

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Liothyronine Sodium 20 micrograms Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 20 micrograms liothyronine sodium

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Intravenous injection

Packed as a freeze dried white plug, in a glass vial for reconstitution with 1 or 2ml water for injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Liothyronine Sodium Injection 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

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 of injection to the ampoule, and shaking gently until the solution has dissolved.

4.3 Contraindications

Hypersensitivity to any components of the preparation. 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 ischemia, 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.

Patients with rare hereditary problems of galactose intolerance e.g. galactosaemia, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

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

Effects of liothyronine may be decreased by concomitant sertraline.

The effects of sympathomimetic agents (e.g. adrenaline) 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.

4.6 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.

Lactation:

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

Not relevant.

4.8 Undesirable effects

Side-effects are usually indicative of excessive dosage. Such effects include:

General: Headache, flushing, fever and sweating.

Immune system disorders: hypersensitivity reactions including rash, pruritus and oedema.

Metabolic: weight loss

Nervous system: tremor, restlessness, excitability, insomnia. Rarely, benign intracranial hypertension in children.

Cardiac: anginal pain, cardiac arrhythmias, palpitations, tachycardia.

Gastrointestinal: diarrhoea, vomiting

Musculoskeletal and connective tissue: muscle cramps, muscle weakness, craniostenosis in infants and premature closure of epiphysis in children.

Reproductive: menstrual irregularities (relevant to maintenance therapy)..

Heat intolerance and transient hair loss in children have also been reported with the use of Liothyronine for maintenance therapy.

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

Liothyronine (L-triiodothyronine) is a naturally occurring thyroid hormone. Its biological action is qualitatively similar to that thyroxine, but the effect is more rapid in onset (in a few hours) and the effect disappears within 24 to 48 hours after stopping treatment.

5.2 Pharmacokinetic properties

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

Water for Injection

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

12 months

6.4 Special precautions for storage

Do not store above 25°C.

Keep the vial in the outer carton in order to protect from light.

6.5 Nature and contents of container

3ml hydrolytic clear glass vial with bromobutyl stopper containing 20 micrograms of Liothyronine Sodium in a freeze-dried, sterile white plug, packed into a carton containing 5 vials.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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10 DATE OF REVISION OF THE TEXT

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11 DOSIMETRY (IF APPLICABLE)

**12 INSTRUCTIONS FOR PREPARATION OF
RADIOPHARMACEUTICALS (IF APPLICABLE)**