SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cytomel 25 microgram, tablets
Cytomel 12.5 microgram, tablets
Cytomel 5 microgram, tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cytomel 25 microgram contains liothyronine sodium equivalent to 25 micrograms of liothyronine per tablet.
Cytomel 12.5 microgram contains liothyronine sodium equivalent to 12.5 micrograms of liothyronine per tablet.
Cytomel 5 microgram contains liothyronine sodium equivalent to 5 micrograms of liothyronine per tablet.

Excipients with known effect: sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per tablet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

Cytomel 25 microgram:
White, round, flat tablets with a diameter of 8 mm, a score line on one side and inscribed with "CYTOMEL 25" on the other side. The tablet can be divided into equal doses.

Cytomel 12.5 microgram:
White, round, biconvex tablets with a diameter of 8 mm, a score line on one side and inscribed with "CYTOMEL 12.5" on the other side. The tablet can be divided into equal doses.

Cytomel 5 microgram:
White, round, biconvex tablets with a diameter of 8 mm, a score line on one side and inscribed with "CYTOMEL 5" on the other side. The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1.Therapeutic indications

Cytomel is used in the treatment of hypothyroidism as an adjunct to levothyroxine therapy. Cytomel is indicated for non-toxic goitre. Cytomel can be used in a diagnostic T3 suppression test.

4.2. Posology and method of administration

The Cytomel dosage should be guided by the severity of the symptoms and the patient's response to the treatment.
A physiological dose ratio between levothyroxine and liothyronine is advised (this ratio is probably between 13:1 and 20:1). The optimum dosage is to be individualised on the basis of the clinical picture and laboratory assessments.
All patients should start on a low dosage (e.g. 5 µg) which should be gradually increased. After dose increases, patients should be monitored for any symptoms of hyperthyroidism, cardiovascular and other adverse events.

Paediatric population
There are few data available on the use of liothyronine in the treatment of hypothyroidism (congenital or other) in children. The dosage in children is guided by the clinical response and thyroid hormone functions and depends on the levothyroxine dosage.

Elderly patients
A low initial daily dose is recommended followed by gradual dose increases. There are few data available to support a concrete dosing advice.

Where possible, it is advised to take the daily dose of liothyronine in two divided doses.

4.3.Contraindications

Hypersensitivity to any of the ingredients of Cytomel.
Uncorrected adrenal cortical insufficiency, hypogonadism and nephrotic syndrome.

4.4.Special warnings and precautions for use

When Cytomel is administered after treatment with levothyroxine, the residual activity of levothyroxine should be taken into consideration, as well as the rapid

onset of action of Cytomel. Early in the treatment, Cytomel should be administered at a low dose, followed by gradual, careful dose increases guided by the patient's response to the first weeks of treatment.

Cytomel should not be administered to patients with cardiovascular disorders, especially those with coronary insufficiency, except if treatment with thyroid hormone is formally essential. Careful dosing is advised in those patients.

Cytomel is not recommended in patients with cardiac arrhythmias due to the risk of developing arrhythmias as a result of high T3 levels.

Patients with myxoedema may respond strongly to thyroid preparations and develop adverse reactions (even at low doses). The initial dose should therefore be low and gradually increased.

Severe, long-term hypothyroidism may result in reduced adrenal cortical function, correlating with hypometabolism. The increase in metabolism resulting from treatment with thyroid hormone is more rapid than the recovery of adrenal cortical function, which may result in acute insufficiency. Adequate corticosteroid supplements should be given to patients with adrenal cortical insufficiency before starting Cytomel therapy.

Decreased adrenal cortical function should be corrected before administration of Cytomel in patients with anterior lobe pituitary insufficiency.

As Cytomel displays weak protein binding, the PBI level during treatment is usual lower than the normal level. As with all thyroid preparations, Cytomel may reduce thyroid uptake of ^{131}I, especially if the daily dosage is less than 75 micrograms. This is a transient phenomenon. The ^{131}I test will no longer be affected two weeks after cessation of therapy.

The effect of Cytomel can be confirmed both clinically and in laboratory assessments: T3 ^{131}I resin or RBC uptake test, TBI, basal metabolism and Achilles tendon reflex test.

4.5.Interaction with other medicinal products and other forms of interaction

Cytomel should not be combined with sympathomimetics, especially in the treatment of obesity. The combination is inappropriate and may lead to life-threatening situations.

Initiation of Cytomel may reduce the oral anticoagulant requirement in patients already using oral anticoagulants. This effect does not occur in patients using Cytomel who are due to start oral anticoagulant therapy.

Cytomel should not be taken within 4 hours before or after administration of cholestyramine, as this reduces the absorption.

Initiation of Cytomel therapy may increase the requirement for insulin and oral blood-glucose-lowering agents.

Phenytoin levels may be increased by liothyronine.

Anticonvulsants such as carbamazepine and phenytoin increase thyroid hormone metabolism and may displace thyroid hormones on plasma proteins.

Initiation or cessation of anticonvulsant therapy may change the liothyronine dose requirement.

If liothyronine is administered concomitantly with cardiac glycosides, the cardiac glycoside dose may need to be adjusted.

