the expected maternal benefit indicate that occasional administration of an iodinated contrast medium should not be delayed where the indication for radiological examination in pregnant women is carefully assessed

Fertility

Toxicological studies conducted on reproduction function did not show any effects on reproduction, fertility or foetal or post-natal development.

Breastfeeding

Small quantities of iodinated contrast media are excreted in breast milk. Occasional administration in mothers therefore bears a low risk of causing adverse effects in infants. It is advisable to suspend breastfeeding for 24 hours following administration of an iodinated contrast medium.

4.7. Effects on the ability to drive and use machines

No study on the effect on the ability to drive and use machines has been conducted.

However, this product contains alcohol (see section 4.4.2.10), so an effect on the ability to drive and use machines is possible.

4.8. Undesirable effects

Since marketing, the most frequently reported undesirable effects after administration of all forms of TELEBRIX are: hypersensitivity (particularly anaphylactic reaction, anaphylactoid reaction and anaphylactic shock), urticaria, rash (particularly erythema and maculopapular rash) and reactions at injection site (such as oedema, pain and inflammation).

Hypersensitivity reactions are usually immediate (occurring during administration or within the hour following the start of administration), but they may be delayed (from one hour to several days after administration), and are seen as undesirable cutaneous reactions.

Immediate reactions may consist in one or several successive or concomitant effects, usually cutaneous reactions, respiratory and/or cardiovascular disorders, which may be the early signs of shock. They are rarely fatal.

The undesirable effects are presented in the table below according to System Organ Class; frequency is unknown (cannot be estimated from available data).

List summarising the undesirable effects reported with TELEBRIX GASTRO or another form of TELEBRIX after intravascular administration or instillation:

System Organ Class	**Frequency: undesirable effect**
Immune system disorders	Unknown frequency: anaphylactic shock, anaphylactic reaction, anaphylactoid reaction, hypersensitivity
Endocrine disorders	Unknown frequency: thyrotoxic crisis *, hyperthyroidism*, thyroid disorder*
Nervous system disorders	Unknown frequency: dizziness
Cardiac disorders	Unknown frequency: cardiac arrest, tachycardia
Vascular disorders	Unknown frequency: hypotension
Respiratory, thoracic and mediastinal disorders	Unknown frequency: laryngeal œdema, pneumonia aspiration[1], dyspnoea, sneezing
Gastrointestinal disorders	Unknown frequency: ileus, diarrhoea, nausea, vomiting, abdominal pain
Skin and subcutaneous tissue disorders	Unknown frequency: *Immediate:* angiœdema, urticaria, pruritus, erythema *Delayed:* rash maculo-papular
General disorders and administration site conditions	Unknown frequency: face œdema
Investigations	Unknown frequency: Blood creatinine increased

[1] in patients with swallowing disorders (oral route)

* See section 4.4.1.2. Iodinated contrast media and the thyroid

The following undesirable effects have been reported with other iodinated contrast media or with TELEBRIX via a different route of administration.

Hence, they may occur during administration of TELEBRIX.

System Organ Class	Undesirable effect
Psychiatric disorders	Confusional state, agitation, hallucinations, anxiety
Nervous system disorders	Coma, syncope, brain œdema, convulsion, paresis/paralysis paresthesiae, tremor, amnesia, speech disorders, somnolence, headache, dysgeusia
Eye disorders	Visual impairment, photophobia, blindness transient
Ear and labyrinth disorders	Hearing impaired
Cardiac disorders	Myocardial infarction, angina pectoris, arrhythmia, bradycardia
Vascular disorders	Thrombophlebitis[1], circulatory collapse
Respiratory, thoracic and mediastinal disorders	Respiratory arrest, laryngospasm, bronchospasm, pulmonary oedema, throat tightness, cough
Gastrointestinal disorders	Parotid gland enlargement, salivary hypersecretion, pancreatitis[2]
Reproductive system and breast disorders	Pelvic pain[3]
Skin and subcutaneous tissue disorders	Angioedema, urticaria, pruritus, Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, eczema
Musculoskeletal and connective tissue disorders	Arthralgia[4]
Renal and urinary disorders	Renal failure acute, anuria
General disorders and administration site conditions	Oedema, feeling hot, pain, malaise, injection site extravasation, injection site necrosis[5], injection site pain, injection site inflammation, injection site oedema
Investigations	Electroencephalogram abnormal, blood amylase increased

[1] after intravascular administration

[2] after endoscopic retrograde cholangio-pancreatography (ERCP)

[3] in the event of hysterosalpingography

[4] in the event of arthrography

[5] in the event of extravasation

Undesirable effects in children

The known nature of undesirable effects associated with TELEBRIX GASTRO is the same as that of effects reported in adults. Their frequency cannot be estimated from available data.

4.9. Overdose

Overdose increases the risk of kidney disease and may cause diarrhoea, dehydration, electrolyte

imbalance, haemodynamic and cardiovascular disorders.

With very high doses, fluid and electrolyte losses must be compensated by appropriate rehydration. Renal function must be monitored during at least three days. Haemodialysis may be carried out, if necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: IODINATED CONTRAST MEDIUM (V: miscellaneous)
ATC Code: V08AA05

GASTROINTESTINAL IODINATED CONTRAST AGENT:
Contrast enhancement in the gastrointestinal tract.

5.2. Pharmacokinetic properties

Oral or rectal administration normally results in very limited systemic diffusion. If the intestinal mucosa is normal, less than 5% of the administered dose is found in urine and the rest is eliminated in faeces. On the other hand if the mucosa is damaged, absorption is increased. In the event of perforation, it is total and rapid, with diffusion into the peritoneal cavity, and the product is eliminated in urine (see Section 4.4).

5.3 Preclinical safety data

With oral use (negligible systemic exposure), preclinical data showed no particular risk for humans based on the basis of conventional toxicity studies. With intravenous use (systemic exposure), effects were only observed in animals at doses that were well above the maximum exposure in humans, and consequently have little clinical significance.

6. PHARMACEUTICAL DATA

6.1 List of excipients

Meglumine, sodium calcium edetate, sodium dihydrogen phosphate dihydrate, disodium phosphate dodecahydrate, saccharin sodium, citrus flavour, purified water.

6.2. Incompatibilities

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

6.3. Shelf life

3 years

6.4. Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5. Nature and contents of container

Glass vial / bottle
50 and 100 mL glass vials.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MANUFACTURER

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F-95943 Roissy CdG cedex
France

8. MARKETING AUTORISATION NUMBER(S)

117-64-25639-05

9. REGISTRATION HOLDER

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10. DATE OF APPROVAL/REVISION

The format of this leaflet has been defined by the MOH and its content has been checked and approved- June 2014