SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MON.IYOT-131 0.37 - 7400 MBq (10 µCi – 200 mCi) oral capsule
0.37 - 7400 MBq / Capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:
Sodium iodide …… 0,37 – 7400 MBq

One capsule contains ^{131}I as sodium iodide (^{131}I): 0,37-7400 MBq (10 µCi – 200 mCi) at activity reference date and time.

Iodine-131 has a half-life of 8.02 days. During the reduction of activity, it emits beta (β) and gamma (γ) radiations. 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:

	1 kapsülde bulunabilecek miktar	
	Diagnostic (D)	Therapeutic (T)
Disodium hydrogen phosphate anhidr	400 mg	400 mg
Sodium thiosulphate	0,1 -1 mg	0,1 -1 mg
Sodium carbonat decahydrate	0,02 - 1,1 mg	0,0 - 0,7 mg
Sodium bicarbonate	0,05 - 2,8 mg	0,0 - 1,7 mg
Sodium hydroxide 1M	0,00 - 0,01 mL	0,00 – 0,01mL

See section 6.1 for a full list of excipients

3. PHARMACEUTICAL FORM

Oral capsule
Transparent, colorless hard gelatin capsule containing white to light brown powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the therapy of:
- Thyroid cancer
- Toxic nodular goiter
- Toxic diffused goiter diseases
- Hyperthyroidism

For diagnosis, it is used for scanning thyroid.

4.2 Posology and method of administration

Posology / administration frequency and time

Administration for treatment purposes:
The activity administered for treatment 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:

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

Where:
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 ^{131}I = 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.

Administration for diagnosis purpose:
The following doses are used for adult patients (70 kg).

Thyroid uptake study: 0.2- 3.7 MBq
After thyroid ablation (for metastasis and thyroid remnant): Maximum dosage: 400 MBq
For thyroid imaging: 7.4- 11 MBq

Scanning is generally completed in 4 hours and repeated between 18-24 hours. However, scintigraphy studies are conducted in 72 hours.

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
Application by swallowing orally.

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.

In patients with suspected gastrointestinal disease, great care should be taken when administering Sodium [^{131}I] iodide. The capsules should be swallowed whole with sufficient fluid to ensure clear passage into the stomach and upper small intestine. Concomitant use of H_2 antagonists or proton pump inhibitors is advised.

For instructions on the medicinal product before administration, see section 12.

Additional information on special populations

Renal/hepatic impairment
It may increase the risk of potential adverse effects as the patients with renal disease may extend the duration of stay of I-131 within the body. The therapeutic administration of ^{131}I capsules in patients with significant renal impairment, in which an activity adjustment is necessary, requires special attention.

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

The quantity of dose (activity) to be administered to a child over 10 years and adolescent should be a fraction of the adult dose calculated from formulas depending on the body weight or surface area of the child.

$$\text{Child dose (MBq)} = \frac{\text{Adult dose (MBq)} \times \text{Child weight (kg)}}{70 \text{ kg}}$$

or

$$\text{Child dose (MBq)} = \frac{\text{Adult dose (MBq)} \times \text{Child body surface } (m^2)}{1.73 \ m^2}$$

Child dose (MBq) = Adult dose x Fraction of adult dose

Fraction of adult dose		
3 Kg = 0.1	22 Kg = 0.50	42 Kg = 0.78
4 Kg = 0.14	24 Kg = 0.53	44 Kg = 0.80
6 Kg = 0.19	26 Kg = 0.56	46 Kg = 0.82
8 Kg = 0.23	28 Kg = 0.58	48 Kg = 0.85
10 Kg = 0.27	30 Kg = 0.62	50 Kg = 0.88
12 Kg = 0.32	32 Kg = 0.65	52-54 Kg = 0.90
14 Kg = 0.36	34 Kg = 0.68	56-58 Kg = 0.92
16 Kg = 0.40	36 Kg = 0.71	60-62 Kg = 0.96
18 Kg = 0.44	38 Kg = 0.73	64-66 Kg = 0.98
20 Kg = 0.46	40 Kg = 0.76	68 Kg = 0.99

(Paediatric Task Group, European Association of Nuclear Medicines)

Geriatric population
It is not necessary to adjust dosage for old patients.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Lactation period.
- Established or suspected pregnancy or when pregnancy has not been excluded (see section 4.6.)
- For diagnostic purposes in children under 10 years of age.
- Thyroid scanning except in the follow-up of malignant disease or when ^{123}I or ^{99m}Tc are not available.
- Patients with dysphagia, oesophageal stricture, oesophageal stenosis, oesophagus diverticulum, active gastritis, gastric erosions and peptic ulcer.
- Patients with suspected reduced gastrointestinal motility.