Liothyronine increases catecholamine receptor sensitivity, increasing the response to tricyclic antidepressants.

Some medicinal products may influence thyroid function tests and this should be taken into consideration when monitoring patients undergoing liothyronine therapy.

Concomitant administration of oral contraceptives may result in increased liothyronine dose requirement.

4.6.Fertility, pregnancy and lactation

Pregnancy
Thyroxine is required for normal brain development of the child.
Limited amounts of liothyronine may cross the placenta. However, as liothyronine cannot reach brain cells during embryonal and foetal development, while thyroxine can, Cytomel is not recommended in the treatment of hypothyroidism during pregnancy. The use of liothyronine may lead to material hypothyroxinaemia. Conversion from liothyronine to thyroxine should be initiated as soon as possible in women planning a pregnancy or those whose pregnancy has been confirmed.

Lactation
Liothyronine can be used during lactation. Low levels of liothyronine are excreted in human milk. The amount of L-T3 excreted in human milk during lactation is not sufficient to cause hyperthyroidism, goitre or suppression of TSH secretion in the child, even in mothers on high-dose liothyronine therapy.

4.7.Effects on ability to drive and use machines

There is no data on the effect of Cytomel on the ability to drive and use machines.

4.8.Undesirable effects

Undesirable effects during Cytomel therapy are suggestive of overdose. Overdose may lead to hyperthyroidism; the clinical manifestations are tachycardia, nervousness, headache, anxiety, agitation, hyperkinesis, excessive perspiration. These symptoms disappear a few days after discontinuation of treatment or after lowering the dose.
A few cases of allergic skin reactions have been reported.

Endocrine disorders
Hyperthyroidism

Psychiatric disorders
Nervousness
Anxiety
Agitation

Nervous system disorders
Headaches
Hyperkinesis

Cardiac disorders
Tachycardia

Skin and subcutaneous tissue disorders
Excessive perspiration
Allergic skin reaction

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 the Netherlands Pharmacovigilance Centre Lareb (website: www.lareb.nl).

4.9.Overdose

Increased T3 levels are a more reliable indicator of overdose than increased T4 of free T4 levels.

Patients who have taken an overdose will display strongly increased basal metabolism.

Depending on the level of overdose, discontinuation of treatment with the tablets and testing is advised.

Various cases of sudden cardiac death have been reported in patients after years of levothyroxine misuse.

Symptoms
Alongside worsening of the listed undesirable effects, the following symptoms may be observed:

agitation, confusion, irritability, hyperactivity, headache, perspiration, mydriasis, tachycardia, arrhythmia, tachypnoea, pyrexia, increased stools and convulsions.

Treatment:
Therapy to reduce absorption by administration of activated charcoal can be considered in cases of severe overdose, as well as gastric lavage if it can be performed within 1 hour of administration and only in the event of severe overdose. Further treatment is symptomatic; tachycardia can be controlled in adults with 40-mg doses of propranolol every six hours.

5. PHARMACOLOGICAL PROPERTIES

5.1.Pharmacodynamic properties

Pharmacotherapeutic group: Thyroid hormones - liothyronine
ATC code: H03A A02.

Cytomel possesses the properties of the hormone formed in the thyroid but differs from levothyroxine by labile binding to serum proteins resulting in rapid availability to tissues where it exerts its action as soon as a few hours after administration with the peak effect exerted after 2 to 3 days. This is important for the treatment of severe hypothyroidism. The effect is maintained for 3 days after treatment cessation.

5.2.Pharmacokinetic properties

Absorption is approximately 95%. The biological half-life is 1-2 days.

5.3.Preclinical safety data

No special data.

6. PHARMACEUTICAL PARTICULARS

6.1.List of excipients

Gelatine (E441)
Croscarmellose sodium (E468)
Calcium sulphate dihydrate (E516)
Magnesium stearate (E470b)

6.2.Incompatibilities

Not applicable.

6.3.Shelf life

24 months

6.4.Special precautions for storage

Store in the original package in order to protect from moisture.
Store in the fridge (2-8 °C).
Cytomel can be stored outside the fridge for 1 month, provided that it is stored below 25 °C.

6.5.Nature and contents of container

Each pack of Cytomel contains 3 blister strips, containing 10 tablets per strip.

Cytomel 25 microgram, Cytomel 12.5 microgram and Cytomel 5 microgram tablets are packaged in Alu/Alu blister strips.

6.6. Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

ACE Pharmaceuticals BV
Schepenveld 41
3891 ZK Zeewolde
+31 (0)36-5227201

8. MARKETING AUTHORISATION NUMBER

Cytomel 25 microgram, tablets: RVG 108769
Cytomel 12.5 microgram, tablets: RVG 121884
Cytomel 5 microgram, tablets: RVG 121883

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Cytomel 25 microgram:
Date of first authorisation: 12 November 2010
Date of latest renewal: 12 November 2015

Cytomel 5 and 12.5 microgram:
Date of first authorisation: 18 October 2018

10. DATE OF REVISION OF THE TEXT

Last partial revision concerning sections 2: 14 January 2019