SUMMARY OF PRODUCT CHARACTERISTICS

for

Sodium Iodide (I131) Capsules T, hard capsules

1. NAME OF THE MEDICINAL PRODUCT

Sodium Iodide (I131) Capsules T

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One capsule contains I-131 as sodium iodide: 37-7400 MBq at activity reference time.

Iodine-131 has a half-life of 8.02 days. It decays by emission of gamma radiations of 365 keV (81%), 637 keV (7.3%) and 284 keV (6.0%) and beta radiations of maximal energy of 606 keV to stable Xenon-131.

Excipients with known effect: Sucrose 23 mg, sodium: 63.5 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule, hard.

Transparent hard gelatine capsules containing a white to light brown powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Radioiodine thyroid therapy is indicated for:

- Treatment of Graves' disease, toxic multinodular goitre or autonomous nodules.
- Treatment of papillary and follicular thyroid carcinoma including metastatic disease.
- In the management of thyroid carcinoma, sodium iodide is used to identify thyroid remnant and metastases (after ablation).

Sodium iodide I-131 therapy is often combined with surgical intervention and with antithyroid medicinal products.

4.2 Posology and method of administration

Posology

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

For the treatment of hyperthyroidism

The activity administered depends on the diagnosis, the size of the gland, thyroid uptake, and iodine clearance. 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 Graves' disease, multifocal or disseminated autonomy, the above mentioned target organ doses are related to the overall weight of the thyroid gland, however in the unifocal autonomy, the target organ dose is only related to the weight of the adenoma.

The activity administered is usually in the range of 200-800 MBq but repeated treatment may be necessary.

Patients should be rendered euthyroid medically whenever possible before giving radioiodine treatment for hyperthyroidism.
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 autonomy)

max. uptake I-131= 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 = 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 target organ dose (Gy).

Fixed dose protocols may also be used.

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

For measuring remnant tissue, metastases and recurrence
For post thyroid ablation (for thyroid remnant, metastases and recurrence): A maximum activity of 400 MBq.

Paediatric population
The activity to be administered in children and adolescent should be determined after performing an individual dosimetry (see section 4.4).

Method of administration

The capsule should be taken fasting and with plenty of liquid and swallowed whole. Before giving the capsule to children, in particular to younger children, it should be ensured that the capsule can be swallowed whole. Giving it with mashed food is recommended.

Administration protocol

1 The tin must be removed from the package and the leadpot must be taken out
2 The lid must be turned gently clockwise until a slight resistance is met, then the lid must be lifted from the leadpot leaving the inner vial in the base.
3 The vial, containing the capsule, must be placed into a measuring device to determine the activity.
4 The vial must be replaced in the leadpot and the lid must be mounted on the leadpot without turning.
5 The patient must be asked to unscrew the lid of the leadpot and the vial cap simultaneously by turning it three times counterclockwise.
6 The patient must remove the lid, lift the leadpot, and swallow the capsule.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients, listed in section 6.1
- Pregnancy and lactation.
- 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

Renal impairment

The therapeutic administration of 131I capsules in patients with significant renal impairment, in which an activity adjustment is necessary, requires special attention.

Paediatric population

In the treatment of children and adolescents, the radioiodine treatment of benign thyroid diseases may be performed in justified cases, especially in relapse after use of antithyroid medicinal products or when serious adverse reactions to antithyroid medicinal products do occur. There is no evidence of an increased incidence of cancer, leukemia or mutations in man with respect to patients treated for benign thyroid disease with radioiodine, despite extensive use. In the treatment of children and young people however, account must be taken of the greater sensitivity of child tissue and the greater life expectancy of such patients. The risks must also be weighed against those of other possible treatments. See sections 4.2 and 11.

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.

The capsules should be swallowed whole with sufficient fluid to ensure clear passage into the stomach and upper small intestine. Concomitant use of H2 antagonists or proton pump inhibitors is advised in order to address the possible gastrointestinal reactions.
In case of vomiting, the risk of contamination has to be considered.

