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4 Guideline on core SmPC and Package Leaflet for sodium 5 iodide (^{131}I) therapy capsule

6 Draft

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Keywords	***Radiopharmaceuticals, radionuclide, kit for radiopharmaceutical preparation, core SmPC, core Package Leaflet, sodium iodide (^{131}I) therapy capsule***

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Guideline on core SmPC and Package Leaflet for sodium iodide (^{131}I) therapy capsule

Table of contents

Executive summary

This guideline describes the information to be included in the Summary of Products Characteristics (SmPC) and package leaflet for sodium iodide (^{131}I) therapy capsule.

1. Introduction (background)

This core SmPC has been prepared on the basis of national SmPCs, and taking into account the published scientific literature. Any marketing authorisation application or variation of a marketing authorisation for a radiopharmaceutical product containing sodium iodide (^{131}I) should be accompanied by the required data and documents for the application to be valid.

The indications in section 4.1 are provided as clinical settings sufficiently documented at the time of publication of this core SmPC. However, this list of clinical settings does not waive the need to submit the required studies to support the claimed indication or an extension of indication.

2. Scope

This core SmPC and package leaflet covers sodium iodide (^{131}I) therapy capsule.

3. Legal basis

This guideline has to be read in conjunction with Article 11 of Directive 2001/83 as amended, and the introduction and general principles (4) and part I of the Annex I to Directive 2001/83 as amended.

4. Core SmPC and Package Leaflet for sodium iodide (^{131}I) therapy capsule

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

< ▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.>

1. NAME OF THE MEDICINAL PRODUCT

{(Invented) name strength}, hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One capsule contains sodium iodide (131I) [...] – […] MBq at activity reference time.

Iodine-131 is produced by fission of uranium-235 or by neutron bombardment of stable tellurium in a nuclear reactor. Iodine-131 has a half-life of 8.02 days. It decays by emission of gamma radiations of 365 keV (81.7%), 637 keV (7.2%) and 284 keV (6.1%) and beta radiations of maximal energy of 606 keV to stable Xenon-131.

Excipient(s) with known effect
x mg sodium per capsule.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsule
[Description Product specific]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Radioiodide thyroid therapy is indicated for:
- Hyperthyroidism: Treatment of Graves' disease, toxic multinodular goitre or autonomous nodules.
- Treatment of papillary and follicular thyroid carcinoma including metastatic disease.

Sodium Iodide (131I) therapy is often combined with surgical intervention and with antithyroid medicinal products.

4.2 Posology and method of administration

Posology

The activity to be administered is a matter for clinical judgement. The therapeutic effect is only achieved after several months.

Adults

Treatment of hyperthyroidism
In case of failure or impossibility to pursue the medical treatment, radioactive iodide may be administered to treat the hyperthyroidism.

Patients should be rendered euthyroid medically whenever possible before giving radioiodine treatment for hyperthyroidism.
The activity to be administered depends on the diagnosis, the size of the gland, thyroid uptake and iodine clearance. It is usually in the range of 200-800 MBq for a patient of average weight (70 kg) but repeated treatment up to a cumulative dose of 5000 MBq may be necessary. The therapeutic effect is only achieved after several months.
The activity to be administered may be defined by fixed dose protocols or may be calculated according to the following equation:

$$A\ (MBq) = \frac{\text{Target dose (Gy) x target volume (ml)}}{\text{max. uptake I-131(\%) x effective T ½ (days)}} \times K$$

in case when

target dose	is the target absorbed dose in the whole thyroid gland or in an adenoma
target volume	is the volume of the whole thyroid gland (Graves' disease, multifocal or disseminated autonomy)
max. uptake I-131	is the max. uptake of I-131 in the thyroid gland or nodules in % of the administered activity as established in a test dose
effective T ½	is the effective half life of I-131 in the thyroid gland expressed in days
K	is 24,67

The following target organ doses may be used:

Unifocal autonomy	300 – 400 Gy target organ dose
Multifocal and disseminated autonomy	150 – 200 Gy target organ dose
Graves' disease	200 Gy target organ dose

In the case of Graves' disease, multifocal or disseminated autonomy, the above mentioned target organ doses are related to the overall weight of the thyroid gland mass, however in the case of unifocal autonomy, the target organ dose is only related to the weight of the adenoma. For recommended doses to target organs: see section 11.
Other dosimetric procedures may also be used including sodium pertechnetate (99mTc) thyroid uptake tests to determine the appropriate target organ dose (Gy).
Fixed dose protocols may also be used.

Thyroid ablation and treatment of metastases

The activities to be administered following total or subtotal thyroidectomy to ablate remaining thyroid tissue are in the range of 1850-3700 MBq. It depends on the remnant size and radioiodine uptake. For treatment of metastases, administered activity is in the range of 3700-11100 MBq.

Renal impairment

Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in patients with reduced renal function. The therapeutic use of 131I capsules in patients with significant renal impairment requires special attention. (see section 4.4)

Paediatric population

The use in children and adolescents has to be considered carefully, based upon clinical needs and assessing the benefit/risk ratio in this patient group.

In certain cases the activity to be administered in children and adolescent should be determined after performing an individual dosimetry (see section 4.4).
In children and adolescents, treatment with radioactive iodide of benign thyroid defects is possible in justified cases, in particular in case of relapse after the use of antithyroid medicinal products or in case of severe adverse reaction to antithyroid medicinal products (see section 4.4).

