SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Enolio 10 micrograms/ml Oral Solution

Liothyronine Sodium 10 micrograms/ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of the oral solution contains 10 micrograms liothyronine sodium.

Excipients with known effect:

Sodium methyl parahydroxybenzoate (E 219): 2 mg per 1 ml dose

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution.

Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Liothyronine sodium is indicated in adults and children for the treatment of coma of myxoedema, the management of severe chronic thyroid deficiency and hypothyroid states occurring in the treatment of thyrotoxicosis.

Liothyronine sodium can also be used 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 1 ml (10 micrograms) or 2 ml (20 micrograms) every 8 hours, increasing after one week, if necessary, to the usual recommended daily dose of 6 ml (60 micrograms) in two or three divided doses.

Myxoedema Coma:

6 ml (60 micrograms) given by stomach tube, then 2 ml (20 micrograms) every 8 hours. It is more usual to start treatment with intravenous liothyronine.

Adjunct to carbimazole treatment of thyrotoxicosis:

2 ml (20 micrograms) every 8 hours.

Elderly:

0.5 ml (5 micrograms) daily

Paediatric population:

0.5 ml (5 micrograms) daily

Method of administration

Oral use. This medicinal product should be taken with water.

If necessary, this medicinal product can be administered via a gastric, duodenal or nasal feeding tube (see section 6.6). Rinse the tube twice with at least 10 ml of water following administration.

4.3 Contraindications

- Hypersensitivity to the active substance 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 sodium 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 sodium), pregnancy and breast-feeding (see section 4.6).

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 sodium 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.

Interference with laboratory tests:
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),

This medicinal product contains sodium methyl parahydroxybenzoate which may cause allergic reactions (possibly delayed).

This medicine contains less than 1mmol sodium (23mg) per 5ml dose, that is to say 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 sodium. 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 sodium dose requirements.

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

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

Liothyronine sodium 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 sodium 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.

Interference with laboratory tests:
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 the active substance liothyronine sodium on fertility are available.

4.7 Effects on ability to drive and use machines

Liothyronine sodium has no or negligible influence on the ability to drive and use machines.

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
Immune system disorders	Not known	Hypersensitivity reactions including rash, pruritus and oedema also reported.
Metabolism and nutrition disorders	Not known	Excessive loss of weight
Psychiatric disorders	Not known	Restlessness, excitability, insomnia
Nervous System disorders	Not known	Headache, tremor
Cardiac disorders	Not known	Anginal pain, cardiac arrhythmias, palpitations, tachycardia
Vascular disorders	Not known	Flushing
Gastrointestinal disorders	Not known	Diarrhoea, vomiting
Skin and subcutaneous tissue disorders	Not known	Sweating
Musculoskeletal and connective tissue disorders	Not known	Muscle cramps, muscular weakness
General disorders and administration site conditions	Not known	Fever, flushing and heat intolerance

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 at: 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 sodium 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

Glycerol
Citric acid monohydrate
Sodium citrate
Sodium methyl parahydroxybenzoate (E 219)
Sodium hydroxide
Purified water

6.2 Incompatibilities

Not known.

6.3 Shelf life

30 months

6.4 Special precautions for storage

Store in the original package in order to protect from light.

6.5 Nature and contents of container

Bottle: Type III amber glass bottle

Closure: Polypropylene (PP) child-resistant and tamper evident cap fitted with a low-density polyethylene (LDPE) syringe adaptor and high-density polyethylene (HDPE) screw closure.

Dosing: 5 ml oral syringe (PP barrel and LDPE plunger) with graduations of 0.25 ml

Pack sizes: 50 and 100 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special precautions for disposal.

Feeding tubes

This medicinal product has demonstrated compatibility with medium and large (8-16 Fr) silicone and polyurethane feeding tubes. Studies have not been performed in fine bore tubes (4-6 Fr) and hence this size of tube cannot be recommended.

To flush the feeding tube, rinse twice with at least 10ml of water following administration.

7 MARKETING AUTHORISATION HOLDER

Eclosix Ltd

329 Upper Fourth Street

Milton Keynes

MK9 1EH

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 60170/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17/09/2024

10 DATE OF REVISION OF THE TEXT

24/12/2025