1. NAME OF THE MEDICINAL PRODUCT

Irenat Drops
300 mg sodium perchlorate, oral drops
Sodium perchlorate monohydrate

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution (approximately 15 drops) contains 344.2 mg sodium perchlorate monohydrate (equivalent to 300 mg sodium perchlorate)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral drops

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of hyperthyroidism, for thyroid blockade in the context of radionuclide studies of other organs using radioactively labelled iodine or of immunoscintigraphy to detect tumours using antibodies labelled with radioiodine. For the detection of a congenital iodine organification defect (perchlorate discharge test).

4.2 Posology and method of administration

Posology

Adults receive 4-5 x 10 Irenat drops daily (equivalent to 800-1000 mg sodium perchlorate) or, exceptionally, 5 x 15 Irenat drops daily (equivalent to 1500 mg sodium perchlorate) as an initial dose for the first 1-2 weeks. The mean maintenance dose is 4 x 5 Irenat drops (equivalent to 400 mg sodium perchlorate) per day.

Children between the ages of 6 and 14 are treated throughout with a dose of 3-6 x 1 or 4-6 x 2 Irenat drops (equivalent to 60-240 mg sodium perchlorate) daily.

When used for the perchlorate discharge test following administration of the dose of radioiodine tracer, a single dose is given of 30-50 Irenat drops (equivalent to 600-1000 mg sodium perchlorate) or 300 mg-600 mg/m^2 body surface area in children.

As pretreatment for radionuclide studies not involving the thyroid itself and using radioactively labelled drugs or antibodies containing iodine or technetium, Irenat drops should be administered at doses of 10 – 20 drops (equivalent to 200-400 mg sodium perchlorate) and, in isolated cases, up to 50 drops (equivalent to 1000 mg sodium perchlorate) so as to reduce exposure of the thyroid to radiation and to block uptake of radionuclide into certain compartments.

Method of administration

In view of possible gastrointestinal side effects, Irenat drops should be taken with sufficient water, preferably after eating and, on account of the short duration of action, in 4-6 divided doses over the day.

The duration of use is dependent on the indication and is guided by the clinical picture and tests of thyroid function during treatment.

If remission has not occurred after 2 years of antithyroid therapy or there has already been a recurrence of the hyperthyroidism, patients should be advised of other treatment options (strumectomy / radioiodine therapy) appropriate to their age.

For thyroid blockade prior to radionuclide imaging of other organs (e.g. cerebral scintigraphy) and if radioactively labelled iodine or technetium are being used as the tracer, it is advisable for Irenat drops to be taken daily for 4 days before and, in view of the rebound phenomenon, for 2 to 3 weeks after administration of the nuclide, in combination with thiourea derivatives, to reduce exposure of the thyroid to radiation.

4.3 Contraindications

Irenat drops must not be taken in the following circumstances:
- retrosternal goitre,
- hypersensitivity to perchlorates or to any of the excipients listed in section 6.1;
- if administration of perchlorate has previously given rise to blood count changes, particularly
- agranulocytosis,
- during administration of high-dose iodide in preparation for surgery.

4.4 Special warnings and precautions for use

Regular and repeated monitoring of thyroid function is necessary during antithyroid therapy so as to allow adjustment of the dosage of Irenat drops to the patient's changing metabolism and to avoid over-treatment, which might lead to growth of a goitre and symptoms of hypothyroidism. There is a particular risk of adverse consequences of an inappropriately high dose in the case of intrathoracic goitre. All patients must be informed of the need for regular monitoring of blood count.
Falsely low concentrations of ionised calcium may be measured while using Irenat drops as a result of interference with the electrolyte electrode of blood gas analysers.

4.5 Interaction with other medicinal products and other forms of interaction

Uptake of radioiodine or ^{99m}Tc-pertechnetate is dose-dependently inhibited by perchlorate. The ability of TSH to stimulate radioiodine uptake is not affected by perchlorate.

If perchlorate is used concomitantly with propylthiouracil or thiamazole / carbimazole as antithyroid therapy, the antithyroid effect is enhanced, as the sites of action of the sodium perchlorate and the thiourea derivatives are different.

Concomitant administration of thiamazole causes a positive perchlorate discharge test (even in patients with hyperthyroidism and healthy subjects) as a result of inhibition of iodine organification.

Concomitant administration of iodine (e.g. iodine-containing medicines or radiographic contrast agents, perioperative use of high-dose iodide) reduces the effect of Irenat drops.

4.6 Fertility, pregnancy and lactation

Irenat drops should not be taken during pregnancy, as insufficient experience is available regarding a possible risk to the unborn child. Irenat drops cross the placenta to the fetus unhindered. The fetal thyroid gland may react more sensitively to antithyroid drugs than an adult thyroid.
No studies are available on secretion of sodium perchlorate in breast milk. If treatment with Irenat drops is necessary during lactation, breast-feeding should be ceased.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

Evaluation of undesirable effects is based on the following frequencies:

common	(≥1% to <10%)
uncommon	(≥0.1% to <1%)
rare	(≥0.01% to <0.1%)
very rare	(<0.01% or unknown)

The occurrence of undesirable effects is dose-dependent.