Method of administration

The capsule is administered orally on an empty stomach. The capsules should be swallowed whole with abundant drink to ensure clear passage into the stomach and upper small intestine. In patients with suspected gastrointestinal disease, great care should be taken when administering Sodium Iodide (131I) capsules. Concomitant use of H2-antagonists or proton pump inhibitors is advised.
In case of administration to children, especially to younger children, it has to be ensured that the capsule can be swallowed whole without chewing. It is recommended to give the capsule with mashed food.
For patient preparation, see section 4.4.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Pregnancy and breastfeeding lactation (see section 4.6).
- Patients with dysphagia, oesophageal stricture, oesophagal stenosis, oesophagus diverticulum, active gastritis, gastric erosions and peptic ulcer.
- Patients with suspected reduced gastrointestinal motility.

4.4 Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions
If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification
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.
There is little evidence of an increased incidence of cancer, leukaemia or mutations in patients after treatement with radioiodine for benign thyroid diseases, despite its extensive use. In the treatment of malignant thyroid diseases, in a study conducted on patients with doses of iodine–131 higher than 3700 MBq a higher incidence of bladder cancer was reported. Another study reported a slight increase in leukaemia in patients receiving very high doses. Therefore total cumulative doses greater than 26000 MBq are not recommended.

Gonadal function in males
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.

Patients with renal impairment
Careful consideration of the benefit/risk ratio in these patients is required since an increased radiation exposure is possible. In these patients it may be necessary to adjust the posology.

Patient preparation

Patients should be encouraged to increase oral fluids and urged to void as often as possible to reduce bladder radiation, especially after high activities e.g. for the treatment of thyroid carcinoma. Patients with bladder voiding problems should be catheterised after administration of high activities of radioiodine.
To avoid sialadenitis which may occur after high dose radioiodine administration, the patient should be advised to take sweets or drinks containing citric acid (lemon juice, vitamin C) to stimulate saliva excretion before therapy. Other pharmacological protection measures may be used additionally.
Iodide overload from food or medicinal treatment should be investigated before administration of iodide see 4.5. A low iodine diet prior to therapy is recommended to enhance uptake into functioning thyroid tissue.
Thyroid replacement should be stopped prior to radioiodine administration for thyroid carcinoma to ensure adequate uptake. It is recommended to stop triiodothyronine treatment for a period of 14 days and to stop thyroxine treatment for a period of 4 weeks. They should be restarted two days after treatment.
Carbimazole and propylthiouracil should be stopped 1 week prior to treatment of hyperthyroidism and restarted several days after treatment.
The radioiodine treatment of Graves' disease should be performed under concomitant treatment of corticosteroids, particularly when endocrine ophthalmopathy is present.

After the procedure
Close contact with infants and pregnant women should be restricted for an appropriate period of time.
In case of vomiting, the risk of contamination has to be considered.
Patients receiving therapy of the thyroid should be re-examined at appropriate intervals.

Paediatric population
Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11). When treating children and young adults, account must be taken of the greater sensitivity of child tissue and the greater life expectancy of such patients. The risks should be weighed against those of other possible treatments. See sections 4.2 and 11.
The radioiodine treatment of benign thyroid diseases of children and adolescents may be performed only in justified cases, especially in relapse after use of antithyroid medicinal products or in case of serious adverse reactions to antithyroid medicinal products. There is no evidence of an increased incidence of cancer, leukemia or mutations in humans with respect to patients treated for benign thyroid disease with radioiodine, despite extensive use.
Persons who have received radiotherapy of the thyroid as children and adolescents, should be re-examined once a year.

Specific warnings
<This medicinal product contains [...] mg of sodium per dose. To be taken into account by patients on a controlled sodium diet.>
<This medicinal product contains [...] mg of sucrose per capsule. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.>
Precautions with respect to environmental hazard are in section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

Many pharmacologically active substances interact with radioiodide. Various interaction mechanisms exist which can affect the protein binding, the pharmacokinetics or the dynamic effects of labelled iodide. As a consequence, it should be considered that the thyroid uptake might be reduced. Therefore, a full drug history should be taken and relevant medicinal products are required to be withheld prior to the administration of sodium iodide (131I).
For example, the treatment with the following substances should be discontinued:

Active substances	**Withdrawal period before administration of iodine-131**

Active substances	Withdrawal period before administration of iodine-131
Antithyroid medicinal products (e.g. carbimazole, methimazole, propyluracil), perchlorate	1 week before starting treatment till several days after
Salicylates, corticosteroids, sodium nitroprusside, sodium sulfobromophthalein, anticoagulants, antihistamines, antiparasitics, penicillins, sulphonamides, tolbutamide, thiopental	1 week
Phenylbutazone	1 - 2 weeks
Containing iodine expectorants and vitamins	approximately 2 weeks
Thyroid hormone preparations	Triiodothyronine 2 weeks thyroxine 6 weeks
Benzodiazepines, lithium	approximately 4 weeks
Amiodarone*	3-6 months
Containing iodine preparations for topical use	1 - 9 months
Water-soluble iodine-containing contrast media	6 to 8 weeks
Lipo-soluble iodine-containing contrast media	up to 6 months

* Due to the long half-life of amiodarone, iodine uptake in the thyroid tissue can be decreased for several months.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient. If a differentiated thyroid carcinoma is diagnosed during pregnancy, the treatment with iodine-131 should be postponed after childbirth.

Contraception in males and females

Contraception for 6 months (for patients with benign thyroid conditions) or 12 months (for patients with thyroid cancer) is recommended for both sexes after therapeutic administration of Sodium Iodide (131I). 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. Sperm banking should be considered for young men who have extensive disease and therefore may need high iodine-131 therapeutic doses.

Pregnancy

The use of sodium iodide (131I) is contraindicated during established or suspected pregnancy or when pregnancy has not been excluded because transplacental passage of sodium iodide (131I) 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) (see section 4.3).
Should differentiated thyroid carcinoma be diagnosed during pregnancy, iodine-131 treatment must be postponed until after the pregnancy. Women receiving Sodium Iodide (131I) should be advised not to become pregnant within 6-12 months after administration.