General warnings
Radiopharmaceuticals may 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 by the user in a manner which satisfies both radiological and pharmaceutical quality requirements.

This preparation is likely to result in relatively a high radiation dose to most patients (see sections 4.8 and 11). The administration of high dose radioiodine 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 should be taken concerning the activity eliminated by the patients in order to avoid any contaminations.

Specific warnings
The radiation exposure of the salivary glands should be reduced by stimulating saliva excretion with acidic substances. Other pharmacological protection measures may be used additionally.

A low iodine diet prior to therapy will enhance uptake into functioning thyroid tissue.

Thyroid replacement should be stopped prior to radioiodine administration for thyroid carcinoma to ensure adequate uptake. A period of 14 days is recommended for triiodothyronine and 4-5 weeks for thyroxine. They should be restarted two days after treatment. Similarly carbimazole and propythiouracil should be stopped five days prior to treatment of hyperthyroidism and restarted several days later.

The radioiodine treatment of Graves' disease should be performed under concomitant treatment of corticosteroids.

Capsule T should not be used for thyroid scanning except in the follow-up of malignant disease or when I-123 or Tc-99m are not available.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Patients receiving therapy of the thyroid should be re-examined at appropriate intervals.

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

This medicinal product contains 63.5 mg of sodium per dose. To be taken into account by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Many pharmacologically active substances are known to interact with radioiodide. These may happen by a variety of mechanisms which can affect the protein binding, the pharmacokinetics or influence the dynamic effects of labelled iodide. As a consequence, it should be considered that the thyroid uptake might be reduced. It is therefore necessary to take a full drug history and ascertain whether any medicinal products 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 rest before administration of I-131**
antithyroid agents (e.g. carbimazole, methimazole, propyluracil), perchlorate	withheld 1week before starting treatment till several days after
salicylates, steroids, sodium nitroprusside, sodium sulfobromophthalein, anticoagulants, antihistamines, antiparasitics, penicillins, sulphonamides, tolbutamide, thiopentone	1 week
phenylbutazone	1 - 2 weeks
containing iodine expectorants and vitamins	approx. 2 weeks
thyroid hormone preparations	Triiodothyronine 14 days thyroxine 4-5 weeks
amiodarone*, benzodiazepines, lithium	approx. 4 weeks
containing iodine preparations for topical use	1 - 9 months
containing iodine contrast media	up to 1 year

* In case of amiodarone, a reduced uptake in the thyroid gland during several months is possible due to the long half-life of this agent.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Sodium iodide I-131 is contraindicated during established or suspected pregnancy or when pregnancy has not been excluded (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. When it is necessary to administer a radioactive medicinal product to women of childbearing potential, information should always be sought about pregnancy.

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. Should differentiated thyroid carcinoma be diagnosed during pregnancy, radioactive iodine treatment must be postponed until after the pregnancy. Women receiving sodium iodide I-131 should be advised NOT to become pregnant within 6-12 months after administration.

Contraception in males and females

Women are advised to use contraception for a time period of 6 -12 months. As a precaution, men should not father a child for a time period of 6 months after radioiodine treatment to allow the replacement of irradiated by non-irradiated spermatozoa.

Breastfeeding

Before administering a radioactive medicinal product to a mother who is breast-feeding consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breast-feeding and as to whether the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion activity in breast milk. Breast-feeding should be discontinued after sodium iodide I-131 administration.

4.7 Effects on ability to drive and use machines

Sodium Iodide (I131) Capsule T has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The frequencies of reported adverse reactions were derived from the medical literature. The safety profile of sodium iodide I-131 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 dose regimens which are used. Therefore, the reported adverse reactions were grouped by their occurrence in treatment of benign or malignant disease, even though the administered doses and dose regimens were usually not indicated in the respective publications and might not have been in line with the posology recommendations in this SPC.

Frequent occurring adverse reactions are: hypothyroidism, transient hyperthyroidism, salivary and lacrimal gland disorders, and local radiation effects. In cancer treatment additionally gastrointestinal adverse reactions and bone marrow suppression may frequently occur.

