

## **1. NAME OF THE MEDICINAL PRODUCT**

Eltroxin 50mcg tablets  
Levothyroxine 50mcg tablets

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains 50 micrograms levothyroxine sodium BP

## **3. Pharmaceutical Form**

Tablet.

White, uncoated, biconvex tablets engraved on one face "FW21" and a scoreline on the other.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Recommended clinical indications: Control of hypothyroidism, congenital hypothyroidism and juvenile myxoedema.

### **4.2 Posology and method of administration**

Adults:

Initially 50 to 100 micrograms daily, preferably taken before breakfast. Adjust at three to four week intervals by 50 micrograms until normal metabolism is steadily maintained: this may require doses of 100 to 200 micrograms daily.

For patients over 50 years, it is not advisable to exceed 50 micrograms daily initially and where there is cardiac disease, 25 micrograms daily or 50 micrograms on alternate days is more suitable initially. In this condition the daily dose may be increased by 25 micrograms at intervals of perhaps 4 weeks. For patients younger than 50 years, and in the absence of heart disease, a serum Levothyroxine (T4) level of 70 to 160 nanomols per litre, or a serum thyrotrophin level of less than 5 milli-units per litre should be targeted. For patients aged over 50 years, with or without cardiac disease, clinical response is probably a more acceptable criteria of dosage rather than serum levels.

A pre-therapy ECG is valuable because ECG changes due to hypothyroidism may be confused with ECG evidence of cardiac ischaemia. If too rapid an increase in metabolism is produced (causing diarrhoea, nervousness, rapid pulse, insomnia, tremors, and sometimes anginal pain where there is latent cardiac ischaemia), dosage must be reduced, or withheld, for a day or two, and then re-started at a lower dose level.

Elderly:

As for patients aged over 50 years.

Paediatric patients:

The maintenance dose is generally 100 to 150 micrograms per m<sup>2</sup> body surface area.

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.

For children with acquired hypothyroidism, the initial recommended dosage is 12.5-50 micrograms per day. The dose should be increased gradually every 2 to 4 weeks according to the clinical findings and thyroid hormone and TSH values until the full replacement dose is reached.

Infants should be given the total daily dose at least half an hour before the first meal of the day.

When applicable:

Tablets are to be disintegrated in some water (10 to 15 ml) and the resultant suspension, which must be prepared freshly as required, is to be administered with some more liquid (5 to 10 ml).

### **4.3 Contra-indications**

Thyrotoxicosis. Hypersensitivity to any components of Eltroxin tablets.

### **4.4 Special warnings and precautions for Use**

Levothyroxine should be introduced very gradually in patients aged over 50 years (see section 4.2) and those with long standing hypothyroidism to avoid any sudden increase in metabolic demands.

Patients with panhypopituitarism or other causes predisposing to adrenal insufficiency may react to levothyroxine treatment, and it is advisable to start corticosteroid therapy before giving levothyroxine to such patients.

Levothyroxine sodium should be used with caution in patients with cardiovascular disorders, including angina, coronary artery disease, hypertension, and in the elderly who have a greater likelihood of occult cardiac disease.

An ECG before starting treatment with levothyroxine is advised, as changes induced by hypothyroidism may be confused with evidence of ischaemia.

Thyroid replacement therapy may cause an increase in dosage requirements of insulin or other anti-diabetic therapy. Care is needed for patients with diabetes mellitus, and diabetes insipidus.

See note above regarding withdrawal of treatment.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

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.

## 4.5 Interaction with other medicinal products and other forms of interaction

### *Interactions affecting other drugs:*

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

Blood sugar levels are raised and dosage of anti-diabetic agents may require adjustment.

Tricyclic anti-depressants response may be accelerated because levothyroxine increases sensitivity to catecholamines; concomitant use may precipitate cardiac arrhythmias.

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

If levothyroxine therapy is initiated in digitalised patients, the dose of digitalis may require adjustment. Hyperthyroid patients may need their digoxin dosage gradually increased as treatment proceeds because initially patients are relatively sensitive to digoxin.

False low plasma concentrations have been observed with concurrent anti-inflammatory treatment such as phenylbutazone or acetylsalicylic acid and levothyroxine therapy.

Propranolol: levothyroxine (thyroxine) accelerates metabolism of propranolol.

Isolated reports of marked hypertension and tachycardia have been reported with concurrent ketamine administration.

### *Interactions affecting Levothyroxine:*

Anti-convulsants, such as carbamazepine and phenytoin, enhance the metabolism of thyroid hormones and may displace them from plasma proteins.

Initiation or discontinuation of anti-convulsant therapy may alter levothyroxine dosage requirements.

Effects of Levothyroxine may be decreased by concomitant sertraline.

Absorption of levothyroxine (thyroxine) possibly reduced by antacids, calcium salts, cimetidine, oral iron, sucralfate, colestipol, polystyrene sulphonate resin and cholestyramine.

Metabolism of levothyroxine (thyroxine) accelerated by rifampicin, barbiturates, and primidone. (may increase requirements for levothyroxine (thyroxine) in hypothyroidism)

Imatinib: plasma concentration of levothyroxine (thyroxine) possibly reduced by imatinib.

