Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Eltroxin 25 microgram Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 25 micrograms levothyroxine sodium anhydrous.
Excipients: contains Lactose 30.49mg
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.
White uncoated biconvex tablets engraved on one face “FW41” and a score line on the other. The scoreline is to allow breaking for ease of swallowing.

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 (2 to 4 tablets 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 thyroxine (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 criterion of dosage, rather that 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.

Children: For infants with congenital hypothyroidism and juvenile myxoedema, a suitable starting dose is 25 micrograms daily, followed by increments of 25 micrograms every two to four weeks until mild toxic symptoms develop. Dosage is then slightly reduced.

In children aged more than 1 year, the starting dose is 2.5 to 5.0 micrograms/Kg/day. For children, the highest dose consistent with freedom from toxic effects should be given.

The dosage should be guided by the clinical response, growth assessment and appropriate thyroid function tests.

Clinically, a normal pulse rate, and absence of diarrhoea or constipation are the most useful indicators of a suitable dosage.

Thyrotrophin levels may remain elevated during the first year of life in children with neonatal hypothyroidism due to re-setting of the hypothalamic-pituitary axis.

Treatment with Eltroxin should be withdrawn, when appropriate, by gradual reduction of dosage over several weeks to avoid possible effects of rebound hypothyroidism and interaction with other therapies due to sudden withdrawal of levothyroxine treatment.

Note: Eltroxin tablets of 50 mcg and 100 mcg are available.

Method of administration: Oral.

4.3 Contraindications

Thyrotoxicosis. Hypersensitivity to any components of Eltroxin tablets.

4.4 Special warnings and precautions for use

Patient 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

Special care is needed for the elderly and for patients with symptoms of myocardial insufficiency, or ECG evidence of myocardial infarction. Thyroid replacement therapy may cause an increase in dosage requirements of insulin or other anti-diabetic therapy. Care is needed for patients with diabetes mellitis and diabetes insipidus. See note above regarding withdrawal of treatment.

Levothyroxine sodium should be used with caution in patients with cardiovascular disorders, including angina, coronary artery disease, hypertention, and in the elderly who have a greater likelihood of occult cardiac disease. An ECG before starting treatment with levothroxine is advised, as changes induced by hypothyroidism may be confused with evidence of ischaemia. Levothyroxine should be introduced very gradually in elderly patients and those with long standing hypothyroidism to avoid any sudden increase in metabolic demands.

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 levothyroxin sodium therapy, and may be related to the effect of thyroid hormone on seizure threshold.

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

Anti-coagulants: 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. Phenytoin levels may be increased by levothyroxine.

Anti-convulsants, such as carbamazepine and phenytoin, enhance the metabolism of thyroid hormones.

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

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. The effects of sympathomimetic agents (e.g. adrenaline (epinephrine)) 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.

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

Amiodarone may affect thyroid function tests and this must be considered when monitoring a patient on levothyroxine therapy.

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

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

Imatinib: plasma concentration of levothyroxine (thyroxine) possibly reduced by imatinib.
Propranolol: levothyroxine (thyroxine) accelerates metabolism of propranolol.

Oestrogen, oestrogen containing products and oral contraceptives may increase the requirement of thyroid therapy dosage. Conversely, androgens and corticosteroids may decrease serum concentrations of Levothyroxine-binding globulins.

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

Lovastatin has been reported to cause one case each of hypothyroidism and hyperthyroidism in two patients taking levothyroxine.

4.6 Fertility, 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:

Immune System Disorders: hypersensitivity reactions including rash, pruritus and oedema also reported.

Metabolic disorders: Fever, Heat intolerance

Nervous system disorders: tremor, restlessness, excitability, headache, insomnia, flushing, sweating

Cardiac disorders: anginal pain, cardiac arrhythmias, palpitations, tachycardia.

Gastrointestinal disorders: diarrhoea, vomiting.

Musculoskeletal and connective tissue disorders: Muscle cramps, muscular weakness.

Other symptoms: Transient hair loss in children

Thyroid crisis have occasionally been reported following massive or chronic intoxication and cardiac arrhythmias, heart failure, coma and death have occurred.

4.9 Overdose

Symptoms of mild to moderate overdose: fever, angina, tachycardia, arrhythmias, muscle cramps, headache, restlessness, flushing, sweating, diarrhoea. Reduction of dose or withdrawal of therapy reverses mild overdose effects.

Symptoms of severe overdose: this may resemble thyroid crisis with collapse and coma. Signs and symptoms of hyperthyroidism may be delayed for up to 5 days due to the gradual peripheral conversion of levothyroxine to triiodothyronine. Overdosage following recent ingestion of tablets can be treated using gastric lavage.

Treatment is symptomatic. Tachycardia may be controlled in an adult by 40mg doses of propanolol given every 6 hours. Other symptoms may be controlled by Diazepam and/or chlorpromazine as appropriate. Antithyroid drugs such as propylthiouracil and lithium are unlikely to be of benefit to prevent thyrotoxic crisis due to delayed absorption/onset of action.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: HO3AAO1

Pharmacotherapeutic group: Thyroid hormones.

Eltroxin is a tablet containing levothyroxine sodium used for the treatment of hypothyroidism. Levothyroxine is deiodinated in peripheral tissues to form triiodothyronine which is thought to be the active tissue form of thyroid hormone. Triiodothyronine has a rapid action but a shorter duration of activity than levothyroxine.

The chief action of levothyroxine is to increase the rate of cell metabolism.

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 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
Lactose
Maize starch
Powdered acacia
Magnesium Stearate

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

18 months.

6.4 Special precautions for storage

Polypropylene Container: Do not store above 25°C. Store in the original package in order to protect from light and moisture.

Blisters: Do not store above 25°C. Keep blister in the outer carton in order to protect from light and moisture.

6.5 Nature and contents of container

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

Aluminium foil with PVC/PVdC film blisters containing 28, 56, 112 or 1000 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA0899/020/001

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21 July 2011