SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sodium iodide (^{131}I) injection, CIS bio international 111 MBq/mL, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains 111 MBq of sodium iodide (^{131}I) at calibration date.
The total activity per vial varies from 80 MBq to 1110 MBq at calibration date.

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 radiation 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 with known effect :

Each mL of sodium iodide (^{131}I) contains 4.3 mg of sodium .

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear and colorless solution with a pH ranging between 6 and 8.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<u>Pretherapeutic and therapeutic indications</u>

- Sodium iodide may be given as a "tracer" dose to study radioiodine kinetics. An estimation of the thyroid uptake and effective half life obtained with a tracer amount, can be used to calculate the activity required for radioiodine therapy.

- In the management of thyroid carcinoma, after thyroidectomy, sodium iodide is used to identify thyroid remnant and metastases.

- Radioiodine thyroid therapy is indicated in the treatment of:

- Hyperthyroidie: Graves disease, toxic multinodular goitre or autonomous nodules.
- Papillary and/or follicular thyroid carcinoma including metastatic disease and thyroid remnant tissue. Sodium iodide (^{131}I) therapy is often combined with surgical intervention or with antithyroid medications.

4.2 Posology and method of administration

Pretherapeutic use

The recommended activities for an adult patient (70 kg) are as follows :

- For metastases and thyroid remnant imaging post thyroid ablation:: a maximum activity of 400 MBq.

Therapeutic use

The activity administered is a matter for clinical judgement, possibly determined from individual dosimetry. The therapeutic effect is only achieved after several months.

- For the treatment of hyperthyroidism

Patients should be rendered euthyroid medically whenever possible before giving radioiodine treatment for hyperthyroidism. In the event of failure or inability to continue medical treatment, radioactive iodine can be administered to treat hyperthyroidism.
The activity administered is usually in the range of 200 - 800 MBq but re-treatment **after six months** is indicated for persisting hyperthyroidism with cumulative activities of up to 5,000 MBq.

The dose required depends on the diagnosis, the size of the gland, thyroid uptake and iodine clearance.

The following target organ doses may be used for posology calculation:

- unifocal autonomy 300 - 400 Gy
- multifocal and disseminated autonomy 150 - 200 Gy
- Graves' disease 200 Gy

In Graves' disease, multifocal or disseminated autonomy, the above mentioned target organ doses are related to the overall volume of the thyroid gland, however in the unifocal autonomy, the target organ dose is only related to the volume of the adenoma.

The activity to be administered may be calculated according to the following equation:

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

Legend:

target dose	=	is the target absorbed dose in the whole thyroid gland or in an adenoma
target volume	=	volume of the whole thyroid gland (Graves' disease, multifocal or disseminated) or volume of the adenoma (unifocal autonomy)
max. uptake I-131	=	maximal uptake of I-131 in the thyroid gland or nodules in % of the administered activity as established in a test dose
effective T ½	=	effective half-life of I-131 in the thyroid gland
K	=	24.67

Other dosimetric procedures may also be used including sodium pertechnetate (Tc-99m) thyroid uptake tests to determine the appropriate dose to the target organ (Gy).

Fixed dose protocols may also be used.

- For thyroid ablation and treatment of metastases

The administered activities following total or sub total thyroidectomy to ablate remaining thyroid tissue are in the range of 1850 - 3700 MBq. It depends on the remnant size and radioiodine uptake. In subsequent treatment for metastases, administered activity is in the range 3700 - 11000 MBq.

Renal impairment
Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

An adjustment of the posology should be considered.

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

In children and adolescents, treatment of benign thyroid disease with radioiodine is possible in justified cases, especially in cases of recurrence after using anti-thyroid medicines or severe adverse reactions to these agents (see section 4.4).

Method of administration
For multidose use.
For patient preparation, see section 4.4.
Sodium iodide (^{131}I) is administered by intravenous route.

Acquisition of images:
For evaluation of thyroid uptake, scans are usually performed at 4 hours, and repeated between 18 and 24 hours after injection.

For thyroid scintigraphy images should be obtained at 72 hours after injection.
Whole-body imaging may be performed 5 to 7 days after thyroid ablative therapy.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Pregnancy (see section 4.6).
- Breastfeeding (see section 4.6).
- Patients with active gastritis, gastric erosions, and peptic ulcer.