Breast-feeding

Before administering radiopharmaceuticals to a mother who is breast-feeding, consideration should be given to the possibilitiy 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 (131I) administration and should not be resumed. (see section 4.3).
For radioprotection reasons following therapeutic doses, it is recommended to avoid close contact between mother and infants for at least one week.

Fertility
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 serum FSH serum levels have been described after administration greater than 3700 MBq.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive or use machines have been performed.

4.8 Undesirable effects

The frequencies of reported adverse reactions were derived from the medical literature. The safety profile of sodium iodide (131I) differs widely according to the doses administered, while the doses to be administered are dependent on the type of treatment (i.e. treatment of benign or malignant disease). Moreover, the safety profile depends on the cumulative doses administered and the dosing intervals which are used. Therefore, the reported adverse reactions were grouped by their occurrence in treatment of benign or malignant disease.
Frequently occurring adverse reactions are: hypothyroidism, transient hyperthyroidism, salivary and lacrimal gland disorders, and radiation local effects. In cancer treatment additionally gastro-intestinal adverse reactions and bone marrow suppression may frequently occur.
The following tables include reported adverse reactions sorted by system organ classes. Symptoms, which are rather secondary to a group-syndrome (e.g. sicca syndrome) are subsumed in parenthesis behind the respective syndrome.
The following table presents how the frequencies are reflected in this section:
Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000) and not known (frequency cannot be estimated from the available data).

Adverse reactions after treatment of benign disease

System organ class	***Adverse reaction***	***Frequency***
Immune system disorders	Anaphylactoid reaction	Not known
Endocrine disorders	Permanent hypothyroidism, hypothyroidism	Very common
	Transient hyperthyroidism	Common
	Thyreotoxic crisis, thyroiditis, hypoparathyroidism (blood calcium decreased, tetany)	Not known
Eye disorders	Endocrine ophthalmopathy (in Graves' disease)	Very common
	Sicca syndrome	Not known

System organ class	*Adverse reaction*	*Frequency*
Respiratory, thoracic and mediastinal disorders	Vocal cord paralysis	Very rare
Gastrointestinal disorders	Sialoadenitis	Common
General disorders and administration site conditions	Local swelling	Not known
Skin and subcutaneous tissue disorders	Iodide induced acne	Not known

335 **Adverse reactions after treatment of malignant disease**

System organ class	*Adverse reaction*	*Frequency*
Neoplasms benign, malignant and unspecified (including cysts and polyps)	Leukaemia	Uncommon
	Solid cancers, Bladder cancer, colon cancer, gastric cancer, breast cancer	Not known
Blood and lymphatic system disorders	erythropenia, bone marrow failure	Very common
	Leukopenia, thrombocytopenia	Common
	Aplastic anemia, Permanent or severe bone marrow suppression	Not known
Immune system disorders	Anaphylactoid reaction	Not known
Endocrine disorders	Thyreotoxic crisis, transient hyperthyroidism	Rare
	Thyroiditis (transient leucocytosis), hypoparathyroidism (blood calcium decreased, tetany), hypothyroidism, hyperparathyroidism	Not known
Nervous system disorders	Parosmia, anosmia	Very common
	Brain oedema	Not known
Eye disorders	Sicca syndrome (conjunctivitis, dry eyes, nasal dryness)	Very common
	Nasolacrimal duct obstruction (lacrimation increased)	Common
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Common

System organ class	*Adverse reaction*	*Frequency*
	Throat constriction*, Pulmonary fibrosis, respiratory distress, obstructive airways disorder, pneumonia, tracheitis, vocal cord dysfunction (vocal cord paralysis, dysphonia, hoareseness), oropharyngeal pain, stridor	Not known
Gastrointestinal Disorders	Sialoadenitis (dry mouth, salivary gland pain, salivary gland enlargement, dental caries, tooth loss), radiation sickness syndrome, nausea, ageusia, anosmia, dysgeusia, decreased appetite	Very common
	Vomiting	Common
	Gastritis, dysphagia	Not known
Renal and urinary disorders	Radiation cystitis	Not known
Reproductive system and breast disorders	Ovarian failure, menstrual disorder	Very common
	Azoospermia, oligospermia, decreased fertility male	Not known
Congenital, familial and genetic disorders	Congenital hypothyroidism	Not known
General disorders and administration site conditions	Flu-like illness, headache, fatigue, neck pain	Very common
	Local swelling	Common

* especially in existing tracheal stenosis

Description of selected undesiderable effects

General advice

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. In all cases it is necessary to ensure that the risks of the radiation are less than those of the disease itself. The effective dose after therapeutic doses of sodium iodide (131I) is higher than 20 mSv and the effective dose equivalent when the administered dose is 11100 MBq (with thyroid uptake 0%) is 799,2 mSv.

Thyroid and parathyroid glands disorders

Hypothyroidism may occur, depending on the dose, as a delayed result of treatment for hyperthyroidism with radioiodine.

In the treatment of malignant disease, hypothyroidism is often reported as an adverse reaction; however the treatment of malignant diseases with radioiodine generally follows thyroidectomy.

