For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

ELTROXIN TABLETS
(12.5 mcg / 25 mcg / 37.5 mcg / 50 mcg / 75 mcg / 88 mcg / 100 mcg / 125 mcg)

1. GENERIC NAME

Thyroxine Sodium Tablets I.P. 12.5 mcg / 25 mcg / 37.5 mcg / 50 mcg/ 75 mcg / 88 mcg / 100 mcg / 125 mcg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

For information related to Child Resistant Packaging, please refer below link: bit.ly/GSK-India-CR2

ELTROXIN TABLETS 12.5 mcg

Each uncoated tablet contains:
Thyroxine Sodium (as anhydrous) I.P. 12.5 mcg

Excipients: Lactose, Sodium Citrate, Starch Maize, Acacia powder, Magnesium Stearate, Purified water* (*evaporates during processing).

ELTROXIN TABLETS 25 mcg

Each uncoated tablet contains:
Thyroxine Sodium (as anhydrous) I.P. 25 mcg

Excipients: Lactose, Sodium Citrate, Starch Maize, Acacia powder, Magnesium Stearate, Purified water* (*evaporates during processing).

ELTROXIN TABLETS 37.5 mcg

Each uncoated tablet contains:
Thyroxine Sodium (as anhydrous) I.P. 37.5 mcg

Excipients: Lactose, Sodium Citrate, Starch Maize, Acacia powder, Magnesium Stearate, Purified water* (*evaporates during processing).

ELTROXIN TABLETS 50 mcg

Each uncoated tablet contains:
Thyroxine Sodium (as anhydrous) I.P. 50 mcg

Excipients: Lactose, Sodium Citrate, Acacia Powder, Starch Maize, Magnesium Stearate, Purified water* (*evaporates during processing).

ELTROXIN TABLETS 75 mcg

Each uncoated tablet contains:
Thyroxine Sodium (as anhydrous) I.P. 75 mcg

Excipients: Lactose, Sodium Citrate, Acacia Powder, Starch Maize, Magnesium Stearate, Purified water* (*evaporates during processing).

ELTROXIN TABLETS 88 mcg

Each uncoated tablet contains:
Thyroxine Sodium (as anhydrous) I.P. 88 mcg

Excipients: Lactose, Sodium Citrate, Acacia Powder, Starch Maize, Magnesium Stearate, Purified water* (*evaporates during processing).

ELTROXIN TABLETS 100 mcg

Each uncoated tablet contains:
Thyroxine Sodium (as anhydrous) I.P. 100 mcg

Excipients: Lactose, Sodium Citrate, Methyl Hydroxybenzoate, Propyl Hydroxybenzoate, Starch Maize, Magnesium Stearate, Gelatin, Purified water* (*evaporates during processing).

ELTROXIN TABLETS 125 mcg

Each uncoated tablet contains:
Thyroxine Sodium (as anhydrous) I.P. 125 mcg

Excipients: Lactose, Sodium Citrate, Acacia Powder, Starch Maize, Magnesium Stearate, Purified water* (*evaporates during processing).

3. DOSAGE FORM AND STRENGTH

Uncoated tablets.

For information on strength(s) refer *2. Qualitative and Quantitative Composition* above.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

For the treatment of:

- hypothyroidism.

4.2 Posology and Method of Administration

The total daily dose should be taken in the morning on an empty stomach at least half an hour before breakfast. The tablets should be swallowed whole, without chewing, with some liquid.

Due to lack of data, it is not appropriate to crush *ELTROXIN TABLETS*.

ELTROXIN TABLETS without a score-line must not be halved.

Thyroid hormone therapy / replacement

The dosing information serves as a guideline. The individual daily dose should be determined by laboratory diagnostic tests and clinical examinations. If any residual thyroid function remains, a lower replacement dose may be sufficient.

In elderly patients, patients with coronary heart disease and patients with severe or chronic hypothyroidism, thyroid hormone treatment must be initiated with particular caution, i.e. by selecting a low initial dose and increasing it slowly and at longer intervals, with frequent thyroid hormone monitoring. Experience has shown that a lower dose is also sufficient in patients with a low body weight and in patients with large goitres. A starting dose of 12.5 micrograms can be used, providing that available formulation allow for appropriate dose adaptation.

As T_4 (thyroxine) or fT_4 (free thyroxine) levels may be increased in some patients, determination of the serum TSH (thyroid stimulating hormone) concentration is better suited for monitoring the treatment regimen.

