

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Triiodothyronine 20 Micrograms Powder for Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 20 micrograms liothyronine sodium

Excipient(s) with known effect

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for solution for injection.

White, freeze-dried powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

It is indicated for the treatment of myxoedema coma, usually in conjunction with other measures including the intravenous injection of a corticosteroid.

For the treatment of less severe forms of myxoedema and for maintenance therapy, orally administered liothyronine should be used.

4.2 Posology and method of administration

Posology

Dosage: 5 to 20 micrograms given by slow intravenous injection and repeated at intervals of 12 hours or less if required. The minimal interval between dosing is 4 hours.

An initial dose of 50 micrograms intravenously is used by some physicians, followed by further intravenous injections of 25 micrograms every 8 hours until improvement occurs. The dosage may then be reduced to 25 micrograms intravenously twice daily.

Method of administration: Usually given by intravenous injection, as the alkalinity of the solution may cause irritation of the tissues if given by deep intramuscular injection. The solution is prepared by adding 1 or 2ml water for injection to the ampoule and shaking gently until the solution has dissolved.

Geriatric patients –In elderly patients with severe long-standing hypothyroidism, treatment with liothyronine sodium should be introduced with doses at the low end of the range, with smaller increments and longer intervals between increases as necessary.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

Liothyronine sodium is contraindicated in patients with cardiovascular disorders or angina of effort and thyrotoxicosis.

4.4 Special warnings and precautions for use

Liothyronine must be given with extreme caution in myxoedema coma because too large a dose can precipitate heart failure, especially in the elderly patients and those with ischaemic heart disease.

ECG monitoring can give a useful indication of impending ischaemia; however, changes in ST segment can be confused with similar changes occurring in hypothyroidism.

Liothyronine should be used with caution in patients with long-standing hypothyroidism, cardiovascular disorders, including angina, coronary artery disease, hypertension, and in the elderly, who have a greater likelihood of occult cardiac disease.

In severe and prolonged hypothyroidism, there may be decreased adrenocortical activity. When thyroid replacement therapy is started, metabolism is raised at a greater rate than adrenocortical activity, and this can result in adrenocortical insufficiency. This insufficiency may require supplemental adrenocortical steroids.

Thyroid replacement therapy may cause an increase in the dosage requirement of insulin or other anti-diabetic treatment. Care is needed in patients with diabetes mellitus and diabetes insipidus.

4.5 Interaction with other medicinal products and other forms of interactions

Liothyronine sodium therapy may potentiate the action of anticoagulants (coumarins and phenindione).

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. Phenytoin levels may be increased by liothyronine.

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

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

Liothyronine increases receptor sensitivity to catecholamines thus accelerating the response to tricyclic antidepressants; concomitant use may precipitate cardiac arrhythmias. Effects of liothyronine may be decreased by concomitant sertraline.

A number of drugs may affect thyroid function tests and this should be borne in mind when monitoring patients on liothyronine therapy.

The effects of sympathomimetic agents (e.g. adrenaline, epinephrine and norepinephrine) are also enhanced.

Liothyronine accelerates metabolism of beta-blockers like propranolol.

Metabolism of liothyronine is accelerated by rifampicin, barbiturates, and primidone (may increase requirements for liothyronine in hypothyroidism).

Amiodarone may inhibit the de iodination of thyroxine to tri iodothyronine resulting in a decreased concentration of tri iodothyronine, thereby reducing the effects of thyroid hormones.

Severe hypertension and tachycardia have been reported when ketamine was used in patients taking levothyroxine.

4.6 Fertility, pregnancy and lactation

Pregnancy:

The safety of liothyronine during pregnancy is not known. Any possible risk of congenital abnormalities must be weighed against the risk to the foetus of untreated hypothyroidism in the mother.

Breast-feeding:

Liothyronine is excreted into breast milk in low concentration. This may interfere with neonatal screening programmes.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Side-effects are usually indicative of excessive dosage.

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

Rare (> 1/10,000, < 1/1,000);

Not known: frequency cannot be estimated from the available data

System organ class	Frequency	Undesirable effects
Immune system disorders	Not Known	Hypersensitivity reactions including rash, pruritus and oedema.
Metabolism and nutrition disorders	Not Known	Weight loss
Nervous system disorders	Rare	Benign intracranial hypertension in children.
	Not Known	Tremor, restlessness, excitability, insomnia.
Cardiac disorders	Not Known	Anginal pain, cardiac arrhythmias, palpitations, tachycardia.
Gastrointestinal disorders	Not Known	Diarrhoea, vomiting
Skin and subcutaneous tissue disorders	Not Known	Transient hair loss in children
Musculoskeletal and connective tissue disorder	Not Known	Muscle cramps, muscle weakness, craniostenosis in infants and premature closure of epiphysis in children.
Reproductive system disorders	Not Known	Menstrual irregularities (relevant to maintenance therapy)
General disorders and administration site conditions	Not Known	Headache, flushing, fever and sweating. heat intolerance

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms:

Onset of signs and symptoms occurs within 12 to 24 hours and includes vomiting, diarrhoea, palpitations, anxiety, headache, flushing, agitation, hyperactivity, irritability, sweating, pyrexia, tachycardia and hypertension. In severe cases coma, convulsions, angina and ventricular arrhythmias are seen. Chronic overdose may cause myocarditis. Patients with pre-existing cardiopulmonary disease are more at risk.

Management:

Observe for at least 12 hours post ingestion if symptomatic and monitor pulse, ECG, blood pressure, and temperature. Oral activated charcoal should be used if more than 600 mcg (0.6 mg) has been taken by an adult or 10 micrograms/kg in a child within 1 hour of ingestion. Measurement of thyroid function including T3 levels is necessary if symptomatic or for prognostic purposes (non-urgent). Consider use of a beta blocker for tachycardia, sweating and hypertension. The dose should be adjusted depending on response. A normal heart rate is difficult to achieve and may result in hypotension. The aim of therapy is to keep heart rate at about 120 beat per minute. Symptomatic treatment includes the use of paracetamol for fever. Anticonvulsant therapy may be necessary in severe cases.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Thyroid therapy, Thyroid hormones
ATC code- H03AA02

Liothyronine (L-triiodothyronine) is a naturally occurring thyroid hormone.

5.2 Pharmacokinetic properties

Distribution

Liothyronine is less readily bound to plasma proteins than thyroxine, and about 0.5% exists in the unbound form.

Elimination

The half-life in the blood is about one to two days in euthyroidism.

Thyroid hormones do not readily cross the placenta. Minimal amounts are reported excreted in breast milk.

5.3 Preclinical safety data

No additional data.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dextran 110 freeze dried

Sodium Hydroxide

6.2 Incompatibilities

In the absence of incompatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

12 months.

Reconstituted product should be used immediately and any unused portion should be discarded.

6.4 Special precautions for storage

Do not store above 25°C. Keep the vials in the outer carton in order to protect from light.

6.5 Nature and contents of container

3ml Type I clear glass vial with siliconised bromobutyl rubber stopper, aluminium seal and red flip-off cap.

Pack Size: 5 vials per carton

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

For single use only. Any unused contents must be discarded.

Reconstituted with water for injection.

7 MARKETING AUTHORISATION HOLDER

Mercury Pharma Group Ltd

Capital House

85 King William Street

London

EC4N 7BL

United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA0701/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19 October 1993

Date of last renewal: 19 October 2008

10 DATE OF REVISION OF THE TEXT

March 2019