

NEW ZEALAND DATA SHEET

Levothyroxine Tablets

50 microgram, 100 microgram

Presentations

Tablets containing 50 micrograms (0.05 mg) or 100 micrograms (0.1 mg) anhydrous levothyroxine sodium, which is the monosodium salt of the levorotary isomer of thyroxine.

Levothyroxine 50 microgram (0.05 mg) tablets are white, uncoated, biconvex tablets, engraved with FW21 on one face with a breakline on the other.

Levothyroxine 100 microgram (0.1 mg) tablets are white, uncoated, biconvex tablets, engraved with FW31 on one face with a breakline on the other.

Indications

Levothyroxine is indicated for the treatment of hypothyroidism.

This product should only be prescribed for use in new patients, or those who cannot tolerate other thyroxine products.

Dosage and Administration

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

In younger patients, and in the absence of heart disease, a serum levothyroxine (T4) level of about 70 to 160 nanomols per litre, or a serum thyrotrophin level of less than 5 milli-units per litre, should be aimed at. In those aged over 50, and/or in the presence of heart disease, clinical response is probably a more acceptable criterion of dosage than serum levels.

The tablets must be swallowed whole.

Populations

It is recommended that levothyroxine tablets are only prescribed to patients who are able to swallow whole tablets.

Levothyroxine tablets should be taken on an empty stomach, preferably before breakfast.

Adults

Initially 50 to 100 micrograms daily and adjust at 4 to 6 week intervals by 50 micrograms until normal metabolism is steadily maintained. This may require doses of 100 to 200 micrograms daily.

With patients aged over 50 years, it is not advisable to exceed 50 micrograms a day initially. Where there is cardiac disease 25 micrograms, given as 50 micrograms on alternate days, is more suitable. In this condition the daily dosage may be slowly increased by 25 micrograms increments (given as 50 micrograms on alternate days) at intervals of perhaps four weeks. This dosing regimen is illustrated in **Table 1** below.

Table 1 – Recommended dosage regimen for levothyroxine tablets

DAILY DOSE	DOSING REGIMEN
25 microgram	One 50 microgram tablet on alternate days
50 microgram	One 50 microgram tablet daily
75 microgram	One 50 microgram tablet daily and one 50 microgram tablet on alternate days
100 microgram	One 100 microgram tablet daily
125 microgram	One 100 microgram tablet daily and one 50 microgram tablet on alternate days

Children

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, given as 50 micrograms every other day, is advisable. This may be slowly increased by increments of 25 micrograms (given as 50 micrograms on alternate days) every two to four weeks until optimal response is achieved. This dosing regimen is illustrated in **Table 1** above. 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 25 micrograms to determine the actual prescribed dose.

Contraindications

Hypersensitivity to any component of the preparation.

Thyrotoxicosis.

Warnings and Precautions

Adrenal insufficiency - Patients with panhypopituitarism or other causes predisposing to adrenal insufficiency may react unfavourably to levothyroxine treatment, and it is advisable to initiate corticosteroid therapy before giving levothyroxine sodium in these cases.

Cardiac problems - Special care is needed in patients with symptoms of myocardial insufficiency or ECG evidence of myocardial infarction or ischaemia.

Diabetes - Special care is needed in patients with diabetes mellitus or insipidus. Levothyroxine raises blood sugar levels and this may upset the stability of patients receiving antidiabetic agents.

Patients should be monitored carefully to ensure the correct dose is prescribed.

Potential for bone loss - Subclinical hyperthyroidism may be associated with bone loss. To minimise the risk of osteoporosis, dosage of levothyroxine should be titrated to the lowest possible effective level.

Elderly - Special care is needed in the elderly.

Children - 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.

Use in pregnancy

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.

Use in lactation

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

Effects on ability to drive and use machines

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

Adverse Effects

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

Immune system disorders:

Hypersensitivity reactions such as skin rash and pruritus have been reported.

Metabolism and nutrition disorders:

Increased appetite, abdominal cramps, nausea, vomiting, diarrhoea

Nervous system disorders:

Excitability, insomnia, restlessness, headache, tremors, seizure. Rare cases of pseudotumour cerebri (benign intracranial hypertension) have been reported, especially in children.

Cardiac disorders:

Anginal pain, cardiac arrhythmias, palpitation, tachycardia, increased blood pressure, heart failure, myocardial infarction

Musculoskeletal, connective tissue and bone disorders:

Cramps in skeletal muscle, muscular weakness, decreased bone mineral density. Excessive dose may result in craniosynostosis in infants, and premature closure of epiphyses in children with compromised adult height.

Skin and subcutaneous tissue disorders:

Sweating, flushing, hair loss

Reproductive system and breast disorders:

Menstrual irregularity, impaired fertility

General disorders:

Fatigue, heat intolerance, fever, excessive loss of weight

Interactions

Anticoagulants - 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 - Phenytoin levels may be increased by levothyroxine.

Anticonvulsants - Anticonvulsants such as carbamazepine 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.

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

Sympathomimetic agents - The effects of sympathomimetic agents are also enhanced.

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

Cholestyramine - Cholestyramine given concurrently reduces the gastrointestinal absorption of levothyroxine.

Statins - 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.

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

Increase of thyroxine dosage requirements

- A number of other drugs may decrease absorption of thyroxine sodium, and therefore increase thyroxine dosage requirements. These include antacids (e.g. aluminium hydroxide), bile acid sequestrants (e.g. colestipol), cation exchange resins (e.g. kayexalate), sucralfate, calcium carbonate and ferrous sulphate.
- 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.
- Treatment with imatinib was associated with increased thyroxine dosage requirements in hypothyroid patients.
- Treatment with amiodarone has been associated with multiple effects on thyroid function including increased thyroxine dosage requirements in hypothyroid patients.

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

Overdose

Symptoms

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.

Treatment

Gastric lavage or emesis is required if the patient is seen within several hours of taking the dose.

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

Further Information

Actions

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

Pharmacokinetics

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 diseases 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.

This medicine has been granted provisional consent under section 23 of the Medicines Act 1981, valid until 11 November 2012.

Pharmaceutical Precautions

Excipients

Sodium citrate
Maize starch
Lactose
Acacia powdered
Magnesium stearate
Purified water

Shelf-life

24 months

Special precautions for storage

Store below 25°C. Protect from light.

Package Quantities

50 microgram tablets in blister packaging with PVC/PVdC film (heat treated foil/heat seal lacquer) containing 28 tablets per pack.

100 microgram tablets in blister packaging with PVC/PVdC film (heat treated foil/heat seal lacquer) containing 28 tablets per pack.

Medicine Schedule

Prescription Only Medicine

Sponsor Details

Boucher & Muir (NZ) Ltd t/a Goldshield Healthcare (NZ)
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15 April 2011