Route of Administration

For oral use.

Adults

25 - 50 micrograms/day initially, followed by 100 - 200 micrograms/day (increased at 2 to 4 week intervals in increments of 25 - 50 micrograms).

In most cases, treatment is lifelong when used in hypothyroidism.

Children

Use of *ELTROXIN TABLETS* in neonates, children under 2 years and other children who are not able to swallow the tablet, cannot be recommended because of lack of data on crushed *ELTROXIN TABLETS*. Administering *ELTROXIN TABLETS* in such patients will be solely based on clinical discretion of the prescribing physician.

National treatment guidelines should be followed and the largest dose consistent with freedom from toxic effects should be given.

Elderly

In individual cases, e.g. in the presence of cardiac problems, slow up titration of the levothyroxine sodium dose is recommended, together with regular monitoring of the TSH level.

Renal impairment

There are no relevant data available.

Hepatic impairment

There are no relevant data available.

4.3 Contraindications

ELTROXIN TABLETS are contraindicated in:

- hypersensitivity to the active substance or to any of the excipients (see section *4.4 Special Warnings and Precautions for Use*),
- untreated hyperthyroidism,
- untreated subclinical (suppressed serum TSH level with normal T_3 (tri- iodothyronine) and T_4 levels of any aetiology) or overt thyrotoxicosis,
- untreated adrenal insufficiency,
- untreated pituitary insufficiency,
- acute myocardial infarction,
- acute myocarditis,
- acute pancarditis.

Combination therapy of hyperthyroidism with levothyroxine and anti-thyroid agents is not indicated in pregnancy (see section *4.6 Use in Special Populations).*

4.4 Special Warnings and Precautions for Use

Weight reduction

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 particularly in combination with certain substances for weight reduction, and especially with sympathomimetic amines. In combination with certain weight-reduction agents such as orlistat, reduced control of hypothyroidism may occur. This could be due to a decreased absorption of iodine salts and/ or levothyroxine (see section *4.5 Drug Interactions).*

Switching to another levothyroxine product

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. The values of TSH and T_4 should be measured after four to six weeks. It is recommended that the dose should be adjusted according to the patient's clinical response and the laboratory values.

Situations requiring particular caution

Caution in the following circumstances is required to maintain thyroid balance, namely:

- women who are pregnant or are planning conception (see section *4.6 Use in special populations*),
- hypothyroidism, congenital or acquired in childhood,
- suppressive therapy in patients with previous thyroid cancer, especially if frail or elderly,
- patients with central hypothyroidism,
- patients with cardiac symptoms, or diabetes mellitus or insipidus.

Before starting thyroid hormone therapy

Before starting thyroid hormone therapy, the following diseases or conditions must be excluded or treated:

- coronary heart disease,
- angina pectoris,
- hypertension,
- pituitary and/or adrenocortical insufficiency,
- thyroid autonomy.

Patients requiring frequent monitoring during thyroid hormone therapy

Even relatively mild, medicinal product induced hyperthyroid function must be strictly avoided in cases of coronary heart disease, heart failure, tachyarrhythmias, chronic hypothyroidism or in patients with a history of myocardial infarction. The initial dose and any dose increments should be carefully chosen; 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. In thyroid hormone therapy, more frequent monitoring of thyroid hormone parameters must be performed in these patients.

Secondary hypothyroidism or panhypopituitarism

In secondary hypothyroidism or panhypopituitarism, it must be established whether adrenocortical insufficiency is also present. Treatment with levothyroxine in patients with adrenal insufficiency may cause reactions, including dizziness, weakness, malaise, weight loss, hypotension and adrenal crisis. In case of adrenocorticoid dysfunction, this should be treated before starting the therapy with levothyroxine by adequate replacement treatment to prevent acute adrenal insufficiency (see Section *4.3 Contraindications*). It is advisable to initiate corticosteroid therapy before giving levothyroxine sodium in these cases.

Thyroid autonomy

If thyroid autonomy is suspected, it is recommended that a TRH (thyrotropin-releasing hormone) test or suppression scintigram be performed.

Increased bone resorption in women on long-term levothyroxine sodium therapy

In women, long-term levothyroxine sodium therapy has been associated with increased bone resorption, thereby decreasing bone mineral density. When administering levothyroxine therapy to postmenopausal women, who are at increased risk of osteoporosis, thyroid function should be monitored more frequently to avoid supraphysiological blood levels of levothyroxine and the dosage of levothyroxine should be titrated to the lowest possible level.

