Souhrn plánu řízení rizik podle § 99 odst. 8 písm. a) zákona č. 378/2007 Sb., o léčivech a o změnách některých souvisejících zákonů (zákon o léčivech), ve znění pozdějších předpisů (1)

Euthyrox 38 mikrogramů tablety,

Euthyrox 63 mikrogramů tablety

Administrativní informace:

Léčivá látka/látky	38 mikrogramů sodné soli levothyroxinu (odpovídá 36,95 mikrogramům levothyroxinu) 63 mikrogramů sodné soli levothyroxinu (odpovídá 61,27 mikrogramům levothyroxinu)
Léková forma/formy	tablety
Síla/síly	38 mikrogramů 63 mikrogramů
Držitel rozhodnutí o registraci	Merck spol. s r.o.
Registrační číslo/čísla	56/150/24-C 56/151/24-C
Verze a datum plánu řízení rizik	Verze 6.0 Datum: 26.7.2023

Následující výňatek z plánu řízení rizik (RMP) výše uvedeného léčivého přípravku/léčivých přípravků je souhrnem podstatných informací uvedených ve zmíněném RMP. RMP popisuje opatření, která mají být přijata, aby bylo zajištěno, že tento léčivý přípravek/ty to léčivé přípravky budou používány co nejbezpečněji. Souhrn RMP je potřeba číst spolu se schváleným souhrnem údajů o přípravku/příprav cích a příbalovou informací.

Tento souhrn RMP připravil Státní ústav pro kontrolu léčiv za účelem splnění své zákonné povinnosti týkající se transparentno sti vůči veřejnosti.

1) Zákon č. 378/2007 Sb., o léčivech, ve znění pozdějších předpisů

Summary of the Risk Management Plan for Euthyrox (levothyroxine sodium)

This is a summary of the RMP for Euthyrox. The RMP details important risks of Euthyrox, how these risks can be minimized, and how more information will be obtained about Euthyrox' risks and uncertainties (missing information).

Euthyrox' MRP SPC and its package leaflet give essential information to healthcare professionals and patients on how Euthyrox should be used.

Important new concerns or changes to the current ones will be included in updates of Euthyrox' RMP.

I. The Medicine and What it is Used for

Euthyrox is authorized for (see MRP SPC for the full indication):

Treatment of benign euthyroid goitre

- 75–200 µg/day

Prophylaxis of relapse after surgery for euthyroid goitre:

- 75–200 µg/day

Substitution therapy in hypothyroidism

- Initial dose in adults: 25-50 µg/day
- Initial dose in children: 12.5–50 µg/day
- Maintenance dose in adults: 100-200 µg/day
- Maintenance dose in children: 100-150 µg/m² body surface/day

Suppression therapy in thyroid cancer:

- 150-300 µg/day

Applies only to tablets of 25-100 µg:

Concomitant supplementation during antithyroid drug treatment of hyperthyroidism

- 50-100 µg/day

Applies only to tablets of 150 µg:

Diagnostic use for thyroid suppression testing

- 75 µg/day (½ tablet), Week 4 and 3 prior to test
- 150 µg/day (1 tablet), Week 2 and 1 prior to test

Applies only to tablets of 100 µg and 200 µg:

Diagnostic use for thyroid suppression testing

- 200 µg/day, Week 2 and 1 prior to test

It contains levothyroxine sodium as the active substance, and it is given by oral route of administration.

II. Risks Associated with the Medicine and Activities to Minimize or Further Characterize the Risks

Important risks of Euthyrox, together with measures to minimize such risks and the proposed studies for learning more about Euthyrox' risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorized pack size - the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status - the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including PSUR assessment so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

I.A List of Important Risks and Missing Information

Important risks of Euthyrox are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Euthyrox. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	None
Important potential risks	Circulatory collapse in very low birth (preterm) neonate
Missing information	None

II.B Summary of Important Risks

Circulatory collapse in very low birth (preterm) neonate	
Evidence for linking the risk to the medicine	Postmarketing experience, scientific literature review, and cumulative review of cases.
Risk factors and risk groups	In a Japanese nationwide case-control study, the risk of circulatory collapse was stated to be higher in very low birth weight infants treated with L-T4 than in untreated controls (4.2% vs. 1.8%) (Kawai 2012). Low birth weight (LBW) is a result of preterm labor or intrauterine growth retardation. Approximately 15.5% of all births, or more than 20 million infants worldwide, are born with LBW. There are several causing factors for LBW: Nutritional status and pattern of weight gaining on mother during pregnancy, history of obstetric complications such as abortion or another child with LBW, chronic underlying diseases in mother, alcohol use and smoking. Other factors are prenatal care, hemoglobin and hematocrit level of mother during pregnancy, socioeconomic situation, mother's activity during pregnancy and demographic factors (age, weight, etc.) (Baghianimoghadam 2015).
Risk Minimization Measures	**Routine Risk Minimization Measures** **Routine Risk Communication**: MRP SPC Section 4.4 (Special warnings and precautions for use) **Routine Risk Minimization Activities recommending specific clinical measures to address the risk**: Recommendation for hemodynamic parameters to be monitored when levothyroxine therapy is initiated in very low birth weight preterm in MRP SPC Section 4.4. **Other routine Risk Minimization Measures beyond the Product Information**: Pack size **Legal status**: Restricted medical prescription **Additional Risk Minimization Measures**: None

LBW=Low Birth Weight; MRP=Mutual Recognition Procedure; SPC=Summary of Product Characteristics; T4: (Total) Thyroxine

II.C Post-authorization Development Plan

II.C.1 Studies Which are Conditions of the Marketing Authorization

There are no studies which are conditions of the marketing authorization or specific obligation of Euthyrox.

II.C.2 Other Studies in the Post-authorization Development Plan

There are no other studies required for Euthyrox.