

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Euthyrox[®] 50 microgram Euthyrox[®] 100 microgram

Tablets

The active ingredient: Levothyroxine sodium 50 or 100 mcg.
Inactive ingredients – see section 6.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, refer to the doctor or pharmacist. Keep this leaflet within reach; you may need to read it again. This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar. If you experience any side effects, refer to your doctor or pharmacist. This includes any possible side effects not included in this leaflet. See section 4.

1. WHAT IS THE MEDICINE INTENDED FOR

Levothyroxine, the active substance of Euthyrox, is a synthetic substitute of the natural hormone produced by the thyroid gland, and is used to treat diseases or dysfunction of the thyroid gland. Levothyroxine has an activity identical to that of the natural hormone produced by the thyroid gland. Euthyrox, in various dosages, is used to treat the following conditions:

- benign enlargement of the thyroid gland (benign goitre – swelling of the neck due to enlargement of the thyroid gland) in patients with normal thyroid function
- prevention of recurrence of goitre after surgery
- as a substitute for the natural hormone produced by the thyroid gland, if your thyroid gland does not produce enough thyroxine
- suppression of tumor regrowth in patients with thyroid cancer
- to balance the levels of the hormone produced by the thyroid gland, when hyperthyroidism is treated with medicines that inhibit thyroid gland activity

At a dosage of 100 mcg and above, Euthyrox is used to test thyroid function. The dosages are listed in section 3.

Therapeutic group: Thyroid gland hormone.

2. BEFORE USING THE MEDICINE

In order to ensure the continuity of treatment with preparations containing levothyroxine sodium, switching from one levothyroxine sodium preparation to another should only be done with personal medical consultation and with close monitoring of the patient.

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredient or to any of the other ingredients contained in the medicine (see section 6)
- you suffer from untreated dysfunction of the adrenal gland or pituitary gland or untreated hyperthyroidism (thyrotoxicosis)
- you suffer from a severe heart disease (myocardial infarction or inflammation of the heart)

Do not use this medicine together with medicines that inhibit thyroid activity if you are pregnant (see "Pregnancy and breastfeeding" section below).

Special warnings regarding use of the medicine

Before starting treatment with Euthyrox, tell the doctor if you suffer from any of the following heart diseases:

- disturbed blood flow in the coronary blood vessels (angina pectoris)
- heart failure
- rapid and irregular heartbeat
- high blood pressure
- fatty deposits on the arterial walls (arteriosclerosis)

In these conditions, you should be medically controlled **before** you start taking Euthyrox or before a thyroid suppression test is performed. The levels of hormone that your thyroid gland produces **must** be checked frequently during treatment with Euthyrox. If you are not sure whether any of these conditions apply to you, or if you have any of these diseases but still are not receiving treatment for them, contact your doctor.

Your doctor will determine if you suffer from dysfunction of the adrenal, pituitary or thyroid gland with uncontrolled over-production of thyroid hormones (thyroid autonomy), since in such cases, you must be medically controlled before you start taking Euthyrox or before a thyroid suppression test is performed.

When starting treatment with levothyroxine in premature babies with a very low birth weight, frequently monitor blood pressure, since a rapid drop in blood pressure (circulatory failure) may occur.

An imbalance in thyroid hormones may occur if you need to change your medicine to another levothyroxine-containing preparation. Refer to your doctor if you have questions about switching your medicine. Frequent monitoring (clinical and biological) is necessary during the transition period. Tell the doctor if you experience any side effects since this may indicate a need to adjust (increase or decrease) the dosage.

Tell the doctor:

- If you are in menopause or post-menopause. Due to the risk of osteoporosis, regular checks of your thyroid function may be necessary.
- Before starting, stopping or changing treatment with Orlistat (a medicine used to treat obesity). You may need to be checked more frequently. The dosage may also have to be readjusted.
- If you experience signs of psychotic disorders; you may have to be checked more frequently. The dosage may also have to be readjusted.

Do not use thyroid hormones for weight reduction. Taking thyroid hormones will not cause you to lose weight if your thyroid hormone levels are within the normal range. Severe or even life-threatening side effects may occur if you increase the dosage without consulting your doctor.

Do not take high dosages of thyroid hormones together with certain medicines for weight reduction, such as amfepramone, cathine and phenylpropranolamine, as the risk of severe or even life-threatening side effects may increase.

Drug interactions

If you are taking, have recently taken or may take, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. It is especially important to inform the doctor or pharmacist if you are taking:

Euthyrox may affect the activity of the following medicines:

- Anti-diabetic medicines (blood sugar-lowering medicines): Euthyrox may **reduce** the effect of the anti-diabetic medicine you are taking; therefore, you may need additional blood sugar level tests, especially at the start of Euthyrox treatment. During treatment with Euthyrox, the dosage of the anti-diabetic medicine you are taking may need to be adjusted.
- Coumarin derivatives (medicines used to prevent blood clotting): Euthyrox may **intensify** the effect of these medicines. This may increase the risk of bleeding, especially in elderly people. You may therefore need regular checks of your blood clotting values at the start of and during Euthyrox treatment. During treatment with Euthyrox, the dosage of the medicine you are taking from the coumarin family may need to be adjusted.