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 administered should in every case be as low as reasonably achievable to obtain the required diagnostic information or therapeutic effect.

Renal impairment

Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Paediatric population

For information on the use in paediatric population, see section 4.2

Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11).

There is no evidence of an increased incidence of cancer, leukaemia or mutations in patients after treatment with radioiodine-131 for benign thyroid disease, despite extensive use of this medication.
However, the higher sensitivity of tissue structures and longer life expectancy in children and young adults must be taken in account. The risks must also be weighed up against those of other possible treatments. See sections 4.2 and 11.

There is little evidence of an increased incidence of cancer, leukemia or mutations in human with respect to patients treated for benign thyroid disease with radioiodine, despite extensive use. In the treatment of malignant thyroid disease, a higher incidence of bladder cancer has been reported in one study of patients receiving iodine (^{131}I) greater than 3,700 MBq. Another study has reported a small excess leukemia in patients receiving very high doses. A cumulative total activity higher than 26 GBq is therefore not advisable.

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.

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.

Patient preparation:
Iodine overload from foods or medicinal treatment should be investigated before administration of iodine (see section 4.5). A low iodine diet prior to therapy is recommended to enhance uptake into functioning thyroid tissue.
Patients should be encouraged to increase oral fluids within the first 24 hours and urged to void as often as possible to reduce bladder radiation,. Patients with bladder voiding problems should be catheterised before high activity administration.

In patients with suspected gastrointestinal disease, great care should be taken when administering sodium iodide (^{131}I). Concomitant use of H2 antagonists or proton pump inhibitors is advised.

After the procedure
Exposure of the salivary glands to ionising rays should be reduced by stimulating saliva production using acidic substances (lemon juice, vitamin C).

For radioprotection reasons, it is recommended to avoid close contact with infants and pregnant women. The period of close contact restriction should be adapted to the administered activity and the type of pathology.

The patient should be followed-up at appropriate intervals.

Specific warnings
In Graves' disease, radioiodine treatment may be combined with corticosteroids.

When treating thyroid carcinoma, thyroid replacement therapy should be stopped before radioiodine administration to ensure adequate uptake: stopping for 7 to 14 days beforehand in the case of triiodothyronine and 4 to 5 weeks if taking thyroxine. The replacement treatment can be restarted 2 days after iodine-131 administration.

Similarly, carbimazole and propylthiouracil should be stopped no more than 1 week prior to treatment of hyperthyroidism with iodine 131 and only restarted, if necessary, several days later.

Hyponatraemia:
Serious manifestations of hyponatraemia have been reported after sodium iodide (^{131}I) therapy in elderly patients who have undergone total thyroidectomy. Risk factors include older age, female sex, use of thiazide diuretics and hyponatraemia at the start of sodium iodide (^{131}I) therapy. Regular serum electrolytes measurements shall be considered for these patients.

This medicine contains 4.3 mg of sodium per mL. The amount of sodium may exceed 1 mmol (23 mg) per injection, depending on the volume of solution injected. This amount should be taken into account in patients on a low-salt diet.

For precautions with respect to environmental hazard see section 6.6.

4.5 Interactions with other medicinal products and other forms of interaction

Many pharmacological agents are known to interact with radioiodide. These may do so by a variety of mechanisms which can affect the protein binding, the pharmacokinetics or influence the dynamic effects of labelled iodide. It is therefore necessary to take a full drug history and ascertain whether any medications are required to be withheld prior to the administration of sodium iodide I 131.

For example, the treatment with the following substances should be discontinued:

Active substances	Period of withhold before administration of 131-iodine
Antithyroid agents (carbimazole or other imidazole derivatives such as propylthiouracil) and perchlorate	2 days to 1 week before starting treatment till several days after
Salicylates, steroids, sodium nitroprusside, sodium sulfobromophthalein, anticoagulants, antihistamines, antiparasitics, penicillins, sulphonamides, tolbutamide, thiopental	1 week
Phenylbutazone	1-2 week(s)
Containing iodine expectorants and vitamins	Approx. 2 weeks
Thyroid hormone preparations	Triiodothyronine 7 to 14 days Thyroxine 4-6 weeks
Benzodiazepines, lithium Amiodarone *,	Approx. 4 weeks 3-6 months
Containing iodine preparations for topical use	1-9 months
Water-soluble iodine-containing contrast media Oil-based iodine-containing contrast media	6 to 8 weeks Up to 6 months

