NEW ZEALAND DATA SHEET

1 PRODUCT NAME

ELTROXIN® (25 mcg, 50 mcg, 75 mcg, 100 mcg tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Tablets containing levothyroxine sodium as the active ingredient:
25 microgram tablet contains 27.8 microgram of levothyroxine sodium pentahydrate equivalent to 25 microgram of levothyroxine sodium.*
50 microgram tablet contains 55.6 microgram of levothyroxine sodium pentahydrate equivalent to 50 microgram of levothyroxine sodium.
75 microgram tablet contains 83.4 microgram of levothyroxine sodium pentahydrate equivalent to 75 microgram of levothyroxine sodium.*
100 microgram tablet contains 111.3 microgram of levothyroxine sodium pentahydrate equivalent to 100 microgram of levothyroxine sodium.
(* strengths not currently available)

100 mcg levothyroxine is equivalent in activity to 20 to 30 mcg liothyronine or 60 mg thyroid BP.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Eltroxin 25 microgram (0.025 mg) tablets are white, round, biconvex tablets, debossed with '25' on one face and bisected on the other.

Eltroxin 50 microgram (0.05 mg) tablets are white, round, bevelled tablets, debossed with '50' on one face and 'L01' on the other.

Eltroxin 75 microgram (0.075 mg) tablets are white, round, bevelled tablets, debossed with '75' on one face and 'L02' on the other.

Eltroxin 100 microgram (0.1 mg) tablets are white, round, bevelled tablets, debossed with '100' on one face and 'L10' on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Levothyroxine is indicated for the treatment of hypothyroidism.

4.2 Dose and method of administration

Dose

Thyroxine has a narrow therapeutic index. Appropriate thyroxine dosage is based upon clinical assessment and laboratory monitoring of thyroid function tests. During the initial titration period, careful dosage titration and monitoring is necessary to avoid the consequences of under- or over-treatment. The symptoms of excessive thyroxine dosage are the same as many features of endogenous thyrotoxicosis.

If the dose of thyroxine is increased too rapidly, symptoms such as diarrhoea, nervousness, rapid pulse, insomnia, tremors and sometimes anginal pain where there is latent myocardial ischaemia may occur, and the dosage must be reduced or withheld for a day or two, then restarted at a lower level. A pre-therapy ECG is valuable, as changes induced by hypothyroidism may be confused with ECG evidence of ischaemia.

Thyroxine tablets should preferably be taken on an empty stomach.

Missed dosage – If a scheduled daily dose is missed, the dose should be taken as soon as the patient remembers, unless it is almost time for the patient's next dose. Two doses should not be taken together.

In patients whose medications include levothyroxine and known interfering agents, administration should be separated by at least 4 hours (see Section 4.5 Interactions).

Adults
Initially 50 to 100 micrograms daily and adjusted at four or six week intervals by 50 micrograms until attainment of clinical and biochemical euthyroidism. This may require doses of 100 to 200 micrograms daily.

Patients over 50 years, elderly, or with diabetes or cardiac symptoms
With patients aged over 50 years, it is not advisable to exceed 50 micrograms a day initially. Where there is cardiac disease 12.5 to 25 micrograms is more suitable. In this condition the daily dosage may be slowly increased by 12.5 or 25 micrograms increments at intervals of perhaps four weeks.

The initial dose and any dose increments should be carefully chosen in elderly and in patients with cardiac symptoms, diabetes mellitus or insipidus: too high initial dose or too rapid increase may cause or aggravate symptoms of angina, arrhythmias, myocardial infarction, cardiac failure or a sudden raise in blood pressure.

Paediatric population
In congenital hypothyroidism and juvenile myxoedema, the largest dose consistent with freedom from toxic effects should be given. The dosage is guided by clinical response, growth assessment and appropriate thyroid function tests - clinically normal pulse rate and absence of diarrhoea or constipation are the most useful indicators. Thyrotrophin levels may remain elevated during the first year of life in children with neonatal hypothyroidism due to resetting of the hypothalamic-pituitary axis.

For infants with congenital hypothyroidism a suitable starting dose is 25 micrograms levothyroxine sodium. This may be slowly increased by increments of 12.5-25 micrograms every two to four weeks until optimal response is achieved. The same dosing regimen applies to juvenile myxoedema, except that the starting dose for children older than one year may be 2.5 to 5 micrograms/kg/day. The calculated daily dose equivalent should be rounded to the nearest 12.5 or 25 micrograms to determine the actual prescribed dose.

Method of administration
Eltroxin tablets should be swallowed whole where possible, and taken with a full glass of water.

