## PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

### Summary of risk management plan for Sodium Iodide (I131) Capsules T (Sodium Iodide I-131)

This is a summary of the risk management plan (RMP) for Sodium Iodide (I131) Capsules T. The RMP details important risks of Sodium Iodide (I131) Capsules T, how these risks can be

minimised, and how more information will be obtained about Sodium Iodide (I131) Capsules T's risks and uncertainties (missing information).

Sodium Iodide (I131) Capsules T's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Sodium Iodide (I131) Capsules T should be used.

Important new concerns or changes to the current ones will be included in updates of Sodium Iodide (I131) Capsules T's RMP.

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

Sodium Iodide (I131) Capsules T is authorised for (see SmPC for the full indication):

- Treatment of Graves' disease, toxic multinodular goitre or autonomous nodules.
- Treatment of papillary and follicular thyroid carcinoma including metastatic disease.

It contains Sodium Iodide I-131 as the active substance and it is given by a capsule to be taken orally. The capsule should be taken fasting and with plenty of liquid and swallowed whole.

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

Important risks of Sodium Iodide (I131) Capsules T, together with measures to minimise such 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.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including (Periodic Safety Update Report (PSUR) assessment - so that

immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

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

Important risks of Sodium Iodide (I131) Capsules T are risks that need special risk management activities to further investigate or minimise 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 Sodium Iodide (I131) Capsules T. 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 | • Increased radiation exposure for patients with renal impairment<br>• Foetal exposure and hypothyroidism in neonates (Congenital hypothyroidism)<br>• Exposure during lactation<br>• Secondary malignancies (Leukaemia and solid cancers)*<br>• Gonadal dysfunction in males / (Transient) Infertility* |
| Important potential risks | None |
| Missing information | None |

* Risk only applicable for use of sodium iodide I-131 in the treatment of malignant disease

### II.B Summary of important risks

| **Important identified risk: Increased radiation exposure for patients with renal impairment** | |
|---|---|
| Evidence for linking the risk to the medicine | Patients with renal impairment may have a decrease in the radioiodine clearance, resulting in increased radiation exposure of sodium iodide I-131 administered. As the risk profile is very much dependent on the level of exposure, careful consideration of the benefit/risk ratio in patients with renal impairment is required. In these patients it may be necessary to adjust the posology. |
| Risk factors and risk groups | Sodium iodide I-131 is eliminated predominantly through renal clearance; therefore patients with renal impairment are |

| **Important identified risk: Increased radiation exposure for patients with renal impairment** | |
|---|---|
| | subject to decreased excretion of sodium iodide I-131 and increased radiation exposure. |
| Risk minimisation measures | Routine risk minimisation measures<br>It is indicated that the therapeutic administration of I-131 capsules in patients with significant renal impairment, in which an activity adjustment is necessary, requires special attention.<br>Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings.<br>Additional risk minimisation measures<br>None |

| **Important identified risk: Foetal exposure and hypothyroidism in neonates (Congenital hypothyroidism)** | |
|---|---|
| Evidence for linking the risk to the medicine | The use of sodium iodide I-131 is contraindicated during established or suspected pregnancy or when pregnancy has not been excluded because trans-placental passage of sodium iodide I-131 can cause severe and possibly irreversible hypothyroidism in neonates (the absorbed dose to the uterus for this medicinal product is likely to be in the range 11-511 mGy, and the foetal thyroid gland avidly concentrates iodine during the second and third trimesters). |
| Risk factors and risk groups | The effects of radioiodine exposure are influenced by the timing of dose during foetal development. The foetal thyroid begins to develop in week 3 of gestation, becoming active weeks 10–12 and accumulating iodine from the maternal circulation via the placental iodine pump, and by late gestation, foetal radioiodine concentrations may be many times higher relative to the maternal thyroid. |
| Risk minimisation measures | Routine risk minimisation measures<br>It is indicated that the use of Sodium Iodide I-131 is contraindicated during established or suspected pregnancy or when pregnancy has not been excluded, due to trans-placental passage of sodium iodide I-131 which can cause severe and possibly irreversible hypothyroidism in neonates (the absorbed dose to the uterus for this medicinal product is likely to be in the range 11 511 mGy, and the foetal thyroid gland avidly concentrates iodine during the second and third trimesters). Should differentiated thyroid carcinoma be diagnosed during pregnancy, radioactive iodine treatment must be postponed until after the pregnancy. |