* In the case of amiodarone, decreased iodine uptake by the thyroid gland can last several months mainly due to the long half-life of this medicine.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
When it is necessary to administer radioactive medicinal product to women of childbearing potential, information should always be sought about pregnancy. Any woman who has missed a period should be assumed to be pregnant until proven otherwise.
Alternative techniques which do not involve ionising radiation should be considered.

Contraception in males and females
Women receiving sodium iodide-131 should be advised NOT to become pregnant within 6-12 months after treatment.

After therapeutic treatment with iodine 131, effective contraceptive measures should be implemented and maintained by men and women up to 6 months after treatment for the benign disease and up to 12 months after treatment of thyroid cancer.

Pregnancy
Sodium iodide (^{131}I) is contraindicated during established or suspected pregnancy or when pregnancy has not been excluded, see section 4.3. (due to the fact that the radiation dose absorbed in the uterus for this agent is likely to be around 600 mGy, and foetal thyroid gland avidly concentrates iodine during the second and third trimesters).

Should differentiated thyroid carcinoma be diagnosed during pregnancy, radioactive iodine treatment must be postponed until after the pregnancy.

Breastfeeding
Before administering a radioactive medicinal product to a woman who wants to continue breast-feeding, the possibility of delaying treatment until she has stopped breast-feeding should be considered.

The patient should be asked to stop breast-feeding for at least 6 to 8 weeks prior to iodine (^{131}I) administration and to delay treatment until lactation has stopped.

Breast-feeding should not be resumed after sodium iodide (^{131}I) administration.

For radioprotection reasons, close contact between mother and infant should be avoided for at least for 1 week.

Fertility
Sperm cryopreservation should be considered in young men with disseminated disease who require the administration of high iodine (^{131}I) therapeutic doses.
For activities above 1850 MBq, reversible spermatogenic disorders may occur.

For activities greater than 3700 MBq significant clinical effects including oligospermia, azoospermia, and elevated serum FSH concentrations have been reported.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable Effects

The frequency of the undesirable effects reported is based on the medical literature. The safety profile of sodium iodide (^{131}I) differs widely depending on the activity administered, while the doses to be administered depend on the type of treatment (benign or malignant disease). The safety profile depends on the cumulative doses given and on the dosing intervals. Therefore, the undesirable effects reported are categorised into two groups: those occurring in benign or malignant disease. However, the activity administered and dosing intervals were usually not specified in the relevant publications so it could be that the doses recommended in this SPC were not followed.

Common adverse reactions are: hypothyroidism, transient hyperthyroidism, salivary and lacrimal gland disorders, and local radiation effects. When treating carcinoma, gastrointestinal adverse events and myelosuppression are common.

The following tables show the reported adverse reactions sorted by system organ class. Symptoms that are more likely to be secondary to a syndrome (e.g. Sjögren syndrome) appear in parentheses beside the corresponding 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)
Not known	cannot be estimated from the available data

Adverse reactions after treatment of a benign condition:

MedDRA Body system SOCs	Preferred term	Frequency
Immune system disorders	Anaphylactic reaction	Not known
Endocrine disorders	Permanent hypothyroidism, hypothyroidism	Very common
	Transient hyperthyroidism	Common
	Thyrotoxic crisis, thyroiditis, hypoparathyroidism (blood calcium decreased, tetany)	Not known
Eye disorders	Endocrine ophthalmopathy (in Graves' disease)	Common
	Sjögren syndrome	Not known
Respiratory, thoracic and mediastinal disorders	Vocal cord paralysis	Very rare
Gastrointestinal disorders	Sialadenitis	Common
General disorders and administration site conditions	Local swelling	Not known
Skin and subcutaneous tissue disorders	Iodo acne (acne with skin rash)	Not known

Adverse reactions after treatment of a malignancy:

MedDRA Body system SOCs	Preferred term	Frequency
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Leukaemia	Common
	Neoplasms (bladder cancer, colon cancer, gastric cancer)	Not known
Blood and lymphatic system disorders	Aplastic anemia, erythropenia, bone marrow disorder	Very common
	Leucopénie, thrombocytopénie	Common
	Permanent or serious bone marrow failure	Not known
Immune system disorders	Anaphylactic reaction	Not known
Endocrine disorders	Thyrotoxic crisis, transient hyperthyroidism	Rare
	Thyroiditis, transient leukocytosis, hypoparathyroidism (blood calcium decreased, tetany)	Not known
Nervous system disorders	Parosmia	Very common
	Brain oedema	Not known
Eye disorders	Sjogren's syndrome (conjunctivitis, dry eye, nasal dryness)	Very common
	Obstruction of nasolacrimal duct (lacrimation increased)	Common
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Common
	Throat thighness*, pulmonary fibrosis, respiratory distress, obstructive airway disorder, pneumonia, tracheitis, vocal cord disorder (paralysis vocal cord, dysphonia, hoarseness of voice), oropharyngeal pain, stridor	Not known
Gastrointestinal disorders	Sialadenitis (dryness oral, 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	Cystitis radiation	Not known

MedDRA Body system SOCs	Preferred term	Frequency
Affections des organes de reproduction et du sein	Ovarian failure	Very common
	Azoospermia, Oligospermia, infertility male, menstrual disorder	Not known
Congenital, familial and genetic disorders	Congenital hypothyroidism	Not known
General disorders and administration site conditions	Influenza like illness, headache, fatigue, pain neck	Very common
	Local swelling	Common

* Particularly in cases of existing tracheal stenosis

Thyroid and parathyroid disorders

Treating hyperthyroidism with radioiodine can cause late-onset hypothyroidism, the severity of which is dose dependent. This complication can occur from a few weeks to years after treatment and requires regular monitoring of thyroid function and appropriate hormone replacement therapy. Hypothyroidism consecutive to radioiodine treatment usually does not appear until 6-12 weeks.

In the treatment of malignancies, hypothyroidism is often reported as an adverse reaction; however, radioiodine treatment of malignancies usually follows a thyroidectomy.

The destruction of thyroid follicles caused by exposure to sodium iodide (^{131}I) ionising radiation may exacerbate existing hyperthyroidism after 2-10 days, or even produce a thyrotoxic crisis. Immune hyperthyroidism may sometimes develop after initial normalisation (latency period of 2 to 10 months).

With high dose radioiodine treatment, 1-3 days after administration, 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, transient hyperthyroidism can be observed even after treatment of functional thyroid carcinoma.

Transient hypoparathyroidism has been observed occasionally after treatment with radioactive iodine: this must be monitored and treated appropriately.

Eye disorders

Endocrine ophthalmopathy can progress or a new orbital disease may appear after treating hyperthyroidism or Graves' disease with radioactive iodine. Patients with eye symptoms to be treated for Graves’ disease, should be treated concomitantly with corticosteroids.

Local radiation effects

Vocal cord dysfunction and paralysis have been reported after administration of sodium iodide (^{131}I); however, in some cases, these could also have been caused by the thyroid gland surgery. It is not possible to establish whether the vocal cord dysfunction is caused by the radiation or surgical treatment.

High sodium iodide (^{131}I) tissue uptake can cause local pain, discomfort and oedema in tissues taking up the radionuclide. For example, when treating any remaining thyroid tissue with radioactive iodine, generalised and severe soft tissue pain in the head and neck area is possible.

Radiation-induced pneumonia and pulmonary fibrosis have been observed in patients with diffuse lung metastases of differentiated thyroid cancer, due to the destruction of the metastatic tissue. This mainly occurs after treatment with high-dose radioiodine.

In the treatment of metastasising thyroid carcinomas with Central Nervous System involvement, the possibility of local cerebral oedema and/or an increasing existing cerebral oedema must also be born in mind.

Gastrointestinal disorders

High activity levels can cause gastrointestinal disorders, which usually appear within the first few hours or days of administration. To prevent gastrointestinal disorders, see section 4.4.