The following tables include reported adverse reactions sorted by system organ classes. Symptoms, which are rather secondary to a group-syndrome (e.g. sicca syndrome) are subsumed in parenthesis behind the respective syndrome.

The following table presents how the frequencies are reflected in this section:

Very common:	≥10%
Common:	≥1% and <10%
Uncommon:	≥0.1% and <1%
Rare:	≥0.01% and <0.1%
Very rare:	<0.01%
Not known:	No frequency indications found in the medical literature

Adverse Reactions after Treatment of Benign Disease:

System Organ Class	*Symptom*	*Frequency*
Immune system disorders	Anaphylactoid reaction	Not known
Endocrine disorders	Permanent hypothyroidism, hypothyroidism	Very common
	Transient hyperthyroidism	Common
	Thyreotoxic crisis, thyroiditis, hypoparathyroidism (blood calcium decreased, tetany)	Not known
Eye disorders	Endocrine ophthalmopathy (in Graves`disease)	Common
	Sicca syndrome	Not known
Respiratory thoracic and mediastinal disorders	Vocal cord paralysis	Very rare
Skin and subcutaneous disorders	Iodo acne	Not known
Gastrointestinal Disorders	Sialoadenitis	Common
General disorders and administration site conditions	Local swelling	Not known

Adverse reactions after Treatment of Malignant Disease:

System Organ Class	*Symptom*	*Frequency*
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Leukaemia	Common
	Solid cancers	Not known
Blood and lymphatic system disorders	Aplastic anemia, erythropenia, bone marrow failure	Very common
	Leukopenia, thrombocytopenia	Common
	Permanent or severe bone marrow suppression	Not known
Immune system disorders	Anaphylactoid reaction	Not known
Endocrine disorders	Thyreotoxic crisis, transient hyperthyroidism	Rare
	Thyroiditis (leucocytosis transient), hypoparathyroidism (blood calcium decreased, tetany), hypothyroidism	Not known
Nervous system disorders	Parosmia	Very common
	Brain oedema	Not known

System Organ Class	*Symptom*	*Frequency*
Eye disorders	Sicca syndrome (conjunctivitis, dry eyes, nasal dryness)	Very common
	Nasolacrimal duct obstruction (lacrimation increased)	Common
Respiratory thoracic and mediastinal	Dyspnoea	Common
	Throat constriction*, Pulmonary fibrosis, respiratory distress, obstructive airways disorder, pneumonitis, tracheitis, vocal cord dysfunction (vocal cord paralysis, dysphonia, hoareseness), oropharyngeal pain, stridor	Not known
Gastrointestinal Disorders	Sialoadenitis (dry mouth, salivary gland pain, salivary gland enlargement, dental caries, tooth loss), radiation sickness syndrome, nausea, ageusia, anosmia, dysgeusia, decreased appetite	Very common
	Vomiting	Common
	Gastritis, dysphagia	Not known
Renal and urinary disorders	Cystitis radiation	Not known
Reproductive system and breast disorders	Ovarian failure	Very common
Reproductive system and breast disorders	Azoospermia, oligospermia, decreased fertility 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, neck pain	Very common
	Local swelling	Common

*: especially in existing tracheal stenosis

Detailed description of undesirable effects:

