SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Liothyronine Sodium 10 microgram Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10 micrograms of liothyronine sodium.

Excipients with known effect:

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets

Liothyronine Sodium 10 micrograms Tablets are round, white to off-white-colored tablets, debossed with ‘10’ on one side of the tablet and plain on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Used for the treatment of coma of myxedema, the management of severe chronic thyroid deficiency and hypothyroid states occurring in the treatment of thyrotoxicosis.

Liothyronine Sodium can be used also in the treatment of thyrotoxicosis as an adjunct to carbimazole to prevent sub-clinical hypothyroidism developing during treatment.

Liothyronine Sodium may be preferred for treating severe and acute hypothyroid states because of its rapid and more potent effect, but thyroxine sodium is normally the drug of choice for routine replacement therapy.

4.2 Posology and method of administration

Posology

Adults: Starting dose of 10 or 20 micrograms every 8 hours, increasing after one week, if necessary, to the usual recommended daily dose of 60 micrograms in two or three divided doses.

Myxedema Coma: 60 micrograms given by stomach tube, then 20 micrograms every 8 hours. It is more usual to start treatment with intravenous liothyronine.

Adjunct to carbimazole treatment of thyrotoxicosis: 20 micrograms every 8 hours.

Elderly and Children Patients: 5 micrograms daily.

Method of Administration: Oral

For patients who have difficulty in swallowing a whole tablet, such as the elderly and young children, a whole tablet may be crushed and allowed to dissolve/disperse in a minimum of 20 mL of water. The entire volume of liquid should be consumed to ensure ingestion of the full dose.

The solubility of liothyronine in water enables this as a method of administration.

If a dose lower than 20 micrograms is required, an appropriate tablet strength should be used.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1. Patients with angina of effort or cardiovascular diseases and thyrotoxicosis.

4.4 Special warnings and precautions for use

In severe and prolonged hypothyroidism, adrenocortical activity may be decreased. When thyroid replacement therapy is started, metabolism increases more than adrenocortical activity and this can lead to adrenocortical insufficiency requiring supplemental adrenocortical steroids.

Liothyronine rather than levothyroxine would be the replacement therapy of choice during block and replace treatment of thyrotoxicosis with propylthiouracil (PTU) due to the inhibition by PTU of the peripheral conversion of T4 to T3.

Liothyronine sodium treatment may result in an increase in insulin or anti-diabetic drug requirements. Care is required for patients with diabetes mellitus and diabetes insipidus.

Panhypopituitarism or predisposition to adrenal insufficiency (initiate corticosteroid therapy before starting liothyronine), pregnancy, breast-feeding (see section 4.6 Pregnancy and lactation).

In myxoedema, care must be taken to avoid imposing excessive burden on cardiac muscle affected by prolonged severe thyroid depletion. Particular care is needed in the elderly who have a greater risk of occult cardiovascular disease. Baseline ECG is recommended prior to commencement of liothyronine treatment in order to detect changes consistent with ischaemia. Patients should undergo cardiovascular monitoring, including periodic ECGs, during liothyronine treatment. Liothyronine is contraindicated in established myocardial ischaemia (see section 4.3) in which case, levothyroxine, with cautious dose escalation, is recommended instead.

If metabolism increases too rapidly (causing diarrhoea, nervousness, rapid pulse, insomnia, tremors and sometimes anginal pain where there is latent myocardial ischaemia), reduce dose or withhold for 1-2 days and start again at a lower dose.

TSH levels should be monitored during treatment to reduce the risk of over- or undertreatment. The risks of over-treatment include atrial fibrillation, osteoporosis and bone fractures.

Interferences with laboratory test:

Biotin may interfere with thyroid immunoassays that are based on a biotin/streptavidin interaction, leading to either falsely decreased or falsely increased test results. The risk of interference increases with higher doses of biotin.

When interpreting results of laboratory tests, possible biotin interference has to be taken into consideration, especially if a lack of coherence with the clinical presentation is observed.

For patients taking biotin-containing products, laboratory personnel should be informed when a thyroid function test is requested. Alternative tests not susceptible to biotin interference should be used, if available. (see section 4.5)

<u>Excipients</u>

Information on sodium content

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say is essentially ‘sodium free’.

4.5 Interaction with other medicinal products and other forms of interaction

Liothyronine sodium therapy may potentiate the action of anticoagulants. Phenytoin levels may be increased by liothyronine. Anticonvulsants, such as carbamazepine and phenytoin enhance the metabolism of thyroid hormones and may displace thyroid hormones from plasma proteins. Initiation or discontinuation of anticonvulsant therapy may alter liothyronine dose requirements.