Make sure that you adhere to the recommended time intervals, if you are taking the following medicines:

- Medicines used to bind bile acids and to lower high cholesterol levels (such as cholestyramine or colestipol): Make sure that you take Euthyrox 4 to 5 hours **before** taking these medicines, as these may block the uptake of Euthyrox from the intestine.
- Antacids (medicines used to relieve digestion problems), sucralfate (for the treatment of gastric or intestinal ulcers), other aluminium-containing medicines, iron-containing medicines, calcium-containing medicines: Make sure that you take Euthyrox at least 2 hours **before** taking these medicines, as these may otherwise reduce the effect of Euthyrox.

Tell your doctor or pharmacist if you are taking, have recently taken or may take any of the medicines listed below, as they may **reduce** the effect of Euthyrox:

- Propylthiouracil (a medicine to treat hyperthyroidism)
- Glucocorticoids (steroidal anti-allergic and anti-inflammatory medicines)
- Beta-blockers (blood pressure-lowering medicines that are also used to treat heart diseases)
- Sertraline (a medicine to treat depression)
- Chloroquine or proguanil (a medicine to prevent or treat malaria)
- Medicines that activate certain liver enzymes such as barbiturates (sedatives or sleeping pills) or carbamazepine (a medicine to treat epilepsy, also used to regulate certain types of pain and to control mood disturbances)
- Estrogen-containing medicines used for hormone replacement therapy during and after menopause or for contraception
- Sevelamer (a phosphate-binding medicine used to treat patients with chronic renal failure)
- Tyrosine kinase inhibitors (anti-cancer and anti-inflammatory medicines)
- Orlistat (a medicine used to treat obesity)

Tell your doctor or pharmacist if you are taking, have recently taken or may take any of the medicines listed below, as they may **intensify** the effect of Euthyrox:

- Salicylates (medicines used to relieve pain or to reduce fever)
- Dicumarol (a medicine to prevent blood clotting)
- Furosemide in high doses of 250 mg or higher (a diuretic medicine)
- Clofibrate (a medicine to lower blood lipid levels)

Tell your doctor or pharmacist if you are taking, have recently taken or may take any of the medicines listed below, as they may **affect** the activity of Euthyrox:

- Ritonavir, indinavir, lopinavir (protease inhibitors, medicines to treat HIV infection)
 - Phenytoin (a medicine to treat epilepsy)
- You may need regular checks of your thyroid hormone values. The Euthyrox dosage may have to be adjusted.

Tell your doctor if you are taking amiodarone (a medicine used to treat irregular heartbeat), because this medicine may influence the function and activity of your thyroid gland.

If you need to undergo an x-ray or other diagnostic examinations with iodine-containing contrast agents, tell your doctor that you are taking Euthyrox. You may be required to receive an injection that may influence your thyroid function.

Use of the medicine and food

Tell your doctor if you eat soy products, especially if you alter the proportion of soy products you consume in your diet. Soy-containing products may reduce the uptake of Euthyrox from the intestines, and therefore, the Euthyrox dosage you take may need to be adjusted.

Pregnancy and breastfeeding

If you are pregnant, continue taking Euthyrox. Speak to your doctor about your pregnancy, as the dosage may need to be adjusted.

If you take Euthyrox together with an anti-thyroid medicine to treat overproduction of thyroid hormones, your doctor will advise you to stop Euthyrox treatment when you are pregnant.

If you are breastfeeding, continue taking Euthyrox as directed by your doctor. The amount of medicine that is excreted into breast milk is too small to affect your baby.

Driving and using machines

Studies on this medicine's effect on the ability to drive or operate machines have not been performed. Since levothyroxine is identical to the hormone naturally produced by the thyroid gland, it is not expected that Euthyrox will impair the ability to drive or operate machines.

Important information regarding some of the ingredients of the medicine This medicine contains lactose. If you know that you suffer from an intolerance to certain types of sugar, do not take Euthyrox before you consult your doctor. See section 6 "Further information".

3. HOW SHOULD YOU USE THE MEDICINE

Always use the preparation in accordance with the doctor's instructions. Check with the doctor or pharmacist if you are not sure. The dosage and treatment regimen will be determined by the doctor only.

Your doctor will determine the suitable dose for you based on different examinations and laboratory tests. You will generally start with a low dose, which will be increased every 2 to 4 weeks, until the final individual dose is determined. During the first few weeks of treatment, schedule appointments for laboratory tests. The test results will serve to determine the dose that suits you.

If your baby was born with under-activity of the thyroid gland (hypothyroidism), your doctor may recommend to start with a higher dose as rapid hormone replacement is important. The recommended initial dose is 10 to 15 micrograms per kg body weight for the first 3 months. Thereafter, your doctor will determine the dose that suits your baby.