Thyroid and parathyroid gland disorders

Dose dependent hypothyroidism may occur as a late consequence of radioiodine treatment of hyperthyroidism.
This may manifest itself weeks or years after treatment, requiring suitable timed measurement of thyroid function and appropriate thyroid replacement. Hypothyroidism is generally not seen until 6-12 weeks after sodium iodide I-131 administration.
In treatment of malignant disease hypothyroidism is frequently reported as an adverse reaction, however, radioiodine treatment in malignant disease usually follows thyroidectomy.
The destruction of thyroid follicles caused by the radiation exposure of sodium iodide (I-131) may lead to exacerbation of an already existing hyperthyroidism after 2 – 10 days or even to thyrotoxic crisis. Occasionally, an immune hyperthyroidism may develop after initial normalisation (latency period 2 – 10 months). With high dose radioiodine treatment, the patient may experience transient inflammatory thyroiditis and tracheitis 1-3 days after administration, with a possibility of severe tracheal constriction, especially where there is existing tracheal stenosis.
In rare cases, a temporary hyperthyroidism could be found even after treatment of functional thyroid carcinoma.
Cases of transient hypoparathyroidism have been observed after radioiodine; they must be monitored accordingly and treated with replacement therapy.

Eye disorders
Endocrine ophthalmopathy may progress or new ophthalmopathy may occur after radioiodine therapy of hyperthyroidism or Graves` disease.

Local irradiation effects
Vocal cord dysfunction and paralysis have been reported after administration of sodium iodide I-131, however, in some cases this might also have been caused by thyroid surgery and 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 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 metastasising thyroid carcinomas with CNS involvement, the possibility of local cerebral oedema and/or an increasing existing cerebral oedema must also be born in mind.

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 antiinflammatory treatment but cases have occasionally been described of dose-dependent persistent ageusia and dry mouth. The lack of saliva may lead to infections, e.g. caries and this may result in loss of teeth. For prevention of salivary disorders see section 4.4.

Malfunction of the salivary and/or lacrimal glands with resulting sicca syndrome may also appear with a delay of several months and up to two years after radioiodine therapy. Although sicca syndrome is a transient effect in most cases, the symptom may persist for years in some patients.

Bone marrow depression

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

Secondary malignancies

After higher activities, typically those used in the treatment of thyroid malignancies, an increased incidence of leukaemia has been observed.
There is also evidence for an increased incidence of secondary solid cancers at high activities (more than 7.4 GBq).

Fertility impairment

After radioiodine therapy of thyroid carcinoma, a dose dependent impairment of fertility may occur in men and women.

General advice

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 those of the disease itself. The radiation dose delivered (EDE) after therapeutic doses of sodium iodide I-131 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.

4.9 Overdose

In case of overdose, the risk of high radiation exposure may exist. As the medicinal product is excreted through the kidneys, the overdose of radiation exposure can be reduced by forced diuresis and frequent bladder voiding. Additionally, the blockade of the thyroid gland should be recommended (e.g. with potassium iodide or perchlorate) immediately following suspected overexposure in order to reduce the radiation exposure of the thyroid gland. To reduce the uptake of I-131, emetics can be given.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Therapeutic radiopharmaceuticals Iodine (I-131) compounds.
ATC code: V10XA01.
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. In the small amounts of substance used for diagnostic and therapeutic procedures no pharmacodynamic effects of sodium iodide (I-131) 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 (I-131) 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 I-131 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.

In studies on the dissolution of sodium iodide I-131 capsules it was shown that the dissolution took place within 5 – 12 minutes and that the radioactivity was homogeneously spread over the gastric mucosa.

Studies on the serum activities levels showed that after a fast increase, - persisting 10 – 20 minutes -, the equilibrium was reached after approximately 40 minutes. After oral administration of a sodium iodide I-131 solution the equilibrium was measured to be 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 uptake of iodide 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: the age of the patient, the volume of the thyroid, renal clearance, the level of circulating iodide and by other medicinal products (see section 4.5). The iodide clearance by the thyroid is usually 5- 50 ml/min. In case of iodine shortage it is however increased to up to 100 ml/min and during hyperthyroidism to up to 1000 ml/min. In case of iodine overload it can be decreased to 2 – 5 ml/min. Iodide accumulates also in the kidneys.
Small amounts of iodide I-131 are taken up by salivary glands, gastric mucosa and would also be localised in breast milk, the placenta and choroid plexus.

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.

Half-Life

The effective half-life of radioiodine in plasma is in the order of 12 hours whereas that for radioiodine taken up by the thyroid gland is about 6 days. Thus after administration of sodium iodide I-131 approximately 40% of the activity has an effective half-life of 0.4 days and the remaining 60% 8 days.

