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

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

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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) for therapeutic use.

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 possible clinical settings 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) for therapeutic use.

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) for therapeutic use

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 hard capsule contains {...} – {…} MBq sodium iodide (^{131}I) at time of calibration.

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

One hard capsule contains x mg sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsule.
[Product specific]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

Sodium iodide (^{131}I) therapy is often combined with surgical intervention and with antithyroid medicinal products.

4.2 Posology and method of administration

This medicinal product should be administered only by authorised healthcare professionals in designated clinical settings (see section 6.6).

Posology

The activity to be administered is a matter of clinical judgement. The therapeutic effect is only achieved after several weeks. The activity of the capsule should be determined before use.

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 5,000 MBq may be necessary. Re-treatment after 6-12 months is indicated for persisting hyperthyroidism.
The activity to be administered may be defined by fixed dose protocols or may be calculated according to the following equation:

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

under the following conditions

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 volume of the thyroid gland mass, however in the case of unifocal autonomy, the target organ dose is only related to the volume 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).

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 1,850-3,700 MBq. It depends on the remnant size and radioiodine uptake. For treatment of metastases, administered activity is in the range of 3,700-11,100 MBq.

Special populations

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 sodium iodide (^{131}I) in patients with significant renal impairment requires special attention (see section 4.4).

Paediatric population
The use of sodium iodide (^{131}I) in children and adolescents has to be considered carefully, based upon clinical needs and assessing the benefit/risk ratio in this patients group.
In certain cases the activity to be administered in children and adolescents should be determined after performing an individual dosimetry (see section 4.4).
In children and adolescents, treatment of benign thyroid defects with radioactive iodide 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
{(Invented) name strength} is for oral use. The capsules should be taken on an empty stomach. They should be swallowed whole with abundant drink to ensure clear passage into the stomach and upper small intestine.
In case of administration to children, especially to younger children, it must 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 breast-feeding (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 sodium iodide (^{131}I) higher than 3,700 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 26,000 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 balance in these patients is required since an increased radiation exposure is possible. In these patients it may be necessary to adjust the posology.

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.

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 reduce colon radiation exposure, mild laxatives (but not stool softeners which do not stimulate the bowel) may be necessary in patients having less than one bowel movement a day.
To avoid sialadenitis that 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 section4.5). 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.
In patients with suspected gastrointestinal disease, great care should be taken when administering sodium iodide (^{131}I) capsules. Concomitant use of H2-antagonists or proton pump inhibitors is advised.

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.

Specific warnings
<This medicinal product contains {...} mg of sodium per capsule. To be taken into account by patients on a controlled sodium diet.> <This medicinal product contains less than 1 mmol sodium (23 mg) per capsule, i.e. essentially 'sodium- free'.>
<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 (^{131}I).
For example, the treatment with the following substances should be discontinued:

Active substances	**Withdrawal period before administration of sodium iodide (^{131}I)**
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. Women receiving sodium iodide (^{131}I) should be advised not to become pregnant within 6-12 months after administration.

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 (^{131}I). 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 men who have extensive disease and therefore may need high sodium iodide (^{131}I) therapeutic doses.

Pregnancy
The use of sodium iodide (^{131}I) is contraindicated during established or suspected pregnancy or when pregnancy has not been excluded because transplacental passage of sodium iodide (^{131}I) 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).
If a differentiated thyroid carcinoma is diagnosed during pregnancy, sodium iodide (^{131}I) treatment should be postponed until after the childbirth.

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 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 must be discontinued at least 8 weeks before sodium iodide (^{131}I) 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 1,850 MBq. Clinical relevant effects including oligospermia and azoospermia and elevated serum FSH serum levels have been described after administration greater than 3,700 MBq.

4.7 Effects on ability to drive and use machines

Sodium iodide (^{131}I) has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

The frequencies of reported adverse reactions were derived from the medical literature. The safety profile of sodium iodide (^{131}I) 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.