Increase in dosage requirements of insulin or other anti-diabetic therapy

Thyroid replacement therapy may cause an increase in dosage requirements of insulin or other anti-diabetic therapy (see section *4.5 Drug Interactions*). Care is needed for patients with diabetes mellitus and diabetes insipidus.

Partial loss of hair in paediatric patients

Parents of children receiving thyroid agent 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 (see section *4.8 Undesirable Effects*).

Circulatory collapse in low birth weight preterm 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.

Patients with known history of epilepsy

Care is required when levothyroxine is administered to patients with known history of epilepsy. Seizures have been reported rarely in association with the initiation of levothyroxine sodium therapy and may be related to the effect of thyroid hormones on seizure threshold.

Patients with myxoedema

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

Patients with malabsorption syndromes

Levothyroxine sodium absorption is decreased in patients with malabsorption syndromes. It is advised to treat the malabsorption condition to ensure effective levothyroxine treatment with regular levothyroxine dose.

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. 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 Drug Interactions*).

4.5 Drug Interactions

Interactions decreasing levothyroxine absorption

Ion exchange resins
Cholestyramine, calcium, aluminium, magnesium, iron supplements, polystyrene sulfonates, sucralfate, lanthanum, bile acid sequestrants (e.g. colestipol), anion/ cation exchange resins (e.g. kayexelate, sevelamer).

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.
Separate the dosages of thyroxine and the above mentioned medicines as much as possible to avoid interaction in the stomach or the small bowel.

Ciprofloxacin
Ciprofloxacin may decrease the serum concentration of levothyroxine.

Soya products and high-fibre diet

Soya products and high-fibre diet can reduce the intestinal absorption of levothyroxine. In children, there have been reports of a rise in the serum TSH level when they were given a diet containing soya and treatment with levothyroxine for congenital hypothyroidism. Unusually high doses of levothyroxine may be required to achieve normal serum levels of T_4 and TSH. During and upon termination of a diet containing soya, close monitoring of serum T_4 and TSH levels is necessary; a dose adjustment of levothyroxine may be required.

Weight loss agents (including orlistat)

In combination with certain weight-reduction agents, such as orlistat, reduced control of hypothyroidism may occur. This may be due to a decreased absorption of iodine salts and/ or levothyroxine. To avoid this, levothyroxine and weight reduction agents such as orlistat should be administered at least 4 hours apart. Regular monitoring for changes in thyroid function is required (see section *4.4 Special Warnings and Precautions for Use*).

Interactions affecting levothyroxine

Substances inhibiting conversion of T_4 to T_3

Propylthiouracil, glucocorticoids, propranolol, lithium, iodide, oral contrast agents and beta receptor blockers inhibit conversion of T_4 to T_3 and therefore also lower the therapeutic effect.

Amiodarone and iodinated contrast media

Due to their high iodine content the media can initiate both hyperthyroidism and hypothyroidism. Particular caution should be exercised in patients with nodular goitres with possibly undetected autonomy. As a result of this effect of amiodarone on thyroid function, a dose adjustment of levothyroxine sodium may be required.

Salicylates, furosemide, clofibrate

Levothyroxine may be displaced from plasma protein binding by salicylates, high doses (250 mg) of furosemide, clofibrate, and other substances. This leads to an increase in the plasma level of free thyroxine (fT_4).
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.

Oestrogen based contraceptives, medications used in postmenopausal hormone replacement

Levothyroxine requirements may increase during intake of oestrogen based contraceptives or during postmenopausal hormone replacement therapy.

Statins

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

Sertraline, chloroquine/ proguanil

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

Tyrosine kinase inhibitors

Treatment with tyrosine kinase inhibitors (e.g. imatinib and sunitinib) was associated with increased levothyroxine dosage requirements in hypothyroid patients.

Enzyme inducing medications

Effects of drugs inducing cytochrome P-450: Enzyme-inducing drugs such as barbiturates, rifampicin, and other medicinal products containing St John's Wort (Hypericum perforatum L.) may increase hepatic clearance of levothyroxine, resulting in reduced serum concentrations 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.

Protease inhibitors

Clinical symptoms and thyroid function should be carefully monitored in patients concomitantly using levothyroxine and protease inhibitors. 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.

