# Part VI: Summary of the risk management plan

## Summary of risk management plan for Levothyroxine sodium oral solution in single-dose container (levothyroxine sodium)

This is a summary of the risk management plan (RMP) for Levothyroxine sodium oral solution in single-dose container, with the following invented names in the European Economic Area (EEA): Levosintsol (CZ, HU, SK), Levotirsol (IT), Syntroxine Sol (AT, EL), Tirosint Sol (DE, NL, PL), Tirosintsol (DK, NO, SE).

The RMP details important risks of Levothyroxine sodium oral solution, how these risks can be monitored and minimized, and how more information will be obtained about Levothyroxine sodium oral solution risks and uncertainties (missing information).

Levothyroxine sodium oral solution in single-dose container summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how it should be used.

## I. The medicine and what it is used for

Levothyroxine sodium oral solution in single-dose container is indicated for:

- Treatment of benign goitre with euthyroid function
- Prophylaxis against recurrent goitre after resection of a goitre with euthyroid function, depending on postoperative hormone status
- Thyroid hormone replacement in hypothyroidism
- Suppression therapy for malignant thyroid tumour
- Supportive therapy in thyrostatic treatment of hyperthyroidism
- Thyroid suppression test

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

## II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Levothyroxine sodium oral solution in single-dose container together with measures to minimise such risks and the proposed studies for learning more about Levothyroxine sodium oral solution in single-dose container's risks, are outlined below.

Measures to minimise 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 authorised 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 minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

## *II.A List of important risks and missing information*

Important risks of Levothyroxine sodium oral solution in single-dose container are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 Levothyroxine sodium oral solution in single-dose container. 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);

| **Summary of safety concerns** | |
|---|---|
| Important identified risks | Adrenal crisis |
| | Cardiovascular disorders |
| | Thyrotoxicosis |
| Important potential risks | Off label use for weight reduction |
| | Osteoporosis |
| | Seizures in patients with known history of epilepsy |
| | Unintended aspiration in neonates |
| | Circulatory collapse in neonates |
| Missing information | None |

## *II.B Summary of important risks*

| **Important identified risk : Adrenal crisis** | |
|---|---|
| Evidence for linking the risk to the medicine | Published cases and literature review. Moderate evidence. |
| Risk factors and risk groups | Patients with known (previous diagnosis) of adrenal insufficiency and subclinical and unrecognised adrenal insufficiency. |
| Risk minimisation measures | Routine risk minimisation measures:<br>***SmPC sections**: 4.3 – 4.4*<br>***PL section**: 2*<br>Additional risk minimisation measures:<br>No risk minimisation measures |

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|---|---|
| **Important identified risk : Cardiovascular disorders** | |
| Evidence for linking the risk to the medicine | Published cases and literature review. Strong evidence. |
| Risk factors and risk groups | Patients with diagnosed and undiagnosed cardiovascular disorders (angina, heart failure, myocardial infarction, and hypertension etc), elderly. |
| Risk minimisation measures | Routine risk minimisation measures:<br>***SmPC sections**: 4.2 - 4.3 – 4.4 - 4.8 – 4.9*<br>***PL section:** 2 - 3 – 4*<br>Additional risk minimisation measures:<br>No risk minimisation measures |
| **Important identified risk : Thyrotoxicosis** | |
| Evidence for linking the risk to the medicine | Literature review and published individual cases. Strong evidence. |
| Risk factors and risk groups | Individual who misuse intentionally the treatment is more common situation in clinical practice. |
| Risk minimisation measures | Routine risk minimisation measures:<br>***SmPC sections**: 4.3 – 4.4 - 4.8 – 4.9*<br>***PL section:** 2 – 4*<br>Additional risk minimisation measures:<br>No risk minimisation measures |
| **Important potential risk : Off label use for weight reduction** | |
| Evidence for linking the risk to the medicine | Literature review. Published individual cases. |
| Risk factors and risk groups | Massive dose and inappropriate administration of T4 in euthyroid patients is the most common situation. |
| Risk minimisation measures | Routine risk minimisation measures:<br>***SmPC sections**: 4.4*<br>***PL section:** 2*<br>Additional risk minimisation measures:<br>No risk minimisation measures |
| **Important potential risk : Osteoporosis** | |
| Evidence for linking the risk to the medicine | Epidemiological studies some conflicting findings. Low evidence. |

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|---|---|
| Risk factors and risk groups | Post-menopausal women and elderly population. |
| Risk minimisation measures | Routine risk minimisation measures:<br>***SmPC sections**: 4.4*<br>***PL section:** 2*<br>Additional risk minimisation measures:<br>No risk minimisation measures |

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|---|---|
| **Important potential risk : Seizures in patients with known history of epilepsy** | |
| Evidence for linking the risk to the medicine | Literature review. Published cases. Moderate evidence. |
| Risk factors and risk groups | Children and adult with history of seizures. The start of treatment is particularly the critical period. |
| Risk minimisation measures | Routine risk minimisation measures:<br>***SmPC sections**: 4.4*<br>***PL section:** 2*<br>Additional risk minimisation measures:<br>No risk minimisation measures |
| **Important potential risk : Unintended aspiration in neonates** | |
| Evidence for linking the risk to the medicine | Literature review. Low evidence. |
| Risk factors and risk groups | Neonates and infants. vomiting, nasogastric tube, endotracheal tube, gastrointestinal reflux devices |
| Risk minimisation measures | Routine risk minimisation measures:<br>***SmPC sections**: 4.2*<br>***PL section:** 3*<br>Additional risk minimisation measures:<br>No risk minimisation measures |
| **Important potential risk : Circulatory collapse in neonates** | |
| Evidence for linking the risk to the medicine | Literature overview. Moderate evidence. |
| Risk factors and risk groups | Neonates with subclinical and unrecognised adrenal insufficiency. |
| Risk minimisation measures | Routine risk minimisation measures:<br>***SmPC sections**: 4.4*<br>Additional risk minimisation measures:<br>No risk minimisation measures |

No missing information.

## *II.C Post-authorisation development plan*

### II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Levothyroxine sodium oral solution in single-dose container.

### II.C.2 Other studies in post-authorisation development plan

There are no other studies required for Levothyroxine sodium oral solution in single-dose container.