Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Levothyroxine sodium Rowex 150 microgram tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 150 microgram levothyroxine sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

Blue, round (7 mm in diameter), tablet with a score line on one side and "150" debossed on the other side.

The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Treatment of benign euthyroid goitre
- Prophylaxis of relapse after surgery for euthyroid goitre, depending on the post-operative hormone status
- Substitution therapy in hypothyroidism
- Suppression therapy in thyroid cancer
- Diagnostic use for thyroid suppression testing

4.2 Posology and method of administration

Posology
In order to treat each patient according to his/her individual needs, tablets are available with a levothyroxine sodium content ranging from 25 to 200 microgram. Patients therefore usually need to take only one tablet per day.

The dosage recommendations given are only for guidance.

The individual daily dose should be determined on the basis of laboratory tests and clinical examinations. As a number of patients show elevated concentrations of T4 and fT4, basal serum concentration of thyroid-stimulating hormone provides a more reliable basis for following treatment course.

Thyroid hormone therapy should be started at low dose and increased gradually every 2 to 4 weeks until the full replacement dose is reached.

Paediatric population
For neonates and infants with congenital hypothyroidism, where rapid replacement is important, the initial recommended dosage is 10 to 15 micrograms per kg BW per day for the first 3 months. Thereafter, the dose should be adjusted individually according to the clinical findings and thyroid hormone and TSH values.

In older patients, in patients with coronary heart disease, and in patients with severe or long-existing hypothyroidism, special caution is required when initiating therapy with thyroid hormones, that is, a low initial dose (for example 12.5 microgram/day) should be given which should then be increased slowly and at lengthy intervals (e.g., a gradual increment of 12.5 microgram/day fortnightly) with frequent monitoring of thyroid hormones. A dosage, lower than optimal dosage giving complete replacement therapy, consequentially not resulting in a complete correction of TSH level, might therefore need to be considered.

Experience has shown that a lower dose is sufficient in low-weight patients and in patients with a large nodular goitre.

Indication	Recommended Dose (microgram levothyroxine sodium/day)				
Treatment of benign euthyroid goitre	75 - 200				
Prophylaxis of relapse after surgery for euthyroid goitre	75 - 200				
Substitution therapy in hypothyroidism in adults • initial dose • maintenance dose	25 – 50 100 - 200				
Substitution therapy in hypothyroidism in children • initial dose • maintenance dose	12.5 – 50 100 - 150 microgram/m^2 body surface				
Concomitant supplementation during anti-thyroid drug treatment of hyperthyroidism	50 - 100				
Suppression therapy in thyroid cancer	150 - 300				
Diagnostic use for thyroid suppression testing		Week 4 prior to test	Week 3 prior to test	Week 2 prior to test	Week 1 prior to test
	Levothyroxine sodium Rowex 200 microgram	-	-	1 tablet/day	1 tablet/day
	Levothyroxine sodium Rowex 100 microgram	-	-	2 tablet/day	2 tablet/day
	Levothyroxine sodium Rowex 150 microgram	1/2 tablet/day	1/2 tablet/day	1 tablet/day	1 tablet/day

Method of administration
The daily doses can be given in a single administration.

Ingestion: as a single daily dose in the morning on an empty stomach, half an hour before breakfast, preferably with a little liquid (for example, half a glass of water).

Infants receive the entire dose at once at least 30 minutes before the first meal of the day. Tablets are to be disintegrated in some water and the resultant suspension, which must be prepared freshly as required, is to be administered with some more liquid.

Duration of treatment is usually for life in the case of substitution in hypothyroidism and after strumectomy or thyroidectomy and for relapse prophylaxis after euthyroid goitre removal. Concomitant therapy of hyperthyroidism after achieving euthyroid status is indicated for the period in which the anti-thyroid drug is given.

For benign euthyroid goitre, a treatment duration of 6 months up to 2 years is necessary. If the medical treatment was not sufficient within this time, surgery or radioiodine therapy of the goitre should be considered.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Untreated adrenal insufficiency, untreated pituitary insufficiency, and untreated thyrotoxicosis.

- Treatment with levothyroxine must not be initiated in acute myocardial infarction, acute myocarditis, and acute pancarditis.

- Combination therapy of levothyroxine and an antithyroid agent for hyperthyroidism is not indicated during pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

Before starting therapy with thyroid hormones or before performing a thyroid suppression test, the following diseases or medical conditions should be excluded or treated: coronary failure, angina pectoris, arteriosclerosis, hypertension, pituitary insufficiency. Thyroid autonomy should also be excluded or treated before starting therapy with thyroid hormones. In case of adrenocortical dysfunction, this should be treated before starting the therapy with levothyroxine by adequate replacement treatment to prevent acute adrenal insufficiency (see section 4.3).