Elimination

Urinary excretion is 37-75%, faecal excretion is about 10% with almost negligible excretion in sweat.

The urinary excretion is characterised by the renal clearance which constitutes approximately 3 % of the renal flow and is relatively constant from one person to another. It is lower in hypothyroidism and in impaired renal function and higher in hyperthyroidism. In euthyroid patients with normal renal function 50 – 75 % of the administered activity is excreted in urine within 48 hours.

5.3 Preclinical safety data

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents:
Disodium hydrogen phosphate dihydrate
Sodium thiosulphate
Sodium hydrogen carbonate
Sodium hydroxide
Sucrose
Sodium chloride
Water for injections

Capsule shell:
Gelatine

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Sodium iodide (I131) Capsules T expires 2 - 6 weeks after activity reference date and time. Activity reference date and time and expiry date are printed on the label on the outer package.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package. Storage should be in accordance with national regulations for radioactive material.

6.5 Nature and contents of container

1 Capsule in a PETP single dose container.

6.6 Special precautions for disposal and other handling of the product

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

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.

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

7. MANUFACTURED AND RELEASED BY

Mallinckrodt Medical B.V.
Westerduinweg 3
1755 LE Petten
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

January 2011

11. DOSIMETRY

Tabulated radiation dosimetry as reported in ICRP publication n°53 are reported. The ICRP model refers to intravenous administration. Since absorption of radioiodide is rapid and complete, this model is applicable in case of oral administration also but there is a further radiation dose to the stomach wall in addition to that due to gastric and salivary excretion. Assuming that the mean residence time in the stomach is 0.5 hr, the absorbed dose to the stomach increases by about 30% for I-131.

Radiation dose to specific organs, which may not be the target organ of therapy, can be influenced significantly by pathophysiological changes induced by the disease process. As part of the risk-benefit assessment it is advised that the EDE 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.

The radiation exposure is mainly affecting the thyroid. The radiation exposure of the other organs is in the range of thousandths lower than that of the thyroid. It is dependant on the dietary intake of iodine (the uptake of radioactive iodine is in iodine deficient areas increased by up to 90 % and is decreased in iodine rich areas to 5 %). It is further dependant on the thyroid function (Eu-, hyper-, or hypothyroid) 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 blockade of the thyroid.) The radiation exposure of all other organs is correspondingly higher or lower, depending on the degree of accumulation in the thyroid.

IODIDE

Thyroid blocked, uptake 0%

^{131}I 8.04 days

Absorbed dose per unit activity administered (mGy/MBq)

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	3.7E-02	4.2E-02	6.7E-02	1.1E-01	2.0E-01
*Bladder wall	6.1E-01	7.5E-01	1.1E+00	1.8E+00	3.4E+00
Bone surfaces	3.2E-02	3.8E-02	6.1E-02	9.7E-02	1.9E-01
Breast	3.3E-02	3.3E-02	5.2E-02	8.5E-02	1.7E-01
GI-tract					
Stomach wall	3.4E-02	4.0E-02	6.4E-02	1.0E-01	1.9E-01
*Small intestine	3.8E-02	4.7E-02	7.5E-02	1.2E-01	2.2E-01
*ULI wall	3.7E-02	4.5E-02	7.0E-02	1.2E-01	2.1E-01
*LLI wall	4.3E-02	5.2E-02	8.2E-02	1.3E-01	2.3E-01
*Kidneys	6.5E-02	8.0E-02	1.2E-01	1.7E-01	3.1E-01
Liver	3.3E-02	4.0E-02	6.5E-02	1.0E-01	2.0E-01
Lungs	3.1E-02	3.8E-02	6.0E-02	9.6E-02	1.9E-01
Ovaries	4.2E-02	5.4E-02	8.4E-02	1.3E-01	2.4E-01
Pancreas	3.5E-02	4.3E-02	6.9E-02	1.1E-01	2.1E-01
Red marrow	3.5E-02	4.2E-02	6.5E-02	1.0E-01	1.9E-01
Spleen	3.4E-02	4.0E-02	6.5E-02	1.0E-01	2.0E-01
Testes	3.7E-02	4.5E-02	7.5E-02	1.2E-01	2.3E-01
Thyroid	2.9E-02	3.8E-02	6.3E-02	1.0E-01	2.0E-01
Uterus	5.4E-02	6.7E-02	1.1E-01	1.7E-01	3.0E-01
Other tissue	3.2E-02	3.9E-02	6.2E-02	1.0E-01	1.9E-01
Effective dose equivalent (mSv/MBq)	**7.2E-02**	**8.8E-02**	**1.4E-01**	**2.1E-01**	**4.0E-01**