4.3 Contraindications

Hypersensitivity to any component of the preparation.
Thyrotoxicosis.
Acute myocardial infarction
Acute myocarditis
Acute pancarditis.
During pregnancy, combination of levothyroxine and antithyroid agents for the treatment of hyperthyroidism is contraindicated (see section 4.6 Fertility, pregnancy and lactation).

4.4 Special warnings and precautions for use

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

Adrenal insufficiency
Treatment with thyroxine in patients with panhypopituitarism or other causes predisposing to adrenal insufficiency may cause reactions including dizziness, weakness, malaise, weight loss, hypotension and adrenal crisis. It is advisable to initiate corticosteroid therapy before giving levothyroxine sodium in these cases.

Elderly / cardiac symptoms / diabetes
Special care is needed in the elderly and in patients with symptoms of myocardial insufficiency or ECG evidence of myocardial infarction or ischaemia and also those with diabetes mellitus or insipidus.

Levothyroxine raises blood sugar levels and this may upset the stability of patients receiving antidiabetic agents.

Effects on bone mineral density
Subclinical hyperthyroidism may be associated with bone loss. In women, long-term levothyroxine sodium therapy has been associated with increased bone resorption, thereby decreasing bone mineral density, especially in post-menopausal women on greater than replacement doses or in women who are receiving suppressive doses of levothyroxine sodium. The increased bone resorption may be associated with increased serum levels and urinary excretion of calcium and phosphorus, elevations in bone alkaline phosphate and suppressed serum parathyroid hormone levels. To minimize the risk of osteoporosis, dosage of levothyroxine should be titrated to the lowest possible effective level.

Paediatric population
Parents of children receiving levothyroxine should be advised that partial loss of hair may occur during the first few months of therapy, but this effect is usually transient and subsequent regrowth usually occurs.

Thyroxine should not be used for the treatment of obesity or weight loss
In euthyroid patients, doses within the range of daily hormonal requirements are ineffective for weight reduction. Larger doses may produce serious or even life threatening manifestations of toxicity, particularly when given in association with sympathomimetic amines such as those used for anorectic effects.

Malabsorption syndromes
Thyroxine absorption is decreased in patients with malabsorption syndromes. It is advised to treat the malabsorption condition to ensure effective thyroxine treatment with regular thyroxine dose.

Myxoedema
Patients with myxoedema have an increased sensitivity for thyroid hormones; in these patients the starting dose should be low with slow dosing increments.

Pregnancy
During pregnancy, serum thyroxine levels may decrease with a concomitant increase in serum TSH level to values outside the normal range. Patients taking levothyroxine should have their TSH measured during each trimester. An elevated serum TSH level should be corrected by an increase in the dose of levothyroxine. Since postpartum TSH serum levels are similar to preconception values, levothyroxine dosage can be reduced to the pre-pregnancy dose.

Neonates

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.

Effects on laboratory tests

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.

In 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.

4.5 Interaction with other medicines and other forms of interaction

Levothyroxine increases the effect of anticoagulants and it may be necessary to reduce the dose of anticoagulant if excessive hypoprothrombinaemia and bleeding are to be avoided.

Phenytoin levels may be increased by levothyroxine.

Anticonvulsants such as carbamezapine and phenytoin enhance the metabolism of thyroid hormones and may displace them from plasma proteins. Initiation or discontinuation of anticonvulsant therapy may alter levothyroxine sodium dose requirements. Enzyme inducers like rifampicin and barbiturates increase the metabolism and excretion of thyroxine, resulting in increased thyroxine requirements.

Medicines that (partially) inhibit the peripheral transformation of T4 to T3 – like propranolol, amiodarone, lithium, iodide, oral contrast agents, propylthiouracil and glucocorticoids – lower the T3 level and therefore also the therapeutic effect.

If co-administered with cardiac glycosides, adjustment of dosage of cardiac glycoside may be necessary.

The effects of sympathomimetic agents are also enhanced.

Levothyroxine increases receptor sensitivity to catecholamines thus accelerating the response to tricyclic antidepressants.

Cholestyramine, calcium-, aluminium-, magnesium-, iron supplements, polystyrene sulfonates, sucralfate, lanthanum, bile acid sequestrants (e.g. colestipol), anion/cation exchange resins (e.g. kayexalate, sevelamer), and proton pump inhibitors decrease the absorption of thyroxine. Separate the dosages of thyroxine and the above mentioned medicines as much as possible to avoid interaction in the stomach or the small bowel.

Soy-containing compounds and high-fibre diets can decrease the intestinal absorption of thyroxine. Therefore, a dosage adjustment of thyroxine may be necessary, in particular at the beginning or after termination of nutrition with soy supplements.