Salivary and lacrimal gland disorders

Sialadenitis may occur, with oedema and pain in the salivary glands, partial loss of taste and dry mouth. Sialadenitis usually resolves spontaneously or with anti-inflammatories. However, cases have occasionally been observed of a dose-dependent persistent loss of taste and dry mouth, followed by loss of teeth. For information on preventing salivary disorders, see section 4.4.

Lacrimal gland dysfunction and nasolacrimal duct obstruction leading to Sjögren syndrome may occur after several months (up to two years) after radioiodine treatment. Although Sjögren syndrome is transient in the majority of cases, it may persist for several years in some patients.

Myelosuppression

As a late consequence a single administration of over 5000 MBq or in interval of below 6 months are more likely to be associated with reversible or in very rare cases irreversible bone marrow depression may develop, with isolated thrombocytopenia or erythrocytopenia which may be fatal.

Induced cancers

After higher activities, typically those used in the treatment of thyroid malignancies, an increased incidence of leukaemia has been observed. It is therefore recommended not to exceed a cumulative total activity of 26 000 MBq.

An increased incidence of induced solid tumours has also been revealed following administration of high doses (over 7.4 GBq).

Loss of fertility

After treating thyroid cancer with radioactive iodine, a dose-dependent loss of fertility is possible in both men and women.

General warnings

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary effects. 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 from the disease itself. The effective dose after therapeutic activities of Sodium iodide (^{131}I) is higher than 20 mSv.

Paediatric population

Types of adverse reactions in children are expected to be the same as in adults. Based on greater radiation sensitivity of child tissue (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.

4.9 Overdose

The risks relates to the inadvertent administration of excess radioactivity. High radiation exposure through overdose can be reduced by means of immediate administration of thyroid blocking agent, such as potassium perchlorate or potassium iodide, the use of the emetics and promoting a diuresis with frequent voiding of urine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: radiopharmaceutical product for therapeutic use derivated from iodine-131, ATC code:

V10XA01 : therapeutic use

Mechanism of action

The pharmacological active substance is iodine-131 in the form of sodium iodide that is taken up by the thyroid. It decays mainly there during its long residence time and in this manner induces a selective irradiation of this organ.

Pharmacodynamic effects

With therapeutic activity levels, given the quantity of iodine administered, no pharmacological effect is expected.

Over 90% of the radiation effects result from beta minus (β-) radiation which has a mean range in tissue of 0.5 mm. β- radiation decreases cell function and cell division in a dose-dependent manner, leading to cell death. The low mean range and the almost total absence of sodium iodide (^{131}I) uptake outside the thyroid gland means that radiation of non-thyroid tissue is negligible.

5.2 Pharmacokinetic properties

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 or excreted through the kidneys.

Following injection, about 20% of blood iodide is extracted in a single passage through the thyroid gland. Peak thyroid accumulation occurs within 24-48 hours of dosing with about 50% of the maximum at 5 hours. The uptake is influenced by several factors: patient age, volume of the thyroid gland, renal clearance, plasma concentrations of iodide and other drugs (see section 4.5).

Clearance of the iodide by the thyroid gland is generally between 5 and 50 mL/min. In cases of iodine deficiency, however, it increases to 100 mL/min and can reach 1,000 mL/min in cases of hyperthyroidism. In iodine overload cases, it can decrease to 2-5 mL/min. Iodide also accumulates in the kidneys.

Small amounts of iodide (^{131}I) are taken up by salivary glands, gastric mucosa and would also be localised in breast milk, the placenta and choroid plexus. Iodide taken up by the thyroid gland follows the known metabolic pathway of the thyroid hormones and is incorporated into the organic substances from which thyroid hormones are synthesised.

Elimination
Urinary excretion is 37-75 %, faecal excretion is about 10% with almost negligible excretion in the sweat. Urinary excretion is marked by renal clearance, which is about 3% of renal flow and is relatively constant from one person to another. It is lower in cases of hypothyroidism and impaired renal function, and higher in hyperthyroidism. In euthyroid patients with normal renal function, 50 to 75% of the activity administered is excreted in the urine within 48 hours.

Half-life
The effective half-life of radioiodine is about 12 hours in plasma and about 6 days in the thyroid gland. Following the administration of sodium iodide (^{131}I), approximately 40% of the administered activity has an effective half-life of 0.4 days and the remaining 60% a half-life of 8 days.