The destruction of thyroid follicles caused by the radiation exposure of sodium iodide (131I)may lead to exacerbation of an already existing hyperthyroidism within 2 – 10 days or may cause a thyrotoxic crisis. Occasionally, an immune hyperthyroidism may appear after initial normalisation (latency period is 2 – 10 months). After 1-3 days of administration of high dose radioiodine, the patient may experience transient

inflammatory thyroiditis and tracheitis, with a possibility of severe tracheal constriction, especially where there is existing tracheal stenosis.
In rare cases, a temporary hyperthyroidism could be observed even after treatment of a functional thyroid carcinoma.
Cases of transient hypoparathyroidism have been observed after radioiodine administration which should be appropriately monitored and treated with replacement therapy.
Late consequences Dose dependent hypothyroidism may occur as a delayed result of radioiodine treatment of hyperthyroidism. This hypothyroidism may manifest itself weeks or years after the treatment, and monitoring of thyroid function and appropriate hormone replacement therapy are required.
Hypothyroidism does not generally appear until 6 - 12 weeks after radioiodine administration.
Eye disorders
Endocrine ophthalmopathy may progress or new ophthalmopathy may occur after radioiodine therapy of hyperthyroidism or Graves` disease. Radioiodine treatment of Graves disease should be associated with corticosteroids.

Local irradiation effects
Dysfunction and paralysis of vocal cords have been reported after administration of Sodium Iodide (131I);, however, in some cases it cannot be decided whether the dysfunction of the vocal cords was caused by radiation or by surgical treatment.
High tissue uptake of radioiodine can be associated with local pain, discomfort and local oedema e.g. in case of radioiodine treatment of the remnant thyroid gland, a diffuse and severe soft tissue pain may occur in the head and neck region.
Radiation induced pneumonia and pulmonary fibrosis have been observed in patients with diffuse pulmonary metastases from differentiated thyroid carcinoma, due to destruction of metastatic tissue. This occurs mainly after high dose radioiodine therapy.
In the treatment of metastasing thyroid carcinomas with central nervous system (CNS) involvement, the possibility of local cerebral oedema and/or aggravation of existing cerebral oedema should also be considered.
Gastrointestinal disorders
High levels of radioactivity may also lead to gastrointestinal disturbance, usually within the first hours or days after administration. For prevention of gastrointestinal disorders see section 4.4.

Salivary and lacrimal gland disorders
Sialoadenitis may occur, with swelling and pain in the salivary glands, partial loss of taste and dry mouth. Sialoadenitis is usually reversible spontaneously or with anti-inflammatory treatment but cases of dose-dependent persistent ageusia and dry mouth have occasionally been described. The lack of saliva may lead to infections, e.g. caries and this may result in loss of teeth. For prevention of salivary disorders see section 4.4.
Malfunction of the salivary and/or lacrimal glands with resulting sicca syndrome may also appear with a delay of several months and up to two years after radioiodine therapy. Although sicca syndrome is a transient effect in most cases, the symptom may persist for years in some patients.

Bone marrow depression
As a late consequence, reversible bone marrow depression may develop, presenting with isolated thrombocytopenia or erythrocytopenia which may be fatal. Bone marrow depression is more likely to occur after one single administration of more than 5000 MBq, or after repeat administration in intervals below 6 months.

Secondary malignancies
After higher activities, typically those used in the treatment of thyroid malignancies, an increased incidence of leukaemia has been observed. There is evidence of an increased frequency of solid cancers induced by administration of high activities (above 7.4 GBq).

Paediatric population

The type of undesiderable effetcs expected in children are identical to the one in adults. Based on greater radiation sensitivity of child tissues (see section 11) and the greater life expectancy frequency and severity may be different.

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 national reporting system listed in Appendix V.*

[*For the printed material, please refer to the guidance of the annotated QRD template.]

4.9 Overdose

This product must be used by authorize personnel in hospital setting. The risk of overdose is therefore theoretical.
In the event of administration of a radiation overdose, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by frequent micturition and by forced diuresis and frequent bladder voiding. Additionally, the blockade of the thyroid gland should be recommended (e.g. with potassium perchlorate) in order to reduce the radiation exposure of the thyroid gland. To reduce the uptake of iodine-131, emetics can be given.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Therapeutic radiopharmaceuticals, Iodine (131I) compounds.

ATC code: V10XA01.

The pharmacological active substance is iodine-131 in the form of sodium iodide that is taken up by the thyroid. The physical decay takes place essentially in the thyroid gland, where iodide-131 has a long residence time, delivering a selective irradiation to this organ.
In the amount used for therapeutic indications, no pharmacodynamic effects of Sodium Iodide (131I) are to be expected.
More than 90% of the radiation effects result from emitted β radiation which has a mean range of 0.5 mm. The β irradiation will dose dependently decrease cell function and cell division leading to cell destruction. The short range and almost absence of uptake of Sodium Iodide (131I) outside the thyroid lead to a negligible amount of irradiation exposure outside the thyroid gland.

5.2 Pharmacokinetic properties

Absorption

After oral administration, Sodium Iodide (131I) is absorbed rapidly from the upper gastrointestinal tract (90% in 60 minutes). The absorption is influenced by gastric emptying. It is increased by hyperthyroidism and decreased by hypothyroidism.
Studies on the serum activities levels showed that after a fast increase, over 10 to 20 minutes, an equilibrium is reached after about 40 minutes. After oral administration of Sodium Iodide (131I) solution an equilibrium is reached at the same time.

Organ distribution and -uptake

The pharmacokinetics follows that of unlabelled iodide. After entering the blood stream it is distributed in the extra thyroidal compartment. From here it is predominantly taken up by the thyroid that extracts approximately 20% of the iodide in one pass or excreted renally. The iodide uptake in the thyroid reaches a maximum after 24-48 hours, 50% of the maximum peak is reached after 5 hours. The uptake is

influenced by several factors: patient age, thyroid gland volume, renal clearance, plasmatic concentration of iodide and other drugs (see section 4.5). The iodide clearance by the thyroid gland is usually 5- 50 mL/min. In case of iodine deficiency the clearance is increased to 100 mL/min and in case of hyperthyroidism can be up to 1000 mL/min. In case of iodide overload the clearance can decrease to 2 – 5 ml/min. Iodide also accumulates in the kidneys.
Small amounts of sodium iodide (131I) are taken up by salivary glands, gastric mucosa and they would also be localised in breast milk, the placenta and choroid plexus.
The iodide fixed by the thyroid enters the know metabolic path of thyroid hormones and is incorporated in the organic substances entering in the synthesis of thyroid hormones.

