

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. NAME OF THE MEDICINAL PRODUCT

Levothyroxine 100micrograms Tablets (Thyroxine 100 micrograms Tablets).

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100 micrograms Levothyroxine Sodium anhydrous also known as thyroxine sodium tablets.

### 3. PHARMACEUTICAL FORM

Tablet.

White uncoated biconvex tablets engraved on one face FW31 and with a breakline 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 nanomoles 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 2-4 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 (5-10 mL).

### **4.3 Contra-indications**

Thyrotoxicosis. Hypersensitivity to any components of Levothyroxine 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 mellitus and diabetes insipidus.

### **4.5 Interactions with other medicinal products and other forms of interaction**

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.

Acenocoumarol, phenindione and warfarin enhances the effect of Levothyroxine.

Antiepileptics such as carbamazepine, phenobarbital, phenytoin, and primidone accelerate metabolism of Levothyroxine (may increase requirements in hypothyroidism) and may displace them from plasma proteins.

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

If co-administered with cardiac glycosides adjustment of dosage may be necessary.

The effect of sympathomimetic agents are enhanced.

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.

Manufacturer of lofepramine advises to avoid Levothyroxine.

Colestyramine reduces the gastrointestinal absorption of Levothyroxine. Oral contraceptives may increase the requirement of thyroid therapy dosage. Other drugs may affect thyroid function tests and this must be considered when monitoring a patient on Levothyroxine therapy.

Rifampicin accelerates metabolism of Levothyroxine (may increase requirements in hypothyroidism).

Phenylbutazone shows false low total plasma-Levothyroxine concentration.

Amiodarone contain iodine and can cause disorders of Levothyroxine function; both hypothyroidism and hyperthyroidism may occur.

Metabolism of propranolol reduces the effect of Levothyroxine.

Sucralfate reduces absorption of Levothyroxine.

#### **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: anginal pain, cardiac arrhythmias, palpitations, cramps in skeletal muscles, tachycardia, diarrhoea, vomiting, tremors, restlessness, excitability, insomnia, headache, flushing, sweating, excessive loss of weight, and muscular weakness.

#### **4.9 Overdose**

Signs and symptoms may be an exaggeration of the side-effects, as well as agitation, confusion, irritability, hyperactivity, mydriasis, tachypnoea, pyrexia, increased bowel movements and convulsions. The appearance of clinical hyperthyroidism may be delayed for up to five days. Gastric lavage or emesis is required if the patient is seen within several hours of taking the dose. Treatment is symptomatic. Tachycardia may be controlled in an adult by 40mg doses of propranolol given every 6 hours. Other symptoms may be controlled by Diazepam and/or chlorpromazine as appropriate.

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1 Pharmacodynamic properties**

Levothyroxine 100 micrograms Tablets are tablets 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

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## **6. Pharmaceutical Particulars**

### **6.1 List of excipients**

Sodium Citrate

Lactose

Maize starch

Powdered Acacia

Magnesium Stearate

Purified Water

### **6.2 Incompatibilities**

None known.

### **6.3 Shelf life**

36 months for polypropylene containers.

24 months for blister packs.

### **6.4 Special precautions for storage**

Do not store above 25°C and store in the original container.

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

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

Blister packaging PVC/PVdC film (heat treated foil/heat seal lacquer) containing 28, 56 and 112 Levothyroxine tablets.

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

None.

## **7. MARKETING AUTHORISATION HOLDER**

Forley Generics Limited

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CR0 0XT

United Kingdom

## **8. MARKETING AUTHORISATION NUMBER(S)**

PL 16201/0002

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

Aug 2004

**10. DATE OF (PARTIAL) REVISION OF THE TEXT**  
02/09/2010