| **Important identified risk: Foetal exposure and hypothyroidism in neonates (Congenital hypothyroidism)** | |
|---|---|
| | Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings.<br>Additional risk minimisation measures<br>None |

| **Important identified risk: Exposure during lactation** | |
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| Evidence for linking the risk to the medicine | The pharmacokinetics of sodium iodide I-131 follows that of unlabelled iodide. As part of further organ distribution, small amounts of sodium iodide I-131 can also be secreted in breast milk which would be a risk to the infant. Before administering radiopharmaceuticals to a mother who is breast-feeding, consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding, and what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breast-feeding must be discontinued at least 8 weeks before sodium iodide I-131 administration and should not be resumed. This is also to ensure that lactation-associated increase in breast sodium iodide symporter activity has returned to normal. This is to minimize the radiation risk for the mother herself. |
| Risk factors and risk groups | Lactation and post-partum status. |

| **Important identified risk: Exposure during lactation** | |
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| Risk minimisation measures | Routine risk minimisation measures<br>It is indicated that before administering radiopharmaceuticals to a mother who is breast-feeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breast-feeding, and what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breast-feeding should be discontinued after Sodium Iodide I-131 administration.<br>In relation to this risk in the draft core EU SmPC it is indicated in the part on breastfeeding warnings that if the administration is considered necessary, breast-feeding must be discontinued at least 8 weeks before sodium iodide (131-I) administration and should not be resumed (see section 4.3). When the core EU SmPC is final, the product information will be updated accordingly.<br>Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings.<br>Additional risk minimisation measures<br>None |

| **Important identified risk: Secondary malignancies (Leukaemia and solid cancers) *** | |
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| Evidence for linking the risk to the medicine | Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. The radiation dose resulting from therapeutic exposure may result in higher incidence of cancer and mutations. There is little evidence of an increased incidence of cancer, leukaemia or mutations in patients after treatment with radioiodine for benign thyroid diseases, despite its extensive use. After higher activities, typically those used in the treatment of thyroid malignancies, an increased incidence of leukaemia has been observed. There is also evidence for an increased incidence of secondary solid cancers at high activities (more than 7.4 GBq). For each patient, the radiation exposure must be justifiable by the likely benefit. The activity to be administered should in every case be as low as reasonably achievable to obtain the required therapeutic effect. |
| Risk factors and risk groups | Unknown. |
| Risk minimisation measures | Routine risk minimisation measures<br>In relation to this risk in the draft core EU SmPC it is indicated in the warnings that for each patient, the radiation exposure must be justifiable by the likely benefit. The activity to be administered should in every case be as low as reasonably achievable to obtain the required therapeutic |

| **Important identified risk: Secondary malignancies (Leukaemia and solid cancers) *** | |
|---|---|
| | effect. When the core EU SmPC is final, the product information will be updated accordingly.<br>Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings.<br><u>Additional risk minimisation measures</u><br>None |

| **Important identified risk: Gonadal dysfunction in males/(Transient) Infertility*** | |
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| Evidence for linking the risk to the medicine | After radioiodine therapy of thyroid carcinoma, a dose dependent impairment of fertility may occur in men and women. Depending on the activity dose, a reversible impairment of the spermatogenesis could occur in doses above 1850 MBq; clinical relevant effects including oligospermia and azoospermia and elevated FSH serum levels have been described after administration greater than 3700 MBq. Sperm banking should be considered for young men who have extensive disease and therefore may need high iodine-131 therapeutic doses. |
| Risk factors and risk groups | This risk is important to take into account in treatment of patients of childbearing age and younger age groups. |
| Risk minimisation measures | <u>Routine risk minimisation measures</u><br>It is indicated that women are advised to use contraception for a time period of 6 -12 months. As a precaution, men should not father a child for a time period of 6 months after radioiodine treatment to allow the replacement of irradiated by non-irradiated spermatozoa.<br>In relation to this risk in the draft core EU SmPC it is indicated in the warnings that for the use of the sperm bank could be considered to compensate a potential reversible damage of gonadal function in males due to the high therapeutic dose of radioiodine, in the cases of patients with extensive disease. When the core EU SmPC is final, the product information will be updated accordingly.<br>Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings.<br><u>Additional risk minimisation measures</u><br>None |

* Risk only applicable for use of sodium iodide I-131 in the treatment of malignant disease

## 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 Sodium Iodide (I131) Capsules T.

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

There are no studies required for Sodium Iodide (I131) Capsules T.