If co-administered with cardiac glycosides, adjustment of dosage of cardiac glycoside may be necessary. Colestyramine and colestipol given concurrently reduces gastrointestinal absorption of liothyronine.

Liothyronine raises blood sugar levels and this may upset the stability of patients receiving antidiabetic agents.

Liothyronine increases receptor sensitivity to catecholamines thus accelerating the response to tricyclic antidepressants. A number of drugs may affect thyroid function tests and this should be borne in mind when monitoring patients on liothyronine therapy.

Co-administration of oral contraceptives may result in an increased dosage requirement of liothyronine sodium.

Amiodarone may inhibit the deiodination of thyroxine to triiodothyronine resulting in a decreased concentration of triiodothyronine with a rise in the concentration of inactive reverse triiodothyronine.

As with other thyroid hormones, Liothyronine may enhance effects of amitriptyline and effects of imipramine.

Metabolism of thyroid hormones accelerated by barbiturates and primidone (may increase requirements for thyroid hormones in hypothyroidism).

Requirements for thyroid hormones in hypothyroidism may be increased by oestrogens.

Interferences with laboratory test:

Biotin may interfere with thyroid immunoassays that are based on a biotin/streptavidin interaction, leading to either falsely decreased or falsely increased test results (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety during pregnancy is not known. The risk of foetal congenital abnormalities should be weighed against the risk to the foetus of untreated maternal hypothyroidism.

Breast-feeding

Liothyronine sodium is excreted into breast milk in low concentrations.

This may interfere with neonatal screening programmes.

Fertility

No human or animal data on the effect of active substance liothyronine on fertility are available.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

The following effects are indicative of excessive dosage and usually disappear on reduction of dosage or withdrawal of treatment for a day or two.

The undesirable effects are listed below by organ class and the following frequency convention:

Not known: frequency cannot be estimated from the available data.

System Organ Class	**Frequency**	**Adverse events**
Cardiac disorders	Not known	Anginal pain, cardiac arrhythmias, palpitations, tachycardia
Gastrointestinal disorders	Not known	Diarrhoea, vomiting
General disorders and administration site conditions	Not known	Fever, flushing, fever and heat intolerance
Immune system disorders	Not known	Hypersensitivity reactions

		including rash, pruritus and oedema also reported.
Metabolism and nutrition disorders	Not known	Excessive loss of weight
Musculoskeletal and connective tissue disorders	Not known	Muscle cramps, muscular weakness
Nervous system disorders	Not known	Headache, tremor,
Psychiatric disorders	Not known	Restlessness, excitability, insomnia,
Skin and subcutaneous tissue disorders	Not known	Sweating
Vascular disorders	Not known	Flushing

Paediatric population

- Transient hair loss in children (Not Known)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms

If patient is seen within a few hours of overdosage: gastric lavage or emesis.

There may be exaggeration of the side effects as well as agitation, confusion, irritability, hyperactivity, headache, sweating, mydriasis, tachycardia, arrhythmias, tachypnoea, pyrexia, increased bowel movements and convulsions.

Management

Treatment is symptomatic. Tachycardia in adults may be controlled with 40mg propanolol every 6 hours.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Thyroid hormones, ATC code: H03AA02

Mechanism of action

Liothyronine sodium is a naturally occurring thyroid hormone.

The biological action of Liothyronine sodium is quantitatively similar to that of Levothyroxine sodium, but the effects develop in a few hours and disappear within 24 to 48 hours of stopping treatment.

5.2 Pharmacokinetic properties

Absorption

Liothyronine sodium is almost completely absorbed from the gastro-intestinal tract.

Distribution

It is less readily bound to plasma proteins than thyroxine. About 0.5% is in the unbound form.

Elimination

The half-life of liothyronine in euthyroidism is 1 to 2 days. Thyroid hormones do not readily cross the placenta.

Minimal amounts are excreted in breast milk.

5.3 Preclinical safety data

No further relevant data.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol
Maize Starch
Gum Arabic Powder (Acacia)
Sodium Hydroxide
Magnesium Stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Liothyronine Sodium Tablets are proposed for marketing in two pack style i.e., Blister pack and HDPE bottle pack.

Blister Pack

Blister packs: packed in Alu/Alu blisters containing 14, 28, 56, 112 and 100 tablets.

Not all pack sizes may be marketed.

HDPE Pack

HDPE: Packed in HDPE containers with plastic cap containing 100's tablets.

Not all pack sizes may be marketed.

The Blister strips and HDPE bottle are then packed in carton along with the leaflet.

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Strides Pharma UK Ltd.
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United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 13606/0313

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