When initiating levothyroxine therapy in patients at risk of psychotic disorders, it is recommended to start at a low levothyroxine dose and to slowly increase the dosage at the beginning of the therapy. Monitoring of the patient is advised. If signs of psychotic disorders occur, adjustment of the dose of levothyroxine should be considered.

Even slight drug-induced hyperthyroidism must be avoided in patients with coronary failure, cardiac insufficiency or tachycardiac arrhythmias. Hence frequent checks of thyroid hormone parameters must be made in these cases.

In the case of secondary hypothyroidism the cause must be determined before replacement therapy is given and if necessary replacement treatment of a compensated adrenal insufficiency must be commenced.

Where thyroid autonomy is suspected a TRH test should be carried out or a suppression scintigram obtained before treatment.

Haemodynamic parameters should be monitored when levothyroxine therapy is initiated in very low birth weight preterm neonates as circulatory collapse may occur due to the immature adrenal function.

In postmenopausal women with hypothyroidism and an increased risk of osteoporosis supra-physiological serum levels of levothyroxine should be avoided, and, therefore, thyroid function should be checked closely.

Levothyroxine should not be given in hyperthyreotic states other than as concomitant supplementation during anti-thyroid drug treatment of hyperthyroidism.

Thyroid hormones should not be given for weight reduction. In euthyroid patients, treatment with levothyroxine does not cause weight reduction. Substantial doses may cause serious or even life-threatening undesirable effects. Levothyroxine in high doses should not be combined with certain substances for weight reduction, i.e., sympathomimetics (see section 4.9).

If a switch to another levothyroxine-containing product is required, there is a need to undertake a close monitoring including a clinical and biological monitoring during the transition period due to a potential risk of thyroid imbalance. In some patients, a dose adjustment could be necessary.

Hypothyroidism and / or reduced control of hypothyroidism may occur when orlistat and levothyroxine are co-administered (see section 4.5). Patients taking levothyroxine should be advised to consult a doctor before starting or stopping or changing treatment with orlistat, as orlistat and levothyroxine may need to be taken at different times and the dose of levothyroxine may need to be adjusted. Further, it is recommended to monitor the patient by checking the hormone levels in the serum.

For diabetic patients and patients under anticoagulant therapy, see section 4.5.

<u>Interferences with laboratory test</u>

Biotin may interfere with thyroid immunoassays that are based on a biotin/streptavidin interaction, leading to either falsely decreased or falsely increased test results. The risk of interference increases with higher doses of biotin.
When interpreting results of laboratory tests, possible biotin interference has to be taken into consideration, especially if a lack of coherence with the clinical presentation is observed.
For patients taking biotin-containing products, laboratory personnel should be informed when a thyroid function test is requested. Alternative tests not susceptible to biotin interference should be used, if available (see section 4.5).

Levothyroxine sodium Rowex contains sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Anti-diabetic agents

Levothyroxine may reduce the effect of antidiabetic agents. For this reason, blood glucose levels should be checked frequently at the start of thyroid hormone therapy and the dosage of the antidiabetic agent has to be adapted, if necessary.

Coumarin derivates

The effect of anti-coagulant therapy can be intensified as levothyroxine displaces anti-coagulative drugs from plasma proteins, which may increase the risk of haemorrhage, e.g., CNS or gastrointestinal bleeding, especially in elderly patients. Therefore, it is necessary for coagulation parameters to be checked regularly at the start of and during concomitant therapy. If necessary, the dosage of the anti-coagulative drug has to be adapted.

Protease inhibitors

Protease inhibitors (e.g., ritonavir, indinavir, lopinavir) may influence the effect of levothyroxine. Close monitoring of thyroid hormone parameters is recommended. If necessary, the levothyroxine dose has to be adjusted.

Phenytoin

Phenytoin may influence the effect of levothyroxine by displacing levothyroxine from plasma proteins resulting in an elevated fT4 and fT3 fraction. On the other hand phenytoin increases the hepatic metabolisation of levothyroxine. Close monitoring of thyroid hormone parameters is recommended.

Colestyramine, Colestipol

Ingestion of ion exchange resins such as cholestyramine and colestipol inhibits the absorption of levothyroxine sodium. Levothyroxine sodium should therefore be taken 4-5 hours before administration of such products.

Aluminium, iron, and calcium salts

Aluminium-containing drugs (antacids, sucralfate) have been reported in the pertinent literature as potentially decreasing the effect of levothyroxine. Drugs containing levothyroxine should therefore be administered at least 2 hours prior to the administration of aluminium-containing drugs.