The usual dose ranges are listed in the table below. A lower dose may, however, be adequate if:

- you are an elderly patient
- you suffer from a heart disease
- you suffer from severe or long-standing hypothyroidism
- you have low body weight or a large goitre

<i>Indications of Euthyrox</i>	<i>Recommended daily dosage of Euthyrox</i>	
• To treat benign enlargement of the thyroid gland (benign goitre) in patients with normal thyroid function	75 to 200 microgram	
• To prevent recurrence of goitre after surgery	75 to 200 microgram	
• To replace the natural thyroid hormone produced by the thyroid gland, if your thyroid gland does not produce enough thyroxine	Adults	Children
	- Initial dose	25 to 50 microgram
- Maintenance dose	100 to 200 microgram	100 to 150 microgram per m ² of body surface area
• To suppress tumor growth in patients with thyroid cancer	150 to 300 microgram	
• To balance the levels of the hormone produced by the thyroid gland, when over-activity of the thyroid is treated with anti-thyroid medicines	50 to 100 microgram	
• To test thyroid function	150 microgram: Treatment initiation 4 weeks before the test: start with 75 microgram for two weeks, and then 150 microgram until the test	
	200 microgram (2 Euthyrox 100 microgram tablets): Start of treatment: 2 weeks before the test	

Do not exceed the recommended dose

Instructions for use:

- Euthyrox tablets are meant for oral intake.
- Always take the entire daily dose on an empty stomach in the morning (at least half an hour before breakfast), preferably with some liquid, for example, half a glass of water.
- Infants should be given the entire daily dose of Euthyrox at least half an hour before the first meal of the day. Immediately before use, crush the tablet and mix it with a little water, before giving it to the child with a little more liquid. Always prepare a fresh mixture as required.

The tablet has a score line for dividing.

Duration of treatment:

The duration of treatment depends on the medical condition for which you are being treated with Euthyrox. Your doctor will, therefore, discuss with you how long you will need to take this medicine. Most patients need to take Euthyrox for their entire life.

If you accidentally take a higher dosage, you may experience symptoms such as rapid heartbeat, anxiety, agitation or involuntary movements. Seizures may occur in isolated cases in patients with neurological disorders such as epilepsy. In patients at risk for psychotic disorders, symptoms of severe mental disorders (psychoses) may occur. Refer to your doctor if you notice any of the effects listed here.

If you took an overdose or if a child accidentally swallowed the medicine, immediately refer to the doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine

Do not take a double dose to make up for a forgotten dose. Take the next dose at the usual time.

Adhere to the treatment regimen recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with this medicine without consulting the doctor or pharmacist.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have any further questions regarding use of the medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, using Euthyrox may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

You may experience one or more of the following side effects if you take more Euthyrox than prescribed, or if the prescribed dosage is not appropriate (e.g., when the dosage is increased rapidly): Rapid or irregular heartbeat, chest pain, headache, muscle weakness or cramps, flushing (sensation of warmth and redness of the face), fever, vomiting, menstrual irregularity, pseudotumor cerebri (increased intracranial pressure), trembling, restlessness, sleep disturbances, sweating, weight loss, diarrhea.

If you experience any of these side effects, contact your doctor. Your doctor may decide to interrupt therapy for a few days or to reduce the daily dosage until the side effects disappear.

Allergic reactions to any of the ingredients of Euthyrox (see section 6 "Further information"). Allergic reactions can include rash, urticaria and swelling of the face or throat (angio-oedema). If this happens, contact your doctor immediately.

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult the doctor.

Reporting side effects:

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to an online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>

5. HOW SHOULD THE MEDICINE BE STORED

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (Exp. Date) indicated on the package. The expiry date refers to the last day of that month.
- Store below 25°C. Store in the original package to protect from light.
- Do not dispose of medicines via wastewater or household waste. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains – Lactose monohydrate, maize starch, gelatin, croscarmellose sodium, magnesium stearate.

Euthyrox tablets contain lactose:
Each Euthyrox 50 mcg tablet contains 65.948 mg lactose
Each Euthyrox 100 mcg tablet contains 65.895 mg lactose

Euthyrox tablets contain sodium:
Each Euthyrox 50 mcg tablet contains up to 19 mcg sodium
Each Euthyrox 100 mcg tablet contains up to 21 mcg sodium

- What the medicine looks like and contents of the pack – Euthyrox 50, 100 microgram tablets are white, round, flat on both sides, with a beveled edge. The upper surface of the tablet has a score line and the letters EM 50 or EM 100, respectively. Each package contains 30, 50 or 100 tablets. Not all package sizes may be marketed.

• License holder and address – Merck Serono Ltd., 18 Hakishon St., Yavne 81220

• Manufacturer and address – Merck KGaA, Darmstadt, Germany

• Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Euthyrox 50 mcg registration number 147-50-33604-00
Euthyrox 100 mcg registration number 147-51-33605-00

• Revised in August 2020.