Weight loss drugs: Orlistat may decrease levothyroxine absorption which may result in hypothyroidism. To avoid this orlistat and levothyroxine should be administered at least 4 hours apart. Regular monitoring for changes in thyroid function is required.

Thyroxine can increase the need for insulin or oral antidiabetics in patients with diabetes. Lowering the dose of thyroxine can cause hypoglycemia if the insulin or oral antidiabetics dose remains unchanged.

Co-administration of oral contraceptives, as well as a number of other drugs, including oestrogen, tamoxifen, clofibrate, methadone and 5-fluorouracil may increase serum concentration of thyroxine-binding globulin, and therefore increase thyroxine dosage requirements.

Reports indicate that some HMG-CoA reductase inhibitors (statins), such as simvastatin and lovastatin, may increase thyroid hormone requirements in patients receiving thyroxine therapy. It is unknown if this occurs with all statins. Close monitoring of thyroid function and appropriate thyroxine dose adjustments may be necessary when thyroxine and statins are co-prescribed.

A number of drugs may decrease serum concentration of thyroxine-binding globulin, and therefore decrease thyroxine dosage requirements, including androgens and anabolic steroids.

False low plasma concentrations have been observed with concurrent anti-inflammatory treatment such as phenylbutazone or acetylsalicylic acid and thyroxine therapy. Administration of acetylsalicylic acid together with thyroxine results in an initial transient increase in serum free T4. Continued administration results in normal free T4 and TSH concentrations, and therefore, patients become clinically euthyroid.

Treatment with tyrosine kinase inhibitors (eg imatinib and sunitinib) was associated with increased thyroxine dosage requirements in hypothyroid patients.

The concurrent use of sertraline can reduce serum levels of thyroxine (with concomitant increased TSH levels).

Post-marketing cases have been reported indicating a potential interaction between ritonavir containing products and levothyroxine. Thyroid-stimulating hormone (TSH) should be monitored in patients treated with levothyroxine at least the first month after starting and/or ending ritonavir treatment.

A number of drugs may affect thyroid function tests and this should be borne in mind when monitoring a patient on levothyroxine sodium therapy.

There are limited case reports that oral ciprofloxacin may decrease the absorption of levothyroxine. An interval of six hours between the administration of the two medications is recommended and monitoring to changes in thyroid function should be carried out.

St John's Wort
Medicinal products containing St John's Wort (*Hypericum perforatum L.*) may increase the hepatic clearance of levothyroxine, which may lead to reduced serum concentrations of thyroid hormone. Therefore, patients receiving thyroid replacement therapy may need an increase in the thyroid hormone dose when these medicinal products are used concomitantly.

Biotin-containing products
Biotin may interfere with immunoassays for assessing thyroid function based on a biotin/streptavidin interaction, thus leading to falsely decreased or falsely increased test results (see section 4.4 Special warnings and precautions for use).

4.6 Fertility, pregnancy and lactation

Levothyroxine has been taken by a large number of pregnant women and women of childbearing age without any form of definite disturbances in the reproductive process having been observed so far. Thyroid hypo- or hyperactivity in the mother may, however, unfavourably influence the fetal outcome or well-being.

During pregnancy, combination of levothyroxine and antithyroid agents for the treatment of hyperthyroidism is contraindicated.

Levothyroxine is excreted in breast milk in low concentrations and this may be sufficient to interfere with neonatal screening for hypothroidism.

4.7 Effects on ability to drive and use machines

From the pharmacokinetic and pharmacodynamic properties of levothyroxine, treatment with Eltroxin would not be expected to interfere with ability to drive or operate machinery.

4.8 Undesirable effects

The following effects are indicative of excessive dosage and usually disappear on reduction of dosage or withdrawal of treatment for a few days.

The frequency classification for these adverse reactions is not known due to a lack of robust clinical trial data to accurately determine frequency estimates.

Immune system disorders:	Hypersensitivity reactions such as skin rash, pruritis and anaphylactic reactions
Metabolism and nutrition disorders:	Increased appetite, excessive loss of weight
Gastrointestinal disorders	Abdominal cramps, nausea, vomiting and diarrhoea
Nervous system disorders:	Headache, tremors, seizure. Rare cases of pseudotumor cerebri (benign intracranial hypertension) have been reported especially in children.
Psychiatric disorders	Anxiety, emotional lability, nervousness, excitability, insomnia, restlessness, psychotic depression
Cardiac disorders:	Anginal pain, cardiac arrhythmias, palpitations, tachycardia, increased blood pressure, heart failure, myocardial infarction
Endocrine disorders	Hyperthyroidism
Respiratory, thoracic and mediastinal disorders:	Dyspnoea
Skin and subcutaneous tissue disorders:	Sweating, hair loss, angioedema, rash, urticaria
Vascular disorders	Flushing
Musculoskeletal, connective tissue and bone disorders :	Cramps in the skeletal muscle, muscular weakness. Excessive dose may result in

	craniosynostosis in infants, and premature closure of epiphyses in children with compromised adult height.
Investigations	Decreased bone mineral density
Reproductive system and breast disorders:	Menstrual irregularity, impaired fertility
General disorders and administration site conditions:	Fatigue, heat intolerance, fever