Biotransformation
The iodide that has been taken up by the thyroid follows the known metabolism of the thyroid hormones and is incorporated in the organic compounds from which the thyroid hormones are synthesised.
Elimination
Urinary excretion is 37-75%, faecal excretion is about 10% with almost negligible excretion in sweat. Urinary excretion is characterised by the renal clearance, which constitutes about 3% of the renal flow and is relatively constant from one person to another. The clearance is lower in hypothyroidism and in impaired renal function and higher in hyperthyroidism. In euthyroidic patients with normal renal function 50 – 75 % of the administered activity is excreted in urine within 48 hours.

Half-life
The effective half-life of radioiodine in plasma is about 12 hours in blood plasma and about 6 days in the thyroid gland. Thus after administration of Sodium Iodide (131I) about 40% of the activity has an effective half-life of 6 hours and the remaining 60% of 8 days.

Renal impairment
Patients with renal impairment may have a decrease in the radioiodine clearance, resulting in increased radiation exposure of sodium iodide (131I) administered. One study showed, for example, that patients with impaired renal function undergoing continuous ambulatory peritoneal dialysis (CAPD) have a clearance of radioiodine 5 times lower than patients with normal kidney function.

5.3 Preclinical safety data

Because of the small quantities of administered substance compared with the normal intake of iodine with food (40-500 µg/day) no acute toxicity is expected or observed. There are no data available on the toxicity of repeated doses of sodium iodide nor on its effects on reproduction in animals or its mutagenic or carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents:
[Product specific]

Capsule shell:
[Product specific]

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

[Product specific]

6.4 Special precautions for storage

[Product specific].
<Store in the original package to prevent from external radiation exposure.>
Storage of radiopharmaceuticals should be in accordance with national regulations.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

[Product specific]

6.6 Special precautions for disposal <and other handling>

Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the local competent official organisation. Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements.
If at any time in the preparation of this product the integrity of this [container] is compromised it should not be used.

External radiation exposure
The administration of sodium iodide (131I) for therapy may result in significant environmental hazard and creates risks for other persons from external radiation or contamination from spill of urine, vomiting etc. This may be of concern to the immediate family of those individuals undergoing treatment or the general public depending on the level of activity administered.
Radiation protection precautions in accordance with national regulations should therefore be taken.
Administration procedures should be carried out in a way to minimize risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.
When opening the container personnel should be aware that free radioactivity may be registered on monitors. This activity is due to Xe-131m which is formed for 1.17 % in the decay of I-131. Though visible on monitors this does not pose a relevant risk for personnel.
The effective dose rate by inhalation of the Xe-131m formed is 0.1% of the dose rate at 1 m from a lead-shielded capsule.

Procedure for use:
The following procedure should be used when the product is being administered to the patient:
- The patients stomach should be empty when taking the capsule.
- The patient will receive a heavy lead pot, attached in it one capsule in a plastic single dose container
- The patient will unscrew the lid of the lead pot and the container cap simultaneously by turning it three times counter-clockwise
- The patient will remove the lid, lift the lead pot, and swallow the capsule

Precautions and activity data
1.3% of iodine-131 decays via xenon-131m (half-life 12 days) and a small amount of xenon-131m activity may be present in the packaging as a result of diffusion. It is therefore recommended that the transport container be opened in a ventilated enclosure and that, after removal of the capsule, the packaging materials are allowed to stand overnight before disposal to permit the release of absorbed xenon-131m.

In addition, there can be limited leakage of volatile iodine-131 activity from the capsule. The container incorporates a small disc of charcoal in the lid which serves to absorb the iodine that escapes from the capsule. The charcoal disc may become contaminated
with up to 1.3MBq (35μCi) of iodine-131. As a consequence of the charcoal disc, only very small amounts of iodine-131 (typically less than 1.85kBq (50nCi)) may be present in the packaging.

The dose rate for iodine-131 in air due to gamma and X-ray radiation, at one meter from a point source containing one gigabecquerel is 5.7 x 10 -2 mSv/hr.
The activity of a capsule at 12h00 GMT from calibration date can be calculated from the table 1.

Table 1

Day	Coefficient	Day	Coefficient
-6	1,677	5	0,650
-5	1,539	6	0,596
-4	1,412	7	0,547
-3	1,295	8	0,502
-2	1,188	9	0,460
-1	1,090	10	0,422
0	1,000	11	0,387
1	0,917	12	0,355
2	0,842	13	0,326
3	0,772	14	0,299
4	0,708		

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

10. DATE OF REVISION OF THE TEXT

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

11. DOSIMETRY

The data listed below are from ICRP (International Commission on Radiological Protection, Radiation Dose to Patients from Radiopharmaceuticals) publication 53 and 60.
The ICRP model refers to intravenous administration. Since radioiodine absorption is rapid and complete, this model is applicable in case of oral administration also but there is a further radiation dose to the stomach wall in addition to that due to gastric and salivary excretion. Assuming that the mean residence time in the stomach is 0.5 hr, the absorbed radioiodine dose to the stomach wall increases by about 30% for iodine-131.

Radiation dose to specific organs, which may not be the target organ of therapy, can be influenced significantly by pathophysiological changes induced by the disease process. This should be taken into consideration when using the following information.
As part of the risk-benefit assessment it is advised that the effective dose and likely radiation doses to individual target organ(s) are calculated prior to administration. The activity might then be adjusted according to thyroid mass, biological half-life and the "re-cycling" factor which takes into account the physiological status of the patient (including iodine depletion) and the underlying pathology.