Bladder wall contributes to 50.8% of the effective dose equivalent.

Incomplete blockage

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

uptake 0.5%:	3.0E-01	4.5E-01	6.9E-01	1.5E+00	2.8E+00
uptake 1%:	5.2E-01	8.1E-01	1.2E+00	2.7E+00	5.3E+00
uptake 2%:	9.7E-01	1.5E+00	2.4E+00	5.3E+00	1.0E+01

Thyroid uptake 15%

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	3.6E-02	4.3E-02	7.1E-02	1.1E-01	2.2E-01
*Bladder wall	5.2E-01	6.4E-01	9.8E-01	1.5E+00	2.9E+00
Bone surfaces	4.7E-02	6.7E-02	9.4E-02	1.4E-01	2.4E-01
Breast	4.3E-02	4.3E-02	8.1E-02	1.3E-01	2.5E-01
GI-tract					
Stomach wall	4.6E-01	5.8E-01	8.4E-01	1.5E+00	2.9E+00
*Small intestine	2.8E-01	3.5E-01	6.2E-01	1.0E+00	2.0E+00
*ULI wall	5.9E-02	6.5E-02	1.0E-01	1.6E-01	2.8E-01
*LLI wall	4.2E-02	5.3E-02	8.2E-02	1.3E-01	2.3E-01
*Kidneys	6.0E-02	7.5E-02	1.1E-01	1.7E-01	2.9E-01
Liver	3.2E-02	4.1E-02	6.8E-02	1.1E-01	2.2E-01
Lungs	5.3E-02	7.1E-02	1.2E-01	1.9E-01	3.3E-01
Ovaries	4.3E-02	5.9E-02	9.2E-02	1.4E-01	2.6E-01
Pancreas	5.2E-02	6.2E-02	1.0E-01	1.5E-01	2.7E-01
Red marrow	5.4E-02	7.4E-02	9.9E-02	1.4E-01	2.4E-01
Spleen	4.2E-02	5.1E-02	8.1E-02	1.2E-01	2.3E-01
Testes	2.8E-02	3.5E-02	5.8E-02	9.4E-02	1.8E-01
Thyroid	2.1E+02	3.4E+02	5.1E+02	1.1E+03	2.0E+03
Uterus	5.4E-02	6.8E-02	1.1E-01	1.7E-01	3.1E-01
Other tissue	6.5E-02	8.9E-02	1.4E-01	2.2E-01	4.0E-01
Effective dose equivalent (mSv/MBq)	**6.6E+00**	**1.0E+01**	**1.5E+01**	**3.4E+01**	**6.2E+01**