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

Symptoms and Signs

In addition to exaggeration of side effects the following symptoms may be seen: agitation, confusion, irritability, hyperactivity, headache, sweating, mydriasis, tachycardia, arrhythmias, tachypnoea, pyrexia, increased bowel movements and convulsions. The appearance of clinical hyper-thyroidism may be delayed for up to five days. Thyrotoxic crisis has been occasionally reported following massive or chronic intoxication, leading to cardiac arrhythmias, heart failure and coma.

Treatment

The goal of therapy is restoration of clinical and biochemical euthyroid state by omitting or reducing the thyroxine dosage, and other measures as needed depending on clinical status.

Treatment is symptomatic, and tachycardia has been controlled in adults by 40mg doses of propranolol given every 6 hr and other symptoms by diazepam and/or chlorpromazine as appropriate.

Further management should be as clinically indicated or as recommended by the national poisons centre, where available. For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Levothyroxine sodium is the monosodium salt of the levorotary isomer of thyroxine.

Levothyroxine (T4) is a naturally occurring hormone produced by the thyroid gland and converted to the more active hormone triiodothyronine (T3) in peripheral tissues. The precise signals controlling the conversion of T4 to T3 within the cell are not known. The thyroid hormones are required for normal growth and development, particularly of the nervous system. They increase the resting or basal metabolic rate of the whole organism and have stimulatory effects on the heart, skeletal muscle, liver and kidney. Thyroid hormones enhance lipolysis and the utilization of carbohydrate.

100 mcg levothyroxine is equivalent in activity to 20 to 30 mcg liothyronine/triiodothyronine or 60 mg Thyroid BP and/or local pharmacopoeia specification.

5.2 Pharmacokinetic properties

Absorption and Distribution

Following oral administration the absorption of levothyroxine is incomplete and variable especially when taken with food. The amount absorbed increases during fasting conditions.

Levothyroxine is nearly totally bound to serum protein.

Metabolism and Elimination
The main pathway for the metabolism of levothyroxine (T4) is its conversion, by deiodination, to the active metabolite triiodothyronine (T3). Further deiodination of T4 and T3 leads to production of inactive products.

Levothyroxine is eliminated slowly from the body with a half-life of approximately 7 days in a normal person. This may be reduced in hyperthyroid states or increased in hypothyroid patients.

Renal or hepatic disease do not appear to have any significant effect on the disposition of levothyroxine.

In man approximately 20-40% of levothyroxine is eliminated in the faeces and approximately 30-55% of a dose of levothyroxine is excreted in the urine.

5.3 Preclinical safety data
No data included.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Microcrystalline cellulose, Pregelatinised maize starch, Talc, Colloidal anhydrous silica, Magnesium stearate.

6.2 Incompatibilities
Not applicable

6.3 Shelf life
24 months

6.4 Special precautions for storage
Store below 25 °C. Protect from light.

6.5 Nature and contents of container

25 microgram: HDPE bottle with child resistant closure in pack sizes of 200 tablets.
50 microgram: HDPE bottle with child resistant closure in pack sizes of 200 tablets.
75 microgram: HDPE bottle with child resistant closure in pack sizes of 200 tablets.
100 microgram: HDPE bottle with child resistant closure in pack sizes of 200 tablets.

6.6 Special precautions for disposal
No special requirements for disposal

7 MEDICINE SCHEDULE
Prescription Only Medicine

8 SPONSOR
Pharmacy Retailing (NZ) Limited trading as Healthcare Logistics
58 Richard Pearse Drive
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9 DATE OF FIRST APPROVAL

16 November 2006

10 DATE OF REVISION OF THE TEXT

18 December 2024

SUMMARY TABLE OF CHANGES

Section Changed	Summary of New Information
4.3, 4.6	Addition of contraindication for levothyroxine with anti-thyroid agents during pregnancy
4.4	Warning about switching to other levothyroxine containing products
4.4, 4.5	Addition of warning re. biotin interference with thyroid function tests
4.5	Addition of information on potential interaction between levothyroxine and St John's Wort
4.8	Addition of angioedema, rash, urticaria as possible Undesirable effects
4.5, 4.8	Spelling corrections – tamoxifen, diarrhoea, dypnoea
4.8	Update of the reporting URL