Tabulated list of adverse reactions

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).
Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

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

System organ class	*Adverse reaction*	*Frequency*
	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
Respiratory, thoracic and mediastinal disorders	Vocal cord paralysis	Very rare
Gastrointestinal disorders	Sialoadenitis	Common
Hepatobiliary disorders	Hepatic function abnormal	Frequency not know
Skin and subcutaneous tissue disorders	Iodide induced acne	Not known
Congenital, familial and genetic disorders	Congenital hypothyroidism	Not known
General disorders and administration site conditions	Local swelling	Not known

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

System organ class	*Adverse reaction*	*Frequency*
	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
	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

System organ class	*Adverse reaction*	*Frequency*
Hepatobiliary disorders	Hepatic function abnormal	Frequency not know
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 adverse reactions

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 (^{131}I) is 3,108 mSv when the maximal recommended activity of 11,100 MBq is administered (with thyroid uptake 0%).

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 (^{131}I) 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 (^{131}I), 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 5,000 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 authorised personnel in a 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 sodium iodide (^{131}I), emetics can be given.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Therapeutic radiopharmaceuticals, Iodine (^{131}I) compounds, ATC code: V10XA01.

The pharmacological active substance is sodium iodide (^{131}I) in the form of sodium iodide that is taken up by the thyroid. The physical decay takes place essentially in the thyroid gland, where sodium iodide (^{131}I) 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 (^{131}I) 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 (^{131}I) 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 (^{131}I) 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 (^{131}I) solution an equilibrium is reached at the same time.

Distribution and organ 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 1,000 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 (^{131}I) 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 known 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 (^{131}I) 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 (^{131}I) 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 content
[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 on radioactive materials.

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>

General warning
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.

Precautions to be taken before handling or administration of the medicinal product
The administration of sodium iodide (^{131}I) for therapy is likely to result in a relatively high radiation dose to most patients and 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. Suitable precautions in accordance with national regulations should therefore be taken concerning the activity eliminated by the patients in order to avoid any contaminations.
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.

Precautions and activity data
1.3% of iodine (^{131}I) decays via xenon (^{131}mXe) (half-life 12 days) and a small amount of xenon (^{131}mXe) 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 (^{131}mXe).

In addition, there can be limited leakage of volatile iodine-131 activity from the capsule. *[Product specific additional information]*

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 128. The biokinetic model is described as a compartment model including inorganic iodide as well as organically bound iodine released to the body tissues following discharge from the thyroid. The ICRP model refers to oral administration.
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 volume, 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

Unifocal autonomy	Target organ dose 300 – 400 Gy
Multifocal or disseminated autonomy	Target organ dose 150 – 200 Gy
Graves' disease (Morbus Basedow)	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%, oral administration

	Absorbed dose per unit activity administered (mGy/MBq)

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	0.044	0.054	0.086	0.14	0.25
Bone surfaces	0.030	0.037	0.059	0.092	0.18
Brain	0.021	0.026	0.043	0.071	0.14
Breast	0.020	0.025	0.042	0.069	0.13
Gallbladder Wall	0.037	0.048	0.085	0.13	0.21
GI-tract					
Stomach wall	0.87	1.1	1.6	2.8	5.9
Small intest wall	0.035	0.044	0.070	0.11	0.19
Colon wall	0.14	0.18	0.30	0.50	0.92
(ULI wall	0.12	0.15	0.25	0.42	0.75)
(LLI wall	0.17	0.22	0.37	0.61	1.2)
Heart wall	0.062	0.080	0.13	0.20	0.37
Kidneys	0.62	0.080	0.13	0.20	0.37
Liver	0.050	0.065	0.10	0.16	0.30
Lungs	0.053	0.068	0.11	0.18	0.36
Muscles	0.026	0.032	0.051	0.080	0.15
Oesophagus	0.024	0.030	0.049	0.079	0.15
Ovaries	0.038	0.049	0.076	0.11	0.20
Pancreas	0.060	0.073	0.11	0.16	0.28
Red marrow	0.031	0.038	0.061	0.095	0.18
Salivary glands	0.27	0.33	0.44	0.59	0.86
Skin	0.019	0.023	0.038	0.062	0.12
Spleen	0.064	0.077	0.12	0.19	0.34
Testes	0.025	0.033	0.055	0.084	0.15
Thymus	0.024	0.030	0.049	0.079	0.15
Thyroid	2.2	3.6	5.6	0.13	0.25
Urinary bladder wall	0.54	0.71	1.1	1.4	1.8
Uterus	0.045	0.037	0.062	0.10	0.18
Remaining organs	0.029	0.037	0.060	0.10	0.18
Effective dose (mSv/MBq)	**0.28**	**0.40**	**0.54**	**1.1**	**2.0**