Beta blockers may decrease the peripheral conversion of levothyroxine to triiodothyronine. Oestrogen, oestrogen containing product (including hormone replacement therapy) and oral contraceptives may increase the requirement of thyroid therapy dosage. Conversely, androgens and corticosteroids may decrease serum concentrations of Levothyroxine-binding globulins.

#### **4.6 Pregnancy and Lactation**

The safety of levothyroxine treatment during pregnancy is not known, but any possible risk of foetal abnormalities should be weighed against the risk to the foetus of untreated hypothyroidism.

Levothyroxine is excreted in breast milk in low concentrations, and it is contentious whether this can interfere with neonatal screening.

#### **4.7 Effects on Ability to Drive and Use Machines**

None known.

#### **4.8 Undesirable Effects**

Side-effects are usually indicative of excessive dosage and usually disappear on reduction of dosage or withdrawal of treatment for a few days. Such effects include:

General: Headache, flushing, fever and sweating

Immune system disorders: hypersensitivity reactions including rash, pruritus and oedema

Metabolic: weight loss

Nervous system: tremor, restlessness, excitability, insomnia. Rarely, benign intracranial hypertension in children.

Cardiac: anginal pain, cardiac arrhythmias, palpitations, tachycardia

Gastrontestinal: diarrhoea, vomiting

Musculoskeletal and connective tissue: muscle cramps, muscle weakness, craniostenosis in infants and premature closure of epiphysis in children.

Reproductive: menstrual irregularities

Heat intolerance, transient hair loss in children, also reported.

#### **4.9 Overdose**

##### *Symptoms*

In most cases there will be no features. Rarely, features of hyperthyroidism may develop 3-6 days after ingestion, with palpitations, tachycardia, tremor, insomnia and hyperpyrexia. Atrial fibrillation may develop. Convulsions occurred in one child. There may be increased toxicity in those with pre-existing heart disease.

### *Treatment:*

Give oral activated charcoal if more than 10mg has been ingested by an adult or more than 5mg by a child, within 1 hour. If more than 10mg has been ingested by an adult or more than 5mg by a child, take blood 6-12 hours after ingestion for measurement of the free thyroxine concentration. The analysis does not need to be done urgently but can wait until the first working day after the incident. Patients with normal free thyroxine concentrations do not require follow up. Those with high concentrations should have outpatient review 3-6 days after ingestion to detect delayed onset hyperthyroidism. Features of clinical hyperthyroidism should be controlled with beta-blockers, e.g. propranolol.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Eltroxin is a tablet containing the hydrated form of Levothyroxine sodium which is used for the treatment of hypothyroidism. The thyroid gland is dependant upon 2 active principles for it's main hormone activity these are Levothyroxine (tetraiodothyronine) and Tri-iodothyronine (see Goodman and Gilman, 1985). These closely related iodine containing amino acids are incorporated into the glycoprotein thyroglobulin. The chief action of these hormones is to increase the rate of cell metabolism. Levothyroxine is deiodinated in peripheral tissues to form Tri-iodothyronine which is thought to be the active tissue form of thyroid hormone. Tri-iodothyronine is certainly more rapid acting and has a shorter duration of action than Levothyroxine.

### **5.2 Pharmacokinetic properties**

Levothyroxine sodium is incompletely and variably absorbed from the gastrointestinal tract. It is almost completely bound to plasma proteins and has a half-life in the circulation of about a week in healthy subjects, but longer during pregnancy in patients with myxoedema. A large portion of the Levothyroxine leaving the circulation is taken up by the liver. Part of a dose of Levothyroxine is metabolised to triiodothyronine. Levothyroxine is excreted in the urine as free drug, deiodinated metabolites and conjugates. Some Levothyroxine is excreted in the faeces. There is limited placental transfer of Levothyroxine.

### **5.3 Preclinical safety data**

No further data of relevance.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Sodium Citrate BP  
Lactose BP  
Maize starch BP  
Powdered acacia BP  
Magnesium Stearate BP  
Purified Water BP

## **6.2 Incompatibilities**

None known.

## **6.3 Shelf life**

36 months for polypropylene containers.

36 months for blister packs.

## **6.4 Special precautions for storage**

Protect from light.

## **6.5 Nature and contents of container**

Polypropylene container with tamper-evident low density polyethylene lid, containing 28, 56, 100, 112, or 1000 Eltroxin 50mcg tablets.

Blister packaging PVC/PVDC film (heat treated foil/heat seal lacquer) containing 28, 56 and 112 Eltroxin 50mcg tablets.

## **6.6 Instruction for use and handling**

None.

## **7. MARKETING AUTHORISATION HOLDER**

Goldshield Group Limited  
NLA Tower, Croydon  
CR0 0XT  
Trading as Goldshield Pharmaceuticals

## **8. MARKETING AUTHORISATION NUMBER**

PL 10972/0031

## **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

9 November 1993

## **10. DATE OF REVISION OF THE TEXT**

December 2010