Methadone and 5-fluorouracil

Methadone, and 5-fluorouracil may increase serum concentration of thyroxine-binding globulin, and therefore increase levothyroxine dosage requirements.

Interactions affecting other drugs

Antidiabetic agents

Levothyroxine may reduce the anti-hyperglycaemic effect of antidiabetics. Blood glucose levels must therefore be regularly monitored in patients with diabetes, particularly at the start of thyroid hormone therapy. The anti-hyperglycaemic dosage should be adjusted as necessary. Lowering the dose of levothyroxine can cause hypoglycaemia if the insulin or oral antidiabetics dose remains unchanged (see section *4.4 Special Warnings and Precautions for Use*).

Coumarin derivatives

Levothyroxine may potentiate the effect of coumarin derivatives due to plasma protein binding displacement. With concomitant treatment, regular monitoring of blood coagulation is therefore required and the anticoagulant dosage must be adjusted as necessary (dose reduction).

Digitalis preparations

If levothyroxine therapy is initiated in digitalised patients, the dose of digitalis may require adjustment. Serum digitalis glycoside levels may be decreased when a hypothyroid patient becomes euthyroid, necessitating an increase in the dose of digitalis glycosides.

Tricyclic antidepressants

Levothyroxine increases receptor sensitivity to catecholamines thus accelerating the response to tricyclic antidepressants (e.g. amitriptyline, imipramine).

Sympathomimetic agents

The effects of sympathomimetic agents (e.g. adrenaline) are enhanced.

Phenytoin

Phenytoin levels may be increased by levothyroxine.

Interferences with laboratory test

A number of drugs may decrease serum concentration of thyroxine-binding globulin, and therefore decrease levothyroxine 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 levothyroxine therapy.
Administration of acetylsalicylic acid together with levothyroxine results in an initial transient increase in serum free T_4. Continued administration results in normal free T_4 and TSH concentrations, and therefore, patients become clinically euthyroid.

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 Special Warnings and Precautions for Use*).

4.6 Use in Special Populations

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 foetal outcome or well-being.

Levothyroxine requirements may increase during pregnancy due to increased oestrogen levels. Thyroid function should therefore be monitored both during and after pregnancy and the thyroid hormone dose adjusted as appropriate. Since postpartum TSH serum levels are similar to preconception values, levothyroxine dosage can be reduced to the pre-pregnancy dose.

Very small amounts of levothyroxine cross the placenta and its administration using the appropriate doses lacks foetal consequences.

The development of the child depends on the thyroid function of the mother. Thyroxine is necessary to ensure proper brain development of the child. Treatment with levothyroxine should be continued throughout pregnancy to provide the necessary maternal balance in order to have a good progress of pregnancy (and in particular to reduce the risk of fetal hypothyroidism). Clinical and biological monitoring should be started as early as possible, especially during the first half of pregnancy, in order to confirm that the maternal serum TSH

values lie within the trimester-specific pregnancy reference range and to adjust the treatment if necessary.

In any case, it is recommended to have the thyroid hormone values of newborn and mother checked. A maternal postpartum monitoring will adjust treatment as needed.

Particularly during pregnancy and lactation, treatment with thyroid hormones must be consistently administered.

Combination therapy of hyperthyroidism with levothyroxine and anti-thyroid agents is not indicated in pregnancy. In fact, only very small amounts of levothyroxine cross the placenta, while large amounts of anti-thyroid agents pass from mother to child. This can result in foetal hypothyroidism.

See section *4.3 Contraindications* for information on concomitant intake of levothyroxine and anti-thyroid agents during pregnancy.

Suppression tests must not be performed during pregnancy.

Lactation

Even during high dose therapy with levothyroxine, the amount of thyroid hormone secreted into breast milk during breastfeeding is insufficient to induce the development of hyperthyroidism or suppression of TSH secretion in the infant. However, it may be sufficient to interfere with neonatal screening for hypothyroidism.

Suppression tests must not be performed during breastfeeding.

4.7 Effects on Ability to Drive and Use Machines

There are no available studies on the effects on the ability to drive and use machines. As levothyroxine is identical to the naturally occurring thyroid hormone, levothyroxine sodium is not expected to have any influence on the ability to drive and use machines.

4.8 Undesirable Effects

Clinical Trial Data

There are no relevant data available.

Post Marketing Data

Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency.

Frequencies are defined as:

Very common ≥1/10
Common ≥1/100 to <1/10
Uncommon ≥1/1000 to <1/100

Rare ≥1/10000 to <1/1000
Not known (cannot be estimated from the available data).