4.4 Special warnings and precautions for use

RADIOPHARMACEUTICALS SHOULD BE ADMINISTERED ONLY BY NUCLEAR MEDICINE PHYSICIANS IN NUCLEAR MEDICINE CENTERS.

This preparation is likely to result in a relatively high radiation dose to most patients (see sections 4.8 and section 11).

Suitable precautions should be taken concerning the activity eliminated by the patient in order to avoid any contamination.

Iodine-131 for diagnostic studies has not to be used in children under 10 years and is not suitable for administration to children over 10 years old and adolescents unless exceptional circumstances prevail, due to significantly higher radiation exposure compared with the adult.

There is no evidence of an increased incidence of malignancies (cancer, leukaemia or mutations) in man with patients treated for diagnostic purpose with sodium [^{131}I] iodide.

For each patient, exposure to ionising radiation must be justifiable on the basis of likely benefit. The activity administered must be such that the resulting radiation dose is as low as reasonable achievable bearing in mind the need to obtain the intended diagnostic or therapeutic result.

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.

Renal impairment

The therapeutic administration of ^{131}I 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 catheterized after administration of high activities of radioiodine.

The capsules should be swallowed as a 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.

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 propylthiouracil 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, when endocrine ophthalmopathy is present.

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

In patients with known hypersensitivity for gelatine and/ or its metabolites the use of sodium iodide [^{131}I] solution should be preferred for radioiodine treatment.

This medicinal product contains 129.68 mg of sodium per capsule. To be taken into account by patients on a controlled sodium diet.

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 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 1 week 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.

Additional information on special population
There is no additional information on special population

Paediatric population
Interaction study specific to children has not been conducted.

4.6 Pregnancy and lactation

General recommendation
Pregnancy category: X

Women of childbearing potential / Contraception
Administration of sodium iodide I-131 to a woman during pregnancy period can cause serious birth anomalies.

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.

Contraception in males and females

Women are advised to use contraception during treatment period and for a time period of 6 -12 months after treatment.
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.

Pregnancy

MON.IYOT-131 oral capsule is contraindicated during pregnancy period (see Section 4.3).

Sodium iodide I-131 should not be used during established or suspected pregnancy or when pregnancy has not been excluded, due to transplacental passage of sodium iodide I-131 which can cause severe and possibly irreversible hypothyroidism in neonates (the absorbed dose to the uterus for this medicinal product is likely to be in the range 11-511 mGy, and the foetal thyroid gland avidly concentrates iodine during the second and third trimesters) (see section 4.3).

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

Breastfeeding

Before administering radiopharmaceuticals to a mother who is breast-feeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breast-feeding, and what is the most appropriate choice of radiopharmaceutical, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breast-feeding should be discontinued after Sodium Iodide I-131 administration.

Fertility

There may be a decrease in fertility after therapy of thyroid cancer with radioiodine on women and men. Temporary spermatogenesis may occur depending on the dosage. Furthermore, it may cause change in the menstruation period.

4.7 Effects on ability to drive and use machines

MON.IYOT-131 oral capsule has no influence on the ability to drive and use machines or degree of this effect can be neglected.

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 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 local radiation effects. In cancer treatment additionally gastro-intestinal adverse reactions and bone marrow suppression may frequently occur.

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

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

Very common:	≥1/10
Common:	≥1/100 to <1/10
Uncommon:	≥1/1,000 to <1/100
Rare:	≥1/10,000 to <1/1,000
Very rare:	<1/10,000
Not known:	not known (cannot be estimated from the available data)

Adverse Reactions after Diagnostic Use:

System Organ Class	**Symptom**	**Frequency**
Immune system disorders	Hypersensitivity	Not known
Gastrointestinal disorders	Nausea, vomiting	Not known
Congenital and hereditary/genetic disorders	Congenital thyroid disorders	Not known

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 (acne-like rash)	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 e.g. bladder cancer, colon cancer, gastric cancer	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
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, pneumonitis, tracheitis, vocal cord dysfunction (vocal cord paralysis, dysphonia, hoareseness), oropharyngeal pain, stridor	Not known

System Organ Class	Symptom	Frequency
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, which, however, is being accounted for by the preceding 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 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 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 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
Sialadenitis may occur, with swelling and pain in the salivary glands, partial loss of taste and dry mouth. Sialadenitis 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 in 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. Depending on the activity dose, a reversible impairment of the spermatogenesis could be verified in doses above 1850 MBq; clinical relevant effects including oligospermia and azoospermia and elevated serum FSH levels have been described after administration greater than 3700 MBq.