5.3 Preclinical safety data

Because of the small quantities of substance administered compared with the normal food intake of iodine (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

Sodium dihydrogen phosphate, sodium chloride, sodium thiosulfate, sodium hydroxide and water for injections.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

29 days from the day of manufacture.
The expiry date is indicated on each vial label and on the outer packaging.
After the first withdrawal, store in a refrigerator (2°C-8°C) and use within 8 hours.

6.4 Special precautions for storage

Do not store above 25°C.
For storage conditions after first withdrawal of the medicinal product, see section 6.3.
Storage should be in accordance with national regulations for radioactive materials.

6.5 Nature and contents of container

15 mL colourless, European Pharmacopoeia type I, drawn glass vial, closed with a grey rubber stopper and an aluminium capsule.

Pack size: One multidose vial containing from 80 to 1 110 MBq at calibration date.

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 competent official organisation.

Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

Solutions of sodium iodide ^{131}I should be handled strictly under a ventilated hood

The vial must be kept inside its lead shielding. It should never be opened. After disinfection of the stopper, the solution should be aseptically withdrawn through the stopper using sterilized single use needle and syringe.

Solution ready to use.

Before use, packaging, radioactivity and gamma spectrum will be checked.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spills of urine, vomits, and expectorations. Radiation protection precautions in accordance with national regulations must therefore be taken.

The administration of sodium iodide (^{131}I) may result in significant environmental hazard.
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 be taken concerning the activity eliminated by the patients in order to avoid any contaminations.

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

7. MARKETING AUTHORISATION HOLDER

CIS bio international
RN 306 – SACLAY
B.P. 32
91192 GIF-SUR-YVETTE Cedex
FRANCE

8. MARKETING AUTHORISATION NUMBER

Country specific

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Country specific

10. DATE OF REVISION OF THE TEXT

12/2018

11. DOSIMETRY

Tabulated radiation dosimetry is reported from ICRP publication n°53 and 60 (1987).
The ICRP model refers to intravenous administration.

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.

As part of the risk-benefit assessment it is advised that the E (Effective Dose) and likely radiation doses to individual target organ(s) be 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.

Radiation exposure (Thyroid blocked, uptake 0 %)

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	Adults	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	0.040	0.064	0.10	0.19
Small intest	0.038	0.047	0.075	0.12	0.22
ULI wall	0.037	0.045	0.070	0.12	0.21
LLI wall	0.043	0.052	0.082	0.13	0.23
Kidneys	0.065	0.080	0.12	0.17	0.31
Liver	0.033	0.040	0.065	0.10	0.20
Lungs	0.031	0.038	0.060	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**	**0.126**	**0.198**	**0.374**

Bladder wall contributes to 47.6 % of the effective dose.

According to IRCP 60, after injection of 400 MBq (pre-therapeutic indication) the effective dose is about 25.6 mSv. The absorbed doses are 11.6 mGy and 244 mGy for thyroid and bladder wall, respectively.

When 11 100 MBq are administered (therapeutic indication) the effective dose is about 710 mSv. The absorbed doses are 322 mGy and 6770 mGy for thyroid and bladder wall, respectively.

Incomplete blockage

Effective dose equivalent (mSv/MBq) at small uptake in the thyroid

uptake : 0.5 %	0.50	0.79	1.20	2.60	4.90
uptake : 1.0 %	0.90	1.42	2.10	4.70	9.30
uptake : 2.0 %	1.60	2.60	4.20	9.30	17

Radiation exposure (Thyroid uptake: 15 %)

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	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)	**11.1**	**17.9**	**26.8**	**58.7**	**107**

Radiation exposure (Thyroid uptake: 35 %)

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	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	0.16	0.26	0.41	0.71
Effective dose (mSv/MBq)	**25.6**	**41.5**	**62.3**	**137**	**248**

According to IRCP 60, after injection of 11 100 MBq, the Effective Dose is about **284 Sv.** The absorbed doses are **5550 Gy** and **4.5 Gy** for thyroid and bladder wall, respectively.

Radiation exposure (Thyroid uptake: 55 %)

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	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	0.24
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)	**40.2**	**65**	**100**	**214**	**391**

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.