Immune system disorders
Not known: anaphylactic reaction, hypersensitivity reactions including rash, pruritus and oedema

Endocrine disorders
Not known: hyperthyroidism *(*see section *4.9 Overdose)*

Metabolism and nutrition disorders
Not known: increased appetite, osteoporosis at suppressive doses of levothyroxine, especially in postmenopausal women, mainly when treated for a long period *(*see section *4.9 Overdose*)

Psychiatric disorders
Not known: agitation, insomnia, restlessness

Nervous system disorders
Rare: benign intracranial hypertension in children
Not known: tremor, convulsion, headache

Cardiac disorders
Not known: angina pectoris, arrhythmia, palpitations, tachycardia, heart failure, myocardial infarction

Vascular disorders
Not known: flushing, hypertension

Respiratory, thoracic and mediastinal disorders
Not known: dyspnoea

Gastrointestinal disorders
Not known: abdominal pain, nausea, diarrhoea, vomiting

Skin and subcutaneous tissue disorders
Not known: alopecia in children *(*see section *4.4 Special Warnings and Precautions for Use*), hyperhidrosis, allergic reactions of the skin such as erythema, angioedema, rash, urticaria

Musculoskeletal and connective tissue disorders
Not known: muscle spasms, muscular weakness, premature closure of epiphysis in children

Reproductive system and breast disorders
Not known: menstruation irregular

Congenital, familial and genetic disorders
Not known: craniostenosis in infants

General disorders and administration site conditions
Not known: pyrexia, temperature intolerance in children

Investigations
Not known: weight decreased

4.9 Overdose

Symptoms and Signs

Hyperthyroidism may result from treatment imbalance or levothyroxine overdose.
An increased T_3 level is a more reliable sign of an overdose than elevated T_4 or fT_4 levels.

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. Psychiatric symptoms associated with hyperthyroidism may also occur, including affect lability, fatigue, anxiety and nervousness. The appearance of clinical hyperthyroidism may be delayed for up to five days.

In cases of intoxication incidence (suicide attempts) in humans, doses of up to 10 mg levothyroxine have been tolerated without complications. Serious complications, such as a threat to vital functions (respiration and circulation), are not anticipated unless coronary heart disease is present. Nevertheless, cases of thyrotoxic crisis have been occasionally reported following massive or chronic intoxication, leading to seizures, cardiac arrhythmias, heart failure and coma. Individual cases of sudden cardiac death have been reported in patients with many years of levothyroxine abuse.

Exceptional cases of seizures have been reported in epileptic patients when levothyroxine therapy is initiated, particularly when the dose of levothyroxine is increased rapidly (see section *4.4 Special Warnings and Precautions for Use*).

Excessive levothyroxine use may cause decreased bone mineral density, particularly in postmenopausal women (see section *4.4 Special Warnings and Precautions for Use*).

Treatment

Discontinuation of treatment and a follow up examination are recommended, depending on the extent of the overdose. Treatment is mostly symptomatic and supportive - management should be as clinically indicated or as recommended by the national poisons centre, where available.

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

In the event of an acute overdose, gastrointestinal absorption can be reduced by administering medicinal charcoal. For severe beta sympathomimetic effects such as tachycardia, state of anxiety, agitation and hyperkinesia, symptoms can be alleviated with beta receptor blockers (propranolol), diazepam and/ or chlorpromazine. Antithyroid agents are not indicated, as the thyroid is already fully quiescent.

At extremely high doses (suicide attempt), plasmapheresis may be of assistance.

An overdose with levothyroxine demands a prolonged period of monitoring. Onset of symptoms may be delayed by up to 6 days, due to the gradual conversion of levothyroxine to liothyronine.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Thyroid therapy; Thyroid hormones.

ATC Code: H03AA01.

5.1 Mechanism of Action

The action of synthetic levothyroxine is identical to that of the naturally occurring thyroid hormone, which is mainly produced by the thyroid gland. The body cannot differentiate between endogenously produced and exogenous levothyroxine.

5.2 Pharmacodynamic Properties

Following partial conversion to liothyronine (T_3) particularly in the liver and kidney and after passage into bodily cells, the characteristic thyroid hormone effects on development, growth and metabolism are observed, mediated by activation of T_3 receptors.