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.

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

In case of overdose by mistake, laxatives should be administered and stomach cleansing should be performed.

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. 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

It is used for diagnosis and therapy purposes.
Pharmacotherapeutical group:
ATC Code: V09FX03 : Diagnostic radiopharmaceutical
ATC Code: V10XA01: Therapeutic Radiopharmaceutical

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.

5.1 Pharmacodynamic properties

In the small amounts of substance used for diagnostic and therapeutic procedures 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 characteristics

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.

Studies on the serum activities levels showed that after a fast increase, -persisting 10 – 20 minutes-, equilibrium was reached after approximately 40 minutes. After oral administration of a ^{131}I sodium iodide solution the equilibrium was measured to be at the same time.

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.

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 localized 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.

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. The mean urinary excretion in healthy subjects (24 hours urine was investigated) was 2.8 mg/kg in men and 2.7 mg/kg in women.

In euthyroid 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 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.

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
Disodium hydrogen phosphate anhydr
Sodium thiosulphate
Sodium carbonate decahydrate
Sodium bicarbonate
Sodium hydroxide
Hydrochloric acid
Hard gelatin capsule

6.2 Incompatibilities
There is no known incompatibility with MON.IYOT-131 oral capsule.

6.3 Shelf life
30 days as from the date of production.

6.4 Special precautions for storage
It should be stored at room temperature below 25 ºC in original package.
Storage should be in accordance with national regulations for radioactive material.

6.5 Nature and content of container

Inner package: Polypropylene plastic tube
Outer package (from inside to outside): Lead shield, tin box, plastic outer box for transportation.

Content of package for MON.IYOT-131 oral capsule produced in microcure activity:

1 capsule / package
6 capsules / package
20 capsules / package

Content of package for MON.IYOT-131 oral capsule produced in 1 mCi- 200 mCi activity:

1 capsules / package

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

General warnings

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.

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.

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.

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.

Actions for wastes:

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

7. MARKETING AUTHORISATION HOLDER

Curium Nükleer Tıp A.Ş.
TÜBİTAK MAM Teknoparkı
41470 Gebze Kocaeli TURKEY
Tel: +90 262 648 02 00
Fax: +90 262 646 40 39

8. MARKETING AUTHORISATION NUMBER(S)

223/93

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15.03.2010
Date of last renewal: 07.02.2017

10. DATE OF REVISION OF THE TEXT

06.2025

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 hypothroid) 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 8.02 days
Absorbed dose per unit activity administered (mGy/MBq)

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	0.037	0.042	0.067	0.110	0.200
*Bladder wall	0.610	0.750	1.100	1.800	3.400
Bone surfaces	0.032	0.038	0.061	0.097	0.190
Breast	0.033	0.033	0.052	0.085	0.170
GI tract					
Stomach wall	0.034	0.040	0.064	0.100	0.190
*Small intest.	0.038	0.047	0.075	0.120	0.220
*ULI wall	0.037	0.045	0.070	0.120	0.210
*LLI wall	0.043	0.052	0.082	0.130	0.230
*Kidneys	0.065	0.080	0.120	0.170	0.310
Liver	0.033	0.040	0.065	0.100	0.200
Lungs	0.031	0.038	0.060	0.096	0.190
Ovaries	0.042	0.054	0.084	0.130	0.240
Pancreas	0.035	0.043	0.069	0.110	0.210
Red marrow	0.035	0.042	0.065	0.100	0.190
Spleen	0.034	0.040	0.065	0.100	0.200
Testes	0.037	0.045	0.075	0.120	0.230
Thyroid	0.029	0.038	0.063	0.100	0.200
Uterus	0.054	0.067	0.110	0.170	0.300
Other tissue	0.032	0.039	0.062	0.100	0.190
Effective dose equivalent (mSv/MBq)	**0.072**	**0.088**	**0.140**	**0.210**	**0.400**

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%	0.300	0.450	0.690	1.500	2.800
Uptake 1%	0.520	0.810	1.200	2.700	5.300