Thyroid uptake 35%

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	4.2E-02	5.0E-02	8.7E-02	1.4E-01	2.8E-01
*Bladder wall	4.0E-01	5.0E-01	7.6E-01	1.2E+00	2.3E+00
Bone surfaces	7.6E-02	1.2E-01	1.6E-01	2.3E-01	3.5E-01
Breast	6.7E-02	6.6E-02	1.3E-01	2.2E-01	4.0E-01
GI-tract					
Stomach wall	4.6E-01	5.9E-01	8.5E-01	1.5E+00	3.0E+00
*Small intestine	2.8E-01	3.5E-01	6.2E-01	1.0E+00	2.0E+00
*ULI wall	5.8E-02	6.5E-02	1.0E-01	1.7E-01	3.0E-01
*LLI wall	4.0E-02	5.1E-02	8.0E-02	1.3E-01	2.4E-01
*Kidneys	5.6E-02	7.2E-02	1.1E-01	1.7E-01	2.9E-01
Liver	3.7E-02	4.9E-02	8.2E-02	1.4E-01	2.7E-01
Lungs	9.0E-02	1.2E-01	2.1E-01	3.3E-01	5.6E-01
Ovaries	4.2E-02	5.7E-02	9.0E-02	1.4E-01	2.7E-01
Pancreas	5.4E-02	6.9E-02	1.1E-01	1.8E-01	3.2E-01
Red marrow	8.6E-02	1.2E-01	1.6E-01	2.2E-01	3.5E-01
Spleen	4.6E-02	5.9E-02	9.6E-02	1.5E-01	2.8E-01
Testes	2.6E-02	3.2E-02	5.4E-02	8.9E-02	1.8E-01
Thyroid	5.0E+02	7.9E+02	1.2E+03	2.6E+03	4.7E+03
Uterus	5.0E-02	6.3E-02	1.0E-01	1.6E-01	3.0E-01
Other tissue	1.1E-01	1.6E-01	2.6E-01	4.1E-01	7.1E-01
Effective dose equivalent (mSv/MBq)	**1.5E+01**	**2.4E+01**	**3.6E+01**	**7.8E+01**	**1.4E+02**

Thyroid uptake 55%

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	4.9E-02	5.8E-02	1.1E-01	1.7E-01	3.4E-01
*Bladder wall	2.9E-01	3.6E-01	5.4E-01	8.5E-01	1.6E+00
Bone surfaces	1.1E-01	1.7E-01	2.2E-01	3.2E-01	4.8E-01
Breast	9.1E-02	8.9E-02	1.9E-01	3.1E-01	5.6E-01
GI-tract					
Stomach wall	4.6E-01	5.9E-01	8.6E-01	1.5E+00	3.0E+00
*Small intestine	2.8E-01	3.5E-01	6.2E-01	1.0E+00	2.0E+00
*ULI wall	5.8E-02	6.7E-02	1.1E-01	1.8E-01	3.2E-01
*LLI wall	3.9E-02	4.9E-02	7.8E-02	1.3E-01	2.4E-01
*Kidneys	5.1E-02	6.8E-02	1.0E-01	1.7E-01	2.9E-01
Liver	4.3E-02	5.8E-02	9.7E-02	1.7E-01	3.3E-01
Lungs	1.3E-01	1.8E-01	3.0E-01	4.8E-01	8.0E-01
Ovaries	4.1E-02	5.6E-02	9.0E-02	1.5E-01	2.7E-01
Pancreas	5.8E-02	7.6E-02	1.3E-01	2.1E-01	3.8E-01
Red marrow	1.2E-01	1.8E-01	2.2E-01	2.9E-01	4.6E-01
Spleen	5.1E-02	6.8E-02	1.1E-01	1.7E-01	3.3E-01
Testes	2.6E-02	3.1E-02	5.2E-02	8.7E-02	1.7E-01
Thyroid	7.9E+02	1.2E+03	1.9E+03	4.1E+03	7.4E+03
Uterus	4.6E-02	6.0E-02	9.9E-02	1.6E-01	3.0E-01
Other tissue	1.6E-01	2.4E-01	3.7E-01	5.9E-01	1.0E+00
Effective dose equivalent (mSv/MBq)	**2.4E+01**	**3.7E+01**	**5.6E+01**	**1.2E+02**	**2.2E+02**

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

The capsules are ready to use.

For the recommendation how to measure the activity see section 4.2, paragraph administration protocol.

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

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Marketing Authorisation Holder: Soreq Nuclear Research Centre, Yavne 81800, Israel

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