Thyroid low uptake, oral administration

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.051	0.067	0.12	0.20	0.44
Bone surfaces	0.089	0.10	0.14	0.22	0.40
Brain	0.093	0.10	0.13	0.18	0.30
Breast	0.038	0.050	0.10	0.17	0.32
Gallbladder wall	0.043	0.057	0.1.	0.18	0.36
GI-tract					
Stomach wall	0.77	1.0	1.5	2.5	5.3
Small intestine wall	0.033	0.043	0.073	0.11	0.22
(ULI wall	0.12	0.15	0.27	0.49	1.0)
(LLI wall	0.17	0.22	0.39	0.71	1.6)
Heart wall	0.089	0.12	0.21	0.36	0.77
Kidneys	0.27	0.34	0.50	0.84	1.8
Liver	0.093	0.14	0.24	0.46	1.2
Lungs	0.10	0.13	0.22	0.38	0.79
Musclers	0.084	0.11	0.17	0.27	0.48

Oesophagus	0.10	0.15	0.30	0.58	1.1
Ovaries	0.037	0.049	0.080	0.13	0.28
Pancreas	0.064	0.080	0.13	0.21	0.41
Red marrow	0.072	0.086	0.12	0.19	0.37
Salivary glands	0.22	0.27	0.36	0.49	0.72
Skin	0.043	0.053	0.080	0.12	0.25
Spleen	0.069	0.089	0.15	0.26	0.55
Testes	0.024	0.032	0.056	0.095	0.20
Thymus	0.10	0.15	0.30	0.59	1.1
Thyroid	280	450	670	1400	2300
Urinary bladder wall	0.45	0.58	0.89	1.2	1.6
Uterus	0.042	0.054	0.090	0.15	0.28
Remaining organs	0.048	0.1111	0.17	0.25	0.44
Effective dose (mSv/MBq)	**14**	**23**	**34**	**71**	**110**

Thyroid medium uptake, oral administration

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.055	0.074	0.13	0.24	0.55
Bone surfaces	0.12	0.14	0.19	0.30	0.52
Brain	0.13	0.14	0.18	0.24	0.39
Breast	0.048	0.063	0.13	0.23	0.43
Gallbladder wall	0.046	0.063	0.12	0.21	0.45
GI-tract					
Stomach wall	0.71	0.95	1.4	2.4	5.0
Small intestine wall	0.032	0.043	0.075	0.11	0.24
Colon wall	0.14	0.18	0.34	0.63	1.4
(ULI wall	0.12	0.15	0.28	0.53	1.2)
(LLI wall	0.17	0.22	0.40	0.76	1.8)
Heart wall	0.10	0.14	0.25	0.45	1.0
Kidneys	0.27	0.34	0.53	0.93	2.1
Liver	0.12	0.18	0.31	0.62	1.7
Lungs	0.13	0.16	0.28	0.50	1.0
Muscles	0.12	0.15	0.24	0.38	0.66
Oesophagus	0.14	0.22	0.45	0.87	1.7
Ovaries	0.036	0.049	0.082	0.15	0.33
Pancreas	0.066	0.084	0.14	0.24	0.49
Red marrow	0.095	0.11	0.15	0.24	0.48
Salivary glands	0.19	0.24	0.32	0.43	0.64
Skin	0.057	0.070	0.10	0.16	0.33
Spleen	0.023	0.032	0.056	0.10	0.23
Testes	0.023	0.032	0.056	1.0	2.3
Thymus	0.14	0.22	0.45	0.87	1.7
Thyroid	430	690	1000	2200	3600
Urinary bladder wall	0.39	0.51	0,79	1.1	1.5
Uterus	0.040	0.053	0.089	0.15	0.32
Remaining organs	0.11	0.15	0.23	0.33	0.58
Effective dose (mSv/MBq)	**22**	**35**	**53**	**110**	**180**

