SUMMARY OF PRODUCT CHARACTERISTICS

T 4 ® Tablets

-12, -25, -50, -62, -75, -88, -100, -112, -125, -137, -150, -175 & -200 mcg/tab

Levothyroxine sodium

1. NAME OF MEDICINAL PRODUCT:

T4® Tablets *-12, -25, -50, -62, -75, -88, -100, -112, -125, -137, -150, -175 & -200 mcg/tab*

2. QUALITATIVE AND QUANTITAVE COMPOSITION (active ingredient)

The product is provided in the form of lenticular tablets of 12 mcg (μg), 25 mcg, 50 mcg, 62 mcg, 75 mcg, 88 mcg, 100 mcg, 112 mcg, 125 mcg, 137 mcg, 150 mcg, 175 mcg, and 200 mcg of crystalline Levothyroxine Sodium (T4).

3. PHARMACEUTICAL FORM:

Tablets.

SUMMARY OF PRODUCT CHARACTERISTICS

T 4 ® Tablets

-12, -25, -50, -62, -75, -88, -100, -112, -125, -137, -150, -175 & -200 mcg/tab

Levothyroxine sodium

4. CLINICAL DATA

4.1 Therapeutic indications

- Replacement or supplemental therapy in hypothyroidism of any etiology.
- Suppression of pituitary TSH secretion (simple non-edemic goiter, chronic lymphocytic thyroiditis).
- As a test for the suppression of TSH, when there is suspicion for thyroid gland autonomy.
- Thyrotoxicosis in combination with antithyroid drugs.

4.2 Dosage and administration

The dosage must be determined by the level of hypothyroidism, the age of the patient, the individual sensitivity to the medication, as well as, the clinical and laboratory findings.

Initially, the medication is prescribed in low doses which are gradually increased until the optimal maintenance dose is found.

The daily dose is taken in the morning before breakfast.

- ***Adults:*** In primary hypothyroidism, the recommended initial dose is 50-100 mcg (0.05-0.1 mg) per day, while in elderly patients the initial dose is usually 25-50 mcg. The dose after that may be increased by 50 mcg per week until the metabolism is normalized. The usual maintenance dose is 100-200 mcg. If there is cardiovascular problem, the onset is done with 25 mcg per day and

the increase of the dose, where is required, is done with 25 mcg per week.

- ***Children:*** Despite the small body weight, the doses are higher than in the adult. In general, the initial dose until one month of age is 5-10 mcg/kg per day and in the older children the onset is done with 5 mcg/kg. This dose may be adjusted by 25 mcg increments every 2-4 weeks, depending on the clinical and laboratory results.

4.2 Contra-Indications:

- Hyperthyroidism of any etiology (unless it is administered together with antithyroid medications), recent myocardial infarction.
- Also, is contraindicated in untreated adrenal insufficiency because the need of the tissues for adrenal hormones increases (risk of acute adrenal crisis), in uncorrected renal insufficiency and in hypersensitivity to the thyroid hormones.

4.3 Special warnings and precautions during use:

Caution during administration:

- To patients with cardiovascular disorders (hypertension, arrhythmia, coronary insufficiency etc.) or to the elderly in whom there is an increased risk of occult cardiac disease, Levothyroxine therapy should be initiated at lower doses (25-50mcg).

- To patients with uncorrected adrenal cortical insufficiency *(see Contraindications)*.
- To patients with diabetes, the administration of the medication can influence the glycemic balance and adjustment of the dose may be needed.
- Obesity without hypothyroidism is not an indication for prescribing thyroid hormones.
- Lithium binds to thyroid hormones, therefore regular follow-up of the thyroid function is required.

"Due to the low solubility of LEVOTHYROXINE in water, to the molecules light sensitivity, tablets containing this active ingredient could present stability problems as well as problems in their uniformity content. As result of this, patients with hypothyroidism to whom these medications are prescribed for the treatment for their condition, should be monitored closely".

4.5 Drug interactions:

- With medications that reduce Levothyroxine's absorption in the alimentary tube (Aluminium hydroxide, Sucralfate, Iron, Cholestyramine).
- Intensification of the action of anticoagulants (reduction of dose may be necessary).
- Amiodarone contains iodine and can cause hypo or hyperthyroidism.
- Anti-epileptic medications and Rifampin increase Levothyroxine's metabolism.

- Certain medications can interfere with the laboratory findings of patients who undergo therapy with thyroid hormones: Androgens, Estrogens, Contraceptives, Corticosteroids, Salicylates, Iodines.

4.6 Undesirable effects:

These are due to the excess or abrupt increase of the doses. Particularly is possible to see the following:

- Tachycardia
- Palpitations
- Headache
- Anxiety
- Restlessness
- Tremor
- Insomnia
- Chills
- No tolerance to heat
- Muscle weakness
- Cramps
- Sweating
- Fever
- Weight Loss
- Diarrhea and vomiting
- Worsening of an pre-existing cardiopathy

The above undesirable effects disappear with the reduction of dose or the temporary discontinuation of the medication.