Thyroid hormone replacement leads to normalisation of metabolic processes. Thus, for example, a rise in cholesterol due to hypothyroidism is significantly reduced by the administration of levothyroxine.

5.3 Pharmacokinetic Properties

Absorption

Depending to a large extent on the type of galenic formulation, up to ≤ 80% of orally administered levothyroxine is absorbed when taken in the fasting state, mainly from the upper small intestine. Absorption is significantly reduced if the product is administered with food. Peak plasma levels are reached about 2 to 3 hours after ingestion. At the start of oral therapy, onset of action occurs after 3 to 5 days.

Distribution

The volume of distribution is calculated to be about 10 to 12 l. Levothyroxine is approximately 99.97 % bound to specific transport proteins. As this protein hormone binding is not covalent, there is a constant and very rapid exchange between free and bound hormone.

Metabolism

Metabolic clearance for levothyroxine is around 1.2 l plasma/day. It is mainly degraded in the liver, kidney, brain and muscle.

Elimination

The half-life of levothyroxine is about 7 days, although it is shorter in hyperthyroidism (3 to 4 days) and longer in hypothyroidism (about 9 to 10 days). In man, approximately 20 to 40 % of thyroxine is eliminated in the faeces and approximately 30 to 55 % of a dose of levothyroxine is excreted in the urine.

Levothyroxine crosses the placenta only in small amounts. During normal dose therapy, only small amounts of levothyroxine are secreted into breast milk.

Due to its high protein binding, levothyroxine is not amenable to haemodialysis or haemoperfusion.

Special patient populations

Renal impairment

Renal disease does not appear to have any significant effect on the disposition of levothyroxine.

Hepatic impairment

Due to impaired liver function the conversion into T_3 may be decreased and the disposition of levothyroxine may be altered, depending on the severity of decreased hepatic function.

6. NONCLINICAL PROPERTIES

6.1 Animal Toxicology or Pharmacology

Adverse effects observed in single and repeated dose toxicity studies only occurred at high doses.

Acute toxicity

Acute toxicity of levothyroxine is very low.

Chronic toxicity

Chronic toxicity studies were performed in different animal species (rats, dogs). At high doses, signs of hepatopathy, increased occurrence of spontaneous nephrosis and organ weight changes were seen in rats. No significant adverse reactions were observed in dogs.

Mutagenicity

There are no data available with regard to the mutagenic potential of levothyroxine. To date, there has been no suspicion or evidence of offspring damage due to genome changes caused by thyroid hormones. Levothyroxine was not mutagenic in the mouse micronucleus test.

Carcinogenicity

Long term animal studies have not been performed to investigate the tumorigenic potential of levothyroxine.

Reproductive toxicity

Thyroid hormones cross the placenta in very small amounts.

Upon administration of levothyroxine during early pregnancy, in rats, adverse effects, including foetal and neonatal deaths, only occurred at very high doses. Some effects on limb formation in mice and effects on central nervous system development in chinchillas were reported but teratology studies in guinea pigs and rabbits did not reveal increases in congenital abnormalities.

Animal studies regarding effects on fertility are not known. There are no available data regarding impairment of male or female fertility. There is no suspicion or evidence that this might occur.

7. DESCRIPTION

Uncoated tablets.

For further information refer *2. Qualitative and Quantitative Composition* above.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

There are no relevant data available.

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

Tablets in Amber glass bottle with or without CRSF type cap having induction sealing wad.

All presentations may not be marketed in India.

8.4 Storage and Handling Instruction

Store at temperature below 25^{o} C, protected from light and moisture.

Keep out of reach of children.

This product comes in child-resistant packaging.
To open the bottle follow the instruction below:

For more information open the link below:
bit.ly/GSK-India-CR2

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or patients' caregiver as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contra-indications of *ELTROXIN TABLETS*. Patients (and/or patients' caregiver) may also be informed about posology, method of administration and storage/handling information as applicable.

10. DETAILS OF MANUFACTURER

The Manufacturing Site details are mentioned on the label and packaging.

For further information, please contact:
GlaxoSmithKline Pharmaceuticals Limited.
Registered Office:
Dr. Annie Besant Road,
Worli, Mumbai 400 030. India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Manufacturing Licence number is indicated on the label and packaging.

12. DATE OF REVISION

02-JAN-2026

Trade marks are owned by or licensed to the GSK group of companies.

Version: ELT/PI/IN/2026/01

Adapted from Levothyroxine sodium NCDS 07 dated 26 November 2025.