The same applies to medicinal products containing iron and calcium salts.

Salicylates, dicumarol, furosemide, clofibrate

Salicylates, dicumarol, furosemide in high doses (250 mg), clofibrate and other substances can displace levothyroxine sodium from plasma proteins, resulting in an elevated fT4 fraction.

Proton pump inhibitors (PPIs)

Co-administration with PPIs may cause a decrease in the absorption of the thyroid hormones, due to the increase of the intragastric pH caused by PPIs.

Regular monitoring of thyroid function and clinical monitoring is recommended during concomitant treatment. It may be necessary to increase the dose of thyroid hormones.
Care should also be taken when treatment with PPI ends.

Orlistat

Hypothyroidism and / or reduced control of hypothyroidism may occur when orlistat and levothyroxine are taken at the same time. This could be due to a decreased absorption of iodine salts and / or levothyroxine.

Sevelamer

Sevelamer may decrease levothyroxine absorption. Therefore, it is recommended that patients are monitored for changes in thyroid function at the start or end of concomitant treatment. If necessary, the levothyroxine dose has to be adjusted.

Tyrosine kinase inhibitors

Tyrosine kinase inhibitors (e.g. imatinib, sunitinib) may decrease the efficacy of levothyroxine. Therefore, it is recommended that patients are monitored for changes in thyroid function at the start or end of concomitant treatment. If necessary, the levothyroxine dose has to be adjusted.

Propylthiouracil, glucocorticoids, beta-sympatholytics, amiodarone and iodine containing contrast media

These substances inhibit the peripheral conversion of T4 to T3. Due to its high iodine content amiodarone can trigger hyperthyroidism as well as hypothyroidism. Particular caution is advised in the case of nodular goitre with possibly unrecognized autonomy.

Sertraline, chloroquine/proguanil

These substances decrease the efficacy of levothyroxine and increase the serum TSH level.

Enzyme inducing medicinal products

Enzyme inducing medicinal products such as barbiturates, carbamazepine or products containing St John's Wort (Hypericum perforatum L.) may increase hepatic clearance of levothyroxine, resulting in reduced serum concentration of thyroid hormone.

Therefore, patients on thyroid replacement therapy may require an increase in their dose of thyroid hormone if these products are given concurrently.

Estrogens

Women using oestrogen-containing contraceptives or postmenopausal women under hormone-replacement therapy may have an increased need for levothyroxine.

Soy-containing compounds

Soy-containing compounds can decrease the intestinal absorption of levothyroxine. Therefore, a dosage adjustment of Levothyroxine sodium Rowex may be necessary, in particular at the beginning or after termination of nutrition with soy supplements.

Interferences with laboratory test

Biotin may interfere with thyroid immunoassays that are based on a biotin/streptavidin interaction, leading to either falsely decreased or falsely increased test results (see section 4.4).

4.6 Fertility, pregnancy and lactation

Treatment with levothyroxine should be given consistently during pregnancy and breast-feeding in particular. Dosage requirements may even increase during pregnancy. Since elevations in serum TSH may occur as early as 4 weeks of gestation, pregnant women taking levothyroxine should have their TSH measured during each trimester, in order to confirm that the maternal serum TSH values lie within the trimester-specific pregnancy reference range. An elevated serum TSH level should be corrected by an increase in the dose of levothyroxine. Since postpartum TSH levels are similar to preconception values, the levothyroxine dosage should return to the pre-pregnancy dose immediately after delivery. A serum TSH level should be obtained 6–8 weeks postpartum.

Pregnancy

Experience has shown that there is no evidence of drug-induced teratogenicity and/or foeto-toxicity in humans at the recommended therapeutic dose level. Excessively high dose levels of levothyroxine during pregnancy may have a negative effect on foetal and postnatal development.

Combination therapy of hyperthyroidism with levothyroxine and anti-thyroid agents is not indicated in pregnancy. Such combination would require higher doses of anti-thyroid agents, which are known to pass the placenta and to induce hypothyroidism in the infant.

Thyroid suppression diagnostic tests should not be carried out during pregnancy, as the application of radioactive substances in pregnant women is contraindicated.

Breast-feeding

Levothyroxine is secreted into breast milk during lactation but the concentrations achieved at the recommended therapeutic dose level are not sufficient to cause development of hyperthyroidism or suppression of TSH secretion in the infant.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, since levothyroxine is identical to the naturally occurring thyroid hormone, it is not expected that Levothyroxine sodium Rowex has any influence on the ability to drive and use machines.