4.7 Pregnancy and Lactation:

- *Pregnancy:*

Thyroxine does not increase the risk of disorders in the fetus and it can be administered during pregnancy.

Periodically, the levels of TSH should be monitored and in the case where its levels are increased, the administered T4 should be also increased.

- *Lactation:*

Small quantities of the thyroid hormones are excreted into the human milk. However, caution should be paid when these medications are administered to nursing women.

4.8 Effect on the ability to drive or use machinery:

Does not effect on the ability to drive or use machinery.

4.9 Overdose:

The overdose causes symptoms thyrotoxic crisis: Tachycardia, nervousness, diarrhea, sweating, headache etc.

In these cases, the drug should be discontinued for a few days and retreated in smaller doses. Drugs may be administered therapeutically as beta-blockers, sedatives, cholestyramine -which reduces the absorption- and corticosteroids, which inhibit the conversion of T4 to T3. Also, specific treatment (such as heart failure, arrhythmias etc.) where is required.

SUMMARY OF PRODUCT CHARACTERISTICS

T 4 ® Tablets

-12, -25, -50, -62, -75, -88, -100, -112, -125, -137, -150, -175 & -200 mcg/tab

Levothyroxine sodium

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamics

The main thyroid hormones are L-thyroxine (T4) and L-triiodothyronine (T3). The quantities of hormones that are attributable to circulation controlled by thyroid stimulating hormone (TSH) secreted by the anterior pituitary. The secretion of TSH is controlled by the levels of T4 and T3 that are already on circulation and from the release factor of TSH (TRH) that is secreted by the hypothalamus via feedback regulation mechanisms. Thyroid hormones increase cellular oxidative functions in the organization and promote the growth, differentiation and maturation of various tissues, especially the CNS. Containing a significant amount of iodine (59% to 65% and T4, T3).

5.2 Pharmacokinetic:

The absorption of T4 and T3 hormones from the digestive track varies between 50-80%. T4 half life is 7 days, while T3 half life is one day.

5.3 Preclinical Safety Data:

Not Applicable.

SUMMARY OF PRODUCT CHARACTERISTICS

T 4 ® Tablets

-12, -25, -50, -62, -75, -88, -100, -112, -125, -137, -150, -175 & -200 mcg/tab

Levothyroxine sodium

6. PHARMACEUTICAL DATA

6.1. Excipients List

Lactose monohydrate, Sodium starch glycolate, Cellulose microcrystalline, Silicon dioxide colloidal, Magnesium stearate.

Dyes:

T4® 12 μg: Sunset yellow lake E 110 CI 15985

T4® 25 μg: Quinoline yellow lake E 104 CI 47005

T4® 50 μg: Brown lake E 110 CI 15985, E 132 CI 73015, E 124 CI 16255

T4® 62 μg: Blue lake E 132 CI 73015, E 124 CI 16255

T4® 75 μg: Black lake E 151 CI 28440

T4® 88 μg: Azorubin lake E 122 CI 14720

T4® 100 μg: Brown lake E 110 CI 15985, E 132 CI 73015, E 124 CI 16255
Yellow lake No. 6 E 110 CI 15985

T4® 112 μg: Erythrosine lake E 127 CI 45430

T4® 137 μg: Violet (grape) lake E 122 CI 14720, E 133 CI 42090

T4® 150 μg: Green lake (ανοιχτή) E 132 CI 73015, E 104 CI 47005

T4® 175 μg: Blue lake E 132 CI 73015, E 124 CI 16255

T4® 200 μg: Green lake (σκούρο) E 132 CI 73015, E 102 CI 19140

6.2. Incompatibilities:

None known.

6.3 Shelf Life:

It is written on the packaging.

The shelf life of **T4®** is **3 (three)** years from the manufacturing date, when the product is kept closed in its original packaging.

6.4 Special Storage conditions:

Do not store above 25 °C.

Protect from light and humidity.

6.5. Packaging

1) Cardboard box containing 30 tablets packaged per 10 into 3 blisters made of PVC-PVDC and Aluminium foil and a Patient Information Leaflet.

2) Cardboard box containing 30 tablets packaged per 15 into 2 blisters made of PVC-PVDC and Aluminium foil and a Patient Information Leaflet.

7. Marketing Authorization Holder

UNI-PHARMA KLEON TSETIS PHARMACEUTICAL
LABORATORIES S.A.
14th Km National Road 1,
GR-145 64 Kifissia, Greece
Tel.: (+30) 210-80 72 512, 80 72 534
Fax: (+30) 210-80 78 907
URL: www.uni-pharma.gr
E-mail: unipharma@uni-pharma.gr

8. MARKETING AUTHORIZATION NUMBER

9. ISSUE DATE OF THE FIRST MARKETING AUTHORIZATION

10. DATE OF LAST REVISION

25.01.2010.