Thyroid high uptake, oral administration

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.059	0.082	0.15	0.28	0.66
Bone surfaces	0.16	0.18	0.24	0.37	0.65
Brain	0.17	0.18	0.24	0.37	0.65
Breast	0.058	0.077	0.17	0.28	0.54
Gallbladder	0.049	0.068	0.13	0.24	0.54
GI-tract					
Stomach wall	0.66	0.88	1.3	2.2	4.7
Small intestine wall	0.032	0.043	0.077	0.12	0.26
Colon wall	0.14	0.19	0.35	0.68	0.16
(ULI wall	0.12	0.16	0.30	0.58	1.4)
(LLI wall	0.16	0.22	0.42	0.81	2.0)
Heart wall	0.12	0.16	0.30	0.58	1.4
Kidneys	0.27	0.35	0.55	1.0	2.4
Liver	0.14	0.22	0.39	0.79	2.2
Lungs	0.15	0.20	0.35	0.61	1.3
Muscles	0.15	0.19	0.31	0.49	0.86
Oesophagus	0.19	0.28	0.59	1.2	2.3
Ovaries	0.035	0.049	0.084	0.16	0.37
Pancreas	0.068	0.088	0.15	0.27	0.57
Red marrow	0.12	0.14	0.19	0.29	0.59
Salivary glands	0.16	0.20	0.27	0.37	0.55
Skin	0.071	0.087	0.13	0.19	0.41
Spleen	0.075	0.10	0.18	0.33	0.80
Testes	0.22	0.031	0.057	0.11	0.27
Thymus	0.19	0.28	0.59	1.2	2.3
Thyroid	580	940	1400	3000	4900
Urinary bladder wall	0.34	0.44	0.68	0.95	1.3
Uterus	0.038	0.051	0.089	0.16	0.36
Remaining organs	0.15	0.19	0.29	0.42	0,74
Effective dose (mSv/MBq)	**29**	**47**	**71**	**150**	**250**

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

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

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

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

This medicine contains sodium iodide (^{131}I), a radioactive substance which accumulates in certain organs such as, the thyroid gland.

This medicine is radioactive but your doctors consider that the medicine's beneficial effect on your condition outweigh the possible harm from the 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
- breast-feeding

if you have
- swallowing problems
- obstructed gullet
- stomach problems
- reduced stomach or bowel movement

If any of these apply to you, **tell your nuclear medicine doctor.**

Warnings and precautions
Tell the nuclear medicine doctor
- if you have reduced kidney function.
- if you have problems passing urine,
- if you have digestive or stomach problems,
- if protruding eyes are part of the symptoms of the disease you are suffering from (Graves' disease-induced ophthalmopathy).

If any of these apply to you, talk to your nuclear medicine doctor. X may not be suitable for you.
Your doctor will inform you if you need to take any special precautions after using this medicine.
Speak with your nuclear medicine doctor if you have any questions.

Before you take X you should
- follow a low iodine diet .
- drink plenty of water before the start of the procedure so that you pass urine as often as possible in the first hours after taking X.
- be fasting on the day of application.

Children and adolescents
Talk to your nuclear medicine doctor if you are under 18 years old, or if you cannot swallow a capsule.