Common (≥1% to <10%)
- transient rash,
- nausea or retching,
- dry mouth, pharyngeal irritation,
- lymphadenopathy,
- leukopenia,
- purpura,
- febrile arthralgia,
- drug fever.

Uncommon (≥0.1% to <1%)
- initial diarrhoea,
- mild muscle cramps,
- burning in the feet,
- heavy-headedness,
- eosinophilia,
- pruritus,
- jaundice.

An uncommon occurrence is agranulocytosis, which usually resolves rapidly and without sequelae on discontinuing Irenat drops.

Very rare (<0.01%)
- agranulocytosis with a fatal outcome,
- thrombocytopenia or aplastic anaemia with a fatal outcome (incidence approximately 0.1%),
- minimal albuminuria,
- nephrotic syndrome, partially or fully reversible,
- hair loss,
- acne,
- generalised dermatitis,
- urticaria,
- liver damage with acute liver failure,
- erythema nodosum with febrile episodes, antinuclear and anti-erythrocyte antibodies and eosinophilia,
- perforation of a duodenal ulcer.

These extremely rare changes have usually been observed during ongoing treatment with perchlorate, although a causal association could not be proven.

4.9 Overdose

If Irenat drops are taken undiluted, they may (e.g. in children) have a severe local irritant effect, with symptoms such as vomiting, abdominal pain and diarrhoea.

Acute fatal intoxication with perchlorates is not known. Sodium perchlorate is tolerated in quantities of up to several grams. There is no known information on the usefulness of detoxification measures such as gastric lavage, forced diuresis, etc.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: thyroid/antithyroid drugs, ATC code: H03BC

Perchlorate competitively inhibits the thyroid's iodine uptake mechanism, iodination and affects iodisation by flushing the thyroid of iodide that is accumulating but has not yet been incorporated into a thyroglobulin molecule.

Re-utilisation of iodide released outside the thyroid during deiodination of thyroid hormone is also inhibited.

The uptake of iodide split off on administration of iodinated contrast agents may likewise be competitively inhibited by perchlorate. The same applies to uptake of technetium pertechnetate.

Perchlorate takes effect wherever, as in the thyroid, there is an active iodine transport mechanism (e.g. in the salivary gland) and renal excretion of iodide is also increased.

The antithyroid effect is based on the occurrence of iodine depletion.

5.2 Pharmacokinetic properties

Absorption of perchlorate occurs within a matter of minutes. The onset of action in thyroid cells after oral administration is very rapid. After a single dose, the blockade of iodine uptake lasts only a few hours. It is shortened in hyperthyroidism, which means that several doses per day are necessary in order to maintain effective serum concentrations.

When administered as an adjunct to radionuclide scans, the blockade of radionuclide uptake persists even after the subsequent fall in serum perchlorate concentration.

The half-life of perchlorate in humans is not precisely known. Peak tissue levels in the thyroid are attained after 4 hours.

Perchlorate binds to albumin. It is not metabolised *in vivo* and is excreted rapidly and almost completely unchanged via the renal route; > 95% is eliminated after 72 hours.

5.3 Preclinical safety data

a) Acute toxicity
Oral administration of 1 or 2 g showed no toxic effects in humans.

I.v. injection of 250 mg sodium perchlorate in rabbits had no toxic effects, although intracardiac injection of 500 mg induced transient hind leg paralysis.

b) Chronic toxicity
Doses of 250 mg/kg body weight for 40 weeks resulted in no toxic adverse effects in animal studies. In mice, toxic phenomena such as signs of paralysis, skeletal changes, exophthalmos, reduced reactions and hair loss have been described dose-dependently at or above a dosage of 1460 mg/kg BW.

c) Mutagenic and carcinogenic potential
No mutagenicity studies are available for sodium perchlorate.

In rats, the extrathyroid tumour rate on discontinuous long-term treatment with high doses of perchlorate was within the range of the spontaneously expected tumour rate.

Polymorphic changes to breast and thyroid are described, although in no instances was the threshold for malignant changes crossed in animal studies.

d) Reproductive toxicology
Insufficient animal studies are available to be able to rule out a possible embryotoxic/fetotoxic effect of sodium perchlorate.

In the rat, oral administration of a 1% potassium perchlorate solution did not interfere with either implantation or survival of the embryo up to day 13 p. c.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ammonium chloride, magnesium chloride, calcium chloride, purified water

6.2 Incompatibilities

None known

Miscellaneous
Irenat drops should be discontinued at least 3 days prior to thyroid scintigraphy or measurement of radionuclide uptake.

Use during pregnancy and lactation: see section 4.6.

6.3 Shelf life

The shelf life is 4 years. Once opened, vials should not be used for longer than 26 weeks at room temperature.

This medicinal product is not to be used after the expiry date.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Irenat drops are available in a vial containing 40 ml solution.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

6044463.00.00

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09.10.1996
Date of latest renewal: 22.11.2001

10. DATE OF REVISION OF THE TEXT

10/2011

11. GENERAL CLASSIFICATION FOR SUPPLY

Prescription-only