Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Eltroxin 100 microgram Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100 micrograms anhydrous levothyroxine sodium.

Excipients: also contains lactose monohydrate

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

Product imported from the UK:
A white, round tablet, scored on one side and engraved on the other with FW31

The scoreline is to allow for breaking for ease of swallowing and not to divide into equal doses

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 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 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:
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.
The maintenance dose is generally 100 to 150 micrograms per m^2 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).

Treatment with Eltroxin should be withdrawn, when appropriate, by gradual reduction of dosage over several weeks to avoid possible effects of rebound hypothyroidism and interatction with other therapies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

Method of administration: Oral.

4.3 Contraindications

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.

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.

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 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.

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 hormone on seizure threshold.

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 antidiabetic 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 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 phenybutazone 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 possibly reduced by cimetidine, antacids, calcium salts, oral iron, polystyrene sulphonate resins, sucralfate, colestipol and cholestyramine.

Metabolism of levothyroxine (thyroxine) accelerated by rifampicin, barbiturates, primidone and oestrogens (may increase requirement 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 products(including hormone replacement therapy) and oral contraceptives may increase the requirement of thyroid therapy dosage. Conversely, androgens and corticosteroids may decrease serum concerntrations of levothyroxine binding globulins.

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

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.

Metabolic: weight loss.

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

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

Gastrointestinal disorders: diarrhoea, vomiting

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

Reproductive: menstrual irregularities

General: Headache, flushing, fever and sweating

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 dependent 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
Lactose monohydrate
Maize starch
Powdered acacia
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf-life expiry date of this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 25ºC. Store in the original package in order to protect from light and moisture.

6.5 Nature and contents of container

Blister pack containing 28 tablets

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 PARALLEL PRODUCT AUTHORISATION HOLDER

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8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 1328/162/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th February 2012

10 DATE OF REVISION OF THE TEXT

September 2013