Other medicines and X
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines including medicines obtained without a prescription.

Please tell your nuclear medicine doctor if you are taking, or have been given any of the following medicines or substances, since they may affect how wellthis treatment works.
Your doctor may recommend that you stop the following medicines before treatment:

- **medicines to reduce thyroid gland function** such as carbimazole, methimazole, propylthiouracil, perchlorate for 1 week;
- **salicylates:** medicines to reduce pain, fever or inflammation such as aspirin for 1 week;
- **cortisone:** medicines to reduce inflammation or prevent organ transplant rejection for 1 week;
- **sodium nitroprusside:** a medicine to reduce high blood pressure, and also used during an operation for 1 week;
- **sodium sulfobromophtalein:** a medicine to test liver function for 1 week;
- other medicines for 1 week
- to **reduce blood coagulation**
- to **treat parasitic** infestation
- **antihistamines:** used to treat allergies
- **penicillins** and **sulphonamides:** antibiotics
- **tolbutamide:** a medicine to reduce blood sugar
- **thiopental:** an anaesthetic used in operations to reduce brain pressure, and to treat serious epileptic fits
- for 1 week;
- **phenylbutazone:** a medicine to reduce pain and inflammation for 1-2 weeks;
- iodine containing **medicines to help free the airways of sputum** for 2 weeks;
- **iodide**-containing medicines that are used only on a restricted area of the body for 1-9 months;
- iodine containing **contrast agents** up to 1 year
- **vitamins** containing iodine salts for 2 weeks;

- medicines containing **thyroid hormones** such as, levothyroxine (for 6 weeks) or triiodothyronine (for 2 weeks);
- **benzodiazepines:** medicines which calm mood and help patients sleep and relax muscles for 4 weeks;
- **lithium:** a medicine used in the treatment of bipolar disorder for 4 weeks;
- **amiodarone:** a medicine to treat heart rhythm disorders for 3-6 months;

X with food
Your doctor may recommend a low iodine diet before treatment and may ask you to avoid foods such as shellfish and crustaceans.

Pregnancy and breast-feeding
This medicine must not be used during pregnancy. Therefore **you must tell the nuclear medicine doctor before taking X** if there is a possibility you might be pregnant or if you have missed your period, or think you may be pregnant or are planning to have a baby.

If you are pregnant
Do not take X if you are pregnant. Any possibility of pregnancy must be ruled out before using this medicine.

Contraception in males and females
Women should not become pregnant for at least 6 months after using X. Women are advised to use contraception for a time period of 6 months. As a precaution, men should not father a child for a time period of 6 months after treatment with X to allow the replacement of irradiated by non-irradiated spermatozoa.

Fertility
Treatment with X may temporarily reduce fertility in men and women.
In men, high doses of sodium iodide (^{131}I) may affect **sperm production** temporarily. If you would ever like to father a child, speak to your doctor about saving your sperm in a sperm bank.

If you are breast-feeding
Tell your doctor if you are breast-feeding because you should **stop breast-feeding before treatment. Breast-feeding should not be resumed after treatment with X.**

Driving and using machines
It is considered unlikely that X will affect your ability to drive or to use machines.

X contains <sodium> <and> <sugar>

<X contains {...} mg of sodium per dose. This is to be taken into consideration if you are on a controlled sodium diet.> < X contains less than 23 mg of sodium per capsule, i.e. essentially 'sodium-free'.>
<X contains sucrose, a type of sugar.><If you have been told by your doctor that you have an intolerance to <some sugars>, contact your doctor before taking this medicine.>

3. HOW X IS USED

There are strict laws on the use, handling and disposal of radioactive products for medical treatment. X will only be used in specialised, controlled areas.
This medicine will only be given to you by people who are trained and qualified to use it safely. These people will take special care to use this medicine safely and they will talk to you about what they are doing.

The nuclear medicine doctor supervising the procedure will decide on the right dose of X for you. It will be the smallest quantity necessary to get the desired effect.