Doses to the following target organs can be used:
Unique nodule Target organ dose 300 – 400 Gy
Multiple or disseminated nodules Target organ dose 150 – 200 Gy
Basedow disease Target organ dose 200 Gy

The radiation exposure mainly affects the thyroid. The radiation exposure of the other organs is in the range of thousandths lower than that of the thyroid. It depends on the dietary intake of iodine (the uptake of radioiodine is increased up to 90% in iodine deficient areas and it is decreased to 5% in iodine rich areas). It further depends on the thyroid function (eu-, hyper-, or hypothyroidism) and on the presence of iodine accumulating tissues in the body. (e.g. the situation after excision of the thyroid, the presence of iodine accumulating metastases and on thyroid blockade) The radiation exposure of all other organs is correspondingly higher or lower, depending on the degree of accumulation in the thyroid.

Thyroid blocked, uptake 0%

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.037	0.042	0.067	0.11	0.20
* Bladder wall	0.61	0.75	1.1	1.8	3.4
Bone surfaces	0.032	0.038	0.061	0.097	0.19
Breast	0.033	0.033	0.052	0.085	0.17
GI-tract					
Stomach wall	0.034	0.04	0.064	0.1	0.19
* Small intest	0.038	0.047	0.075	0.12	0.22
* ULI wall	0.037	0.045	0.07	0.12	0.21
* LLI wall	0.043	0.052	0.082	0.13	0.23
* Kidneys	0.065	0.08	0.12	0.17	0.31
Liver	0.033	0.04	0.065	0.1	0.2
Lungs	0.031	0.038	0.06	0.096	0.19
Ovaries	0.042	0.054	0.084	0.13	0.24
Pancreas	0.035	0.043	0.069	0.11	0.21
Red marrow	0.035	0.042	0.065	0.10	0.19
Spleen	0.034	0.040	0.065	0.10	0.20
Testes	0.037	0.045	0.075	0.12	0.23
Thyroid	0.029	0.038	0.063	0.10	0.20
Uterus	0.054	0.067	0.11	0.17	0.30
Other tissue	0.032	0.039	0.062	0.10	0.19
Effective dose (mSv/MBq)	**0.064**	**0.081**	**0.13**	**0.20**	**0.37**

Bladder wall contributes to 47.6% of the effective dose.

Incomplete blockage

	Effective dose (mSv/MBq) at small uptake in the thyroid				
Uptake: 0.5%	0.50	0.79	1,2	2,6	4,9
Uptake: 1.0%	0.90	1,4	2,1	4,7	9.3
Uptake: 2.0%	1,6	2,6	4,2	9.3	17

641 **Thyroid uptake 15%**

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.036	0.043	0.071	0.11	0.22
* Bladder wall	0.52	0.64	0.98	1.5	2.9
Bone surfaces	0.047	0.067	0.094	0.14	0.24
Breast	0.043	0.043	0.081	0.13	0.25
GI-tract					
* Stomach wall	0.46	0.58	0.84	1.5	2.9
* Small intest	0.28	0.35	0.62	1.0	2.0
* ULI wall	0.059	0.065	0.10	0.16	0.28
LLI wall	0.042	0.053	0.082	0.13	0.23
* Kidneys	0.060	0.075	0.11	0.17	0.29
Liver	0.032	0.041	0.068	0.11	0.22
Lungs	0.053	0.071	0.12	0.19	0.33
Ovaries	0.043	0.059	0.092	0.14	0.26
Pancreas	0.052	0.062	0.10	0.15	0.27
Red marrow	0.054	0.074	0.099	0.14	0.24
Spleen	0.042	0.051	0.081	0.12	0.23
Testes	0.028	0.035	0.058	0.094	0.18
Thyroid	210	340	510	1100	2000
Uterus	0.054	0.068	0.11	0.17	0.31
Other tissue	0.065	0.089	0.14	0.22	0.40
Effective dose (mSv/MBq)	**11**	**18**	**27**	**59**	**107**

642 **Thyroid uptake 35%**

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.042	0.050	0.087	0.14	0.28
* Bladder wall	0.40	0.50	0.76	1.2	2.3
Bone surfaces	0.076	0.12	0.16	0.23	0.35
Breast	0.067	0.066	0.13	0.22	0.40
GI-tract					
* Stomach wall	0.46	0.59	0.85	1.5	3.0
* Small intest	0.28	0.35	0.62	1.0	2.0
* ULI wall	0.058	0.065	0.10	0.17	0.30
LLI wall	0.040	0.051	0.080	0.13	0.24
Kidneys	0.056	0.072	0.11	0.17	0.29
Liver	0.037	0.049	0.082	0.14	0.27
Lungs	0.090	0.12	0.21	0.33	0.56
Ovaries	0.042	0.057	0.090	0.14	0.27
Pancreas	0.054	0.069	0.11	0.18	0.32
Red marrow	0.086	0.12	0.16	0.22	0.35
Spleen	0.046	0.059	0.096	0.15	0.28
Testes	0.026	0.032	0.054	0.089	0.18
Thyroid	500	790	1200	2600	4700
Uterus	0.050	0.063	0.10	0.16	0.30
Other tissue	0.11	10.16	0.26	0.41	0.71
Effective dose (mSv/MBq)	**26**	**42**	**62**	**137**	**248**

643 **Thyroid uptake 55%**

	Absorbed dose per unit activity administered (mGy/MBq)