Uptake 2%	0.970	1.500	2.400	5.300	10.000

Thyroid uptake 15%

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	0.036	0.043	0.071	0.110	0.220
*Bladder wall	0.520	0.640	0.980	1.500	2.900
Bone surfaces	0.047	0.067	0.094	0.140	0.240
Breast	0.043	0.043	0.081	0.130	0.250
GI tract					
*Stomach wall	0.460	0.580	0.840	1.500	2.900
*Small intest.	0.280	0.350	0.620	1.000	2.000
*ULI wall	0.059	0.065	0.100	0.160	0.280
*LLI wall	0.042	0.053	0.082	0.130	0.230
*Kidneys	0.060	0.075	0.110	0.170	0.290
Liver	0.032	0.041	0.068	0.110	0.220
Lungs	0.053	0.071	0.120	0.190	0.330
Ovaries	0.043	0.059	0.092	0.140	0.260
Pancreas	0.052	0.062	0.100	0.150	0.270
Red marrow	0.054	0.074	0.099	0.140	0.240
Spleen	0.042	0.051	0.081	0.120	0.230
Testes	0.027	0.035	0.058	0.094	0.180
Thyroid	210.000	340.000	510.000	1100.000	2000.000
Uterus	0.054	0.068	0.110	0.170	0.310
Other tissue	0.065	0.089	0.140	0.220	0.400
Effective dose equivalent (mSv/MBq)	**6.600**	**10.000**	**15.000**	**34.000**	**62.000**

Thyroid uptake 35%

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	0.042	0.050	0.087	0.140	0.280
*Bladder wall	0.400	0.500	0.760	1.200	2.300
Bone surfaces	0.076	0.120	0.160	0.230	0.350
Breast	0.067	0.066	0.130	0.220	0.400
GI tract					
*Stomach wall	0.460	0.590	0.850	1.500	3.000
*Small intest.	0.280	0.350	0.620	1.000	2.000
*ULI wall	0.058	0.065	0.100	0.170	0.300
*LLI wall	0.040	0.051	0.080	0.130	0.240
*Kidneys	0.056	0.072	0.110	0.170	0.290

Liver	0.037	0.049	0.082	0.140	0.270
Lungs	0.090	0.120	0.210	0.330	0.560
Ovaries	0.042	0.057	0.090	0.140	0.270
Pancreas	0.054	0.069	0.110	0.180	0.320
Red marrow	0.086	0.120	0.160	0.220	0.350
Spleen	0.046	0.059	0.096	0.150	0.280
Testes	0.026	0.032	0.054	0.089	0.180
Thyroid	500.000	790.000	1200.000	2600.000	4700.000
Uterus	0.050	0.063	0.100	0.160	0.300
Other tissue	0.110	0.160	0.260	0.410	0.710
Effective dose equivalent (mSv/MBq)	**15.000**	**24.000**	**36.000**	**78.000**	**140.000**

Thyroid uptake 55%

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	0.049	0.058	0.110	0.170	0.340
*Bladder wall	0.290	0.360	0.540	0.850	1.600
Bone surfaces	0.110	0.170	0.220	0.320	0.480
Breast	0.091	0.089	0.190	0.310	0.560
GI tract					
*Stomach wall	0.460	0.590	0.860	1.500	3.000
*Small intest.	0.280	0.350	0.620	1.000	2.000
*ULI wall	0.058	0.067	0.110	0.180	0.320
*LLI wall	0.039	0.049	0.078	0.130	0.240
*Kidneys	0.051	0.068	0.100	0.170	0.290
Liver	0.043	0.058	0.097	0.170	0.330
Lungs	0.130	0.180	0.300	0.480	0.800
Ovaries	0.041	0.056	0.090	0.150	0.270
Pancreas	0.058	0.076	0.130	0.210	0.380
Red marrow	0.120	0.180	0.220	0.290	0.460
Spleen	0.051	0.068	0.110	0.170	0.330
Testes	0.026	0.031	0.052	0.087	0.170
Thyroid	790.000	1200.000	1900.000	4100.000	7400.000
Uterus	0.046	0.060	0.099	0.160	0.300
Other tissue	0.160	0.240	0.370	0.590	1.000
Effective dose equivalent (mSv/MBq)	**24.000**	**37.000**	**56.000**	**120.000**	**220.000**

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMEUTICALS

Capsules are provided with its application aparatus like pipette in a cardboard box, in the form of ready to use.