X is given as one single capsule by specialists, who will take responsibility for any necessary precautions.

The doses usually recommended for an adult are:
- 200-800 MBq to treat overactive thyroid gland;
- 1,850-3,700 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 (megabecquerel) is the unit used to measure the amount radioactivity the medicine..

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

How X is given and what the procedure involves
X is given to you as one single capsule.
Your stomach should be empty when you take the capsule.
Take the capsule with plenty of water so that it enters your stomach as quickly as possible.
Young children should take the capsule together with mashed food.
Drink as much water as possible the day after treatment. This will wash away the active substance from your bladder.

Duration of the procedure
Your nuclear medicine doctor will tell you how long the procedure will take.

After you take X
The nuclear medicine doctor will tell you if you need to take any special precautions after receiving this medicine. Particularly, you
- must avoid any close contact with infants and pregnant women for a few days. Your nuclear medicine doctor will tell you how long this should be.
- should drink plenty of fluids and pass urine frequently in order to remove the medicine from your body
- should flush the toilet carefully and wash your hands thoroughly as your bodily fluids will be radioative for a few days
- should have drinks or sweets that contain citric acid, e.g. orange, lemon or limejuice to help produce saliva and stop the saliva building up in your saliva glands
- should have laxatives to stimulate the bowel, if you have less than one bowel movement per day.

Your blood, stools, urine or possible vomit may be radioactive for a few days and should not come into contact with other people.
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.

Frequent adverse reactions are: hypothyroidism (an underactive thyroid gland), temporary hyperthyroidism (an overactive thyroid gland), salivary and tear gland disorders, and local radiation effects. In cancer treatment, additionally stomach and gut side effects and reduction in the production of blood cells in the bone marrow may frequently occur.

If you have a serious allergic reaction, which causes difficulty in breathing or dizziness, or if you have severe overactive thyroid crisis, contact your doctor immediately.

All the side effects with X are listed below, grouped according to the condition X is being used for as they depend on the doses used for the different treatments.

Treatment of overactive thyroid gland
Very common (may affect more than 1 in 10 people):
- underactive thyroid

Common (may affect up to 1 in 10 people):
- a type of 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 tear gland function characterised 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
- thyroid hormone deficiency in the offspring
- abnormal function of the liver

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 blood cells, white blood cells, or both
- disturbance or loss of the sense of smell or taste
- nausea (feeling sick)
- 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

Common (may affect up to 1 in 10 people):

- abnormal, cancerous increase of white blood cells
- lack of white blood cells or platelets
- runny nose
- breathing difficulty
- vomiting
- areas of tissue swelling

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, including that of the bladder, large bowel and stomach
- permanent or severe reduction of blood cell production in the bone marrow
- thyroid inflammation
- reduction or loss of parathyroid hormone production
- increased parathyroid hormone production
- underactive thyroid
- inflammation of the trachea or throat narrowing or both
- proliferation of connective tissue in the lungs
- difficult or wheezy breathing
- lung inflammation
- vocal cord paralysis, hoarseness, reduced ability to produce voice sounds
- mouth and throat pain
- fluid build-up in the brain
- inflammation of the stomach lining
- difficulty in swallowing
- inflammation of the bladder
- disturbed menstrual cycle
- decreased male fertility, low sperm count or loss of sperm
- thyroid hormone deficiency in the offspring
- abnormal function of the liver

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 <nuclear medicine 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. It will be stored 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><carton><bottle> after 'EXP'.

6. Contents of the pack and other information

What X contains
The active substance is sodium iodide (^{131}I)as sodium iodide
Each hard capsule contains {…} MBq of sodium iodide (^{131}I).
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}>.

<Detailed information on this medicine is available on the website of {name of MS Agency (link)}>

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

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

The complete Summary of Product Characteristics (SmPC) of X is provided <as a separate document> <as a tear-off section at the end of the printed leaflet> 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.