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	0.049	0.058	0.11	0.17	0.34
* Bladder wall	0.29	0.36	0.54	0.85	1.6
Bone surfaces	0.11	0.17	0.22	0.32	0.48
Breast	0.091	0.089	0.19	0.31	0.56
GI-tract					
* Stomach wall	0.46	0.59	0.86	1.5	3.0
* Small intest	0.28	0.35	0.62	1.0	2.0
* ULI wall	0.058	0.067	0.11	0.18	0.32
LLI wall	0.039	0.049	0.078	0.13	20.24
Kidneys	0.051	0.068	0.10	0.17	0.29
Liver	0.043	0.058	0.097	0.17	0.33
Lungs	0.13	0.18	0.30	0.48	0.80
Ovaries	0.041	0.056	0.090	0.15	0.27
Pancreas	0.058	0.076	0.13	0.21	0.38
Red marrow	0.12	0.18	0.22	0.29	0.46
Spleen	0.051	0.068	0.11	0.17	0.33
Testes	0.026	0.031	0.052	0.087	0.17
Thyroid	790	1200	1900	4100	7400
Uterus	0.046	0.060	0.099	0.16	0.30
Other tissue	0.16	0.24	0.37	0.59	1.0
Effective dose (mSv/MBq)	**40**	**65**	**100**	**214**	**391**

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

The capsules are ready for use. Determine the activity before use.

<Any unused medicinal product or waste material should be disposed of in accordance with local requirements.>

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu<, and on the website of {name of MS Agency (link)}>.

B. PACKAGE LEAFLET

Package leaflet: Information for the <patient> <user>

{(Invented) name strength hard capsules}

Sodium Iodide (^{131}I)

<▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.> [For medicinal products subject to additional monitoring ONLY]

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What X is and what it is used for

This medicine is a radiopharmaceutical product for therapy only.

X is used in adults, children and adolescents to treat:
- thyroid gland tumours and
- overactive thyroid gland

This medicine contains iodine-131, a radioactive substance which when taken, collects in certain organs such as, the thyroid gland.

The use of X does involve exposure to radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the radiopharmaceutical outweights the risk due to radiation.

2. What you need to know before X is used

X must not be used,
if you are
- allergic to sodium iodide or any of the other ingredients of this medicine (listed in section 6)
- pregnant or breast-feeding

if you have
- swallowing problems
- obstructed gullet

- stomach problems
- reduced abdominal or bowel movement

Warnings and precautions
Inform the nuclear medicine doctor if you have reduced kidney function.
X is given in one single dose by specialists, who will take responsibility for any necessary precautions.
Your doctor will inform you if you need to take any special precautions after using this medicine.
Contact your nuclear medicine doctor if you have any questions.

Before administration of X you should
- adhere to a low iodine diet.
- drink plenty of water before the start of the examination in order to urinate as often as possible during the first hours after administration.
- be fasting.

Children and adolescents
Talk to your nuclear medicine doctor if you are under 18 years old.

Other medicines and X
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines.

Please tell your nuclear medicine doctor if you are taking, or have been administered any of the following medicines/substances, since they may influence the result of this therapy.
Your doctor may recommend that you stop the following medicines before treatment:

a) **medicines to reduce thyroid gland function** such as:
   - carbimazole, methimazole, propyluracil
   - perchlorate
   - for 1 week;

b) **salicylates:** medicines to reduce pain, fever or inflammation such as acetylsalicylic acid for 1 week;
c) **cortisone:** medicines to reduce inflammation or prevent organ transplant rejection
d) **sodium nitroprusside:** a medicine to reduce high blood pressure, and also used during an operation for 1 week;
e) **sodium sulfobromophtalein:** a medicine to test liver function for 1 week;
f) certain medicines
   - to **reduce blood coagulation**
   - to **treat parasitic** infestation
   - **antihistamines:** used to treat allergies
   - **penicillins** and **sulphonamides:** antibiotics
   - **tolbutamide:** a medicine to reduce blood sugar
   - **thiopentone:** used while under anaesthetic to reduce brain pressure, and also to treat extreme epileptic seizures
   - for 1 week;

g) **phenylbutazone:** a medicine to reduce pain and inflammation for 1-2 weeks;
h) iodine containing **medicines to help free the airways of sputum** for 2 weeks;
i) **vitamins** containing iodine salts for 2 weeks;
j) medicines containing **thyroid hormones** such as, thyroxine (for 6 weeks) or triiodothyronine (for 2 weeks);
k) **benzodiazepines:** medicines which calm and initiate sleep and relax muscles for 4 weeks;
l) **lithium:** a medicine to treat depression for 4 weeks;

m) **iodide** containing medicines which are used only on a restricted area of the body for 1-9 months;
n) **amiodarone:** a medicine to treat heart rhythm disorders for 3-6 months;
o) iodine containing **contrast media** up to 1 year

Pregnancy and breast-feeding
You must inform the nuclear medicine doctor before the administration of X if there is a possibility
- you might be pregnant,
- if you have missed your period or
- if you are breast-feeding.

When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.
As a precaution, men should not father a child for a time period of 6 months after radioiodine treatment.

If you are pregnant
Do not take X if you are pregnant. Any possibility of pregnancy must be ruled out before using this medicine. Women should not become pregnant until at least 6 – 12 months after using X. 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.

If you are breast-feeding
Tell your doctor if you are breast-feeding because you should **stop breast-feeding.**

Driving and using machines
No studies on the effect on the ability to drive or use machines have been performed.

X contains <sodium> <and> <sugar>
<If you have been told by your doctor that you have an intolerance to <some sugars>, contact your doctor before taking this medicine.>
<X contains {name the excipient(s)}>
<X contains [..] mg of sodium per dose. To be taken into consideration by patients on a controlled sodium diet.>

3. HOW X IS USED

There are strict laws on the use, handling and disposal of radiopharmaceutical products. X will only be used in special, controlled areas.
This medicine will only be handled and given to you by people who are trained and qualified to use it safely. These persons will take special care for the safe use of this medicine and will keep you informed of their actions.
The nuclear medicine doctor supervising the procedure will decide on the quantity of X to be used in your case. It will be the smallest quantity necessary to get the desired effect.