4.8 Undesirable effects

Where the individual tolerance limit for levothyroxine sodium is exceeded or after overdose it is possible for the following clinical symptoms typical of hyperthyroidism to occur, especially if the dose is increased too quickly at the start of treatment: cardiac arrhythmias (e.g. atrial fibrillation and extrasystoles), tachycardia, palpitations, anginal conditions, cephalalgia, muscular weakness and cramps, flushing, fever, vomiting, disorders of menstruation, pseudotumor cerebri, tremor, restlessness, insomnia, hyperhidrosis, weight loss, diarrhoea.

In such cases the daily dose should be reduced or the medication withdrawn for several days. Therapy may be carefully resumed once the adverse reactions have disappeared.

In case of hypersensitivity to any ingredients of Levothyroxine sodium Rowex allergic reactions particularly of the skin (rash, urticaria) and the respiratory tract may occur. Cases of angioedema have been reported.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system: HPRA Pharmacovigilance; website: www.hpra.ie.

4.9 Overdose

An elevated T3 level is a reliable indicator of overdose, more than elevated T4 or fT4 levels.
After overdose the symptoms of a sharp increase in the metabolic rate occur (see section 4.8).

Depending on the extent of the overdose it is recommended that treatment with the tablets is interrupted and that tests are carried out.

Symptoms consisting of intense beta-sympathomimetic effects such as tachycardia, anxiety, agitation and hyperkinesia can be relieved by betablockers. After extreme doses plasmapheresis may be of help.

In predisposed patients isolated cases of seizures have been reported when the individual dose tolerance limit was exceeded.

Overdose of levothyroxine may result in symptoms of hyperthyroidism and could lead to acute psychosis, especially in patients at risk of psychotic disorders.

Several cases of sudden cardiac death have been reported in patients with long years of levothyroxine abuse.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Thyroid hormones, ATC code: H03A A01

The synthetic levothyroxine contained in Levothyroxine sodium Rowex is identical in effect with the naturally occurring major hormone secreted by the thyroid. It is converted to T3 in peripheral organs and, like the endogenous hormone, develops its specific effects at the T3 receptors. The body is not able to differentiate between endogenous and exogenous levothyroxine.

5.2 Pharmacokinetic properties

Orally given levothyroxine is absorbed almost exclusively in the upper small intestine. Depending on the galenical formulation absorption amounts up to 80 %. t_{max} is approximately 5 to 6 hours.

Following oral administration the onset of action is seen after 3-5 days. Levothyroxine exhibits an extremely high binding to specific transport proteins of about 99.97 %. This protein hormone binding is not covalent and so the bound hormone in plasma is in continuous and very rapid exchange with the fraction of the free hormone.

Due to its high protein binding levothyroxine undergoes neither haemodialysis nor haemoperfusion.

The half-life of levothyroxine is on average 7 days. In hyperthyroidism it is shorter (3-4 days) and in hypothyroidism it is longer (approx. 9-10 days). The volume of distribution amounts to about 10-12 l. The liver contains 1/3 of the entire extra-thyroidal levothyroxine, which is rapidly exchangeable with the levothyroxine in serum. Thyroid hormones are metabolized mainly in the liver, kidneys, brain and muscles. The metabolites are excreted with urine and faeces. The overall metabolic clearance for levothyroxine is about 1.2 l plasma/day.

5.3 Preclinical safety data

Acute toxicity
Levothyroxine has a very slight acute toxicity.

Chronic toxicity
The chronic toxicity of levothyroxine was studied in various animal species (rat, dog). At high doses, signs of hepatopathy, increased occurrence of spontaneous nephroses as well as changes in organ weights were observed in rats.

Reproduction toxicity
Reproductive toxicity studies in animals have not been performed.

Mutagenicity
No information is available on this subject. So far no indications of any kind have become known suggesting damage to the progeny due to changes in the genome caused by thyroid hormones.

Carcinogenicity
No long-term animal studies have been carried out with levothyroxine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose (E460(i))
Pregelatinized starch (E1422)
Silica, Colloidal Anhydrous (E551)
Talc (E553b)
Magnesium stearate (E572)
Indigo carmine lake (E132)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Blister pack
Store below 25°C.

HDPE bottle pack
This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Blister pack

oPA/Alu/PVC//Alu blisters containing 28, 30, 50, 56, 98 and 100 tablets.

HDPE bottle pack

HDPE bottle with a child-resistant polypropylene screw closure and oxygen absorbing canister containing 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

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

Rowex Limited,
Newtown
Bantry
Co. Cork
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0711/354/006

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28th November 2025

10 DATE OF REVISION OF THE TEXT

June 2026