The doses to be administered usually recommended for an adult are:
- 200-800 MBq (megabecquerel, the unit used to express radioactivity) to treat overactive thyroid gland;
- 1850-3700 MBq for partial or complete removal of the thyroid gland and for treating the spread of cancer cells, known as metastases;
- 3700-11100 MBq for follow up treatment of metastases.

MBq is the unit used to measure radioactivity and defines the activity of a quantity of radioactive material.

Use in children and adolescents under 18 years
Lower doses are used for children and adolescents.

Administration of X and conduct of the procedure
Healthcare professionals will give you the capsule and information for you.
Drink plenty of water to ensure the capsule enters your stomach as quickly as possible
Young children should take the capsule together with mashed food.
Drink water as much as possible the day after treatment. This will prevent active substance gathering in the bladder.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure.

After administration of X, you should
- avoid any close contact with infants and pregnant women for an appropriate period of time
- urinate frequently in order to eliminate the medicine from your body

The nuclear medicine doctor will inform you if you need to take any special precautions after receiving this medicine. Contact your nuclear medicine doctor if you have any questions.

If you have been given more X than you should
An overdose is unlikely because you will only receive a single dose of X precisely controlled by the nuclear medicine doctor supervising the procedure. However, in the case of an overdose, you will receive the appropriate treatment.
Should you have any further question on the use of X, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Your doctor has considered that the clinical benefit that you will obtain from the procedure with X overcomes the risk due to radiation.
Side effects are grouped according to the therapies as they depend on the doses administered in the respective type of treatment.
Frequently occurring adverse reactions are: hypothyroidism, transient hyperthyroidism, salivary and lacrimal gland disorders, and local radiation effects. In cancer treatment additionally gastro-intestinal adverse reactions and bone marrow suppression may frequently occur.
When serious allergic reaction occurs, which causes difficulty in breathing or dizziness, or in case of severe overactive thyroid crisis contact your doctor immediately.

Treatment of non-cancerous diseases
Very common, may affect more than 1 in 10 people
- underactive thyroid

Common, may affect up to 1 in 10 people
- certain eye inflammation, called endocrine ophthalmopathy (after treatment of Graves`disease)
- temporarily overactive thyroid
- salivary gland inflammation

Very rare, may affect up to 1 in 10,000 people
- vocal cord paralysis

Frequency not known, frequency cannot be estimated from the available data
- serious allergic reaction which causes difficulty in breathing or dizziness
- severe overactive thyroid crisis
- thyroid inflammation
- reduced gland function characterized with dry eyes

- reduction or loss of parathyroid hormone production with tingling in the hands, fingers, and around the mouth to more severe forms of muscle cramps

Treatment of cancers

Very common, may affect more than 1 in 10 people

- severe reduction in blood cells which can cause weakness, bruising or make infections more likely
- lack of red blood cells
- bone marrow failure with reduction of red and/or white blood cells
- disturbance or loss of the sense of smell or taste
- nausea
- decreased appetite
- failure of function of the ovaries
- flu-like illness
- headache, neck pain
- extreme tiredness or drowsiness
- inflammation causing red, watery and itchy eyes
- salivary gland inflammation with symptoms such as dry mouth, nose and eyes; tooth decay, tooth loss

Stimulate the salivary glands by eating or drinking acidic foods to reduce the frequency of this side effect.

Common, may affect up to 1 in 10 people

- abnormal, cancerous increase of white blood cells
- lack of white blood cells or platelets
- increased streaming
- breathing difficulty
- vomiting
- local swelling of tissue

Rare, may affect up to 1 in 1,000 people

- severe or temporarily overactive thyroid

Frequency not known, frequency cannot be estimated from the available data

- serious allergic reaction which causes difficulty in breathing or dizziness
- cancer, such as on the bladder, large bowel, stomach
- permanent or severe bone marrow suppression
- thyroid inflammation
- reduction or loss of parathyroid hormone production
- underactive thyroid
- inflammation of the trachea and/or throat narrowing
- proliferation of connective tissue in the lungs
- difficulty or wheezy breathing
- lung inflammation
- vocal cord paralysis, hoarseness, reduced ability to produce voice sounds using the vocal organs
- mouth/throat pain
- fluid accumulation in the brain
- inflammation of the stomach lining
- difficulty in swallowing
- inflammation of the bladder
- disturbed menstrual cycle
- decreased male fertility, low or loss of sperm

– thyroid hormone deficiency

If you get any side effects talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet.

Reporting of side effects
If you get any side effects, talk to your <doctor> <or> <,> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V.* By reporting side effects you can help provide more information on the safety of this medicine.

[*For the printed material, please refer to the guidance of the annotated QRD template.]

5. How to store X

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.
The following information is intended for the specialist only.
X must not be used after the expiry date which is stated on the label after 'EXP'.

6. Contents of the pack and other information

What X contains:
The active substance is iodine-131 as sodium iodide
Each capsule contains […] MBq of iodine-131.
The other ingredients are:
[Product specific]

What X looks like and contents of the pack
[Product specific]

Marketing Authorisation Holder and Manufacturer
{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

This leaflet was last revised in <{MM/YYYY}><{month YYYY}>.

<----------->

The following information is intended for medical or healthcare professionals only:

The complete SmPC of X is provided as a separate document in the product package, with the objective to provide healthcare professionals with other additional scientific and practical information about the administration and use of this radiopharmaceutical. Please refer to the SmPC of X.