

## Part II

### Summary of Product Characteristics

#### 1 NAME OF THE MEDICINAL PRODUCT

Sodium Iodide (I131) Capsule D.

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium Iodide (I131), with activity from 3.7 MBq/capsule at activity reference date and time. No carrier added. Contains per 37 MBq (1 mCi) of activity approximately 8 nanograms of iodine.

Sodium Iodide (I 131), Capsule D is supplied as:

3.7 MBq/capsule at activity reference time

2.0 MBq/capsule 1 week after activity reference time

1.1 MBq/capsule 2 weeks after activity reference time

0.6 MBq/capsule 3 weeks after activity reference time

Six colours identify the different strengths of the capsules. Every week, one batch is produced with one specific colour; this colour thus identifies both batch and strength. After six weeks, the colour first used is applied again. The six colours are:

<i>Cap</i>	<i>Body</i>
White opaque	White opaque
Maroon opaque	White opaque
Green opaque	White opaque
Maroon opaque	Maroon opaque
Green opaque	Maroon opaque
Green opaque	Green opaque

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 8.04 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.

For a full list of excipients, see section 6.1

#### 3 PHARMACEUTICAL FORM

Capsule, hard.

#### 4 CLINICAL PARTICULARS

##### 4.1 Therapeutic Indications

- 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, sodium iodide is used to identify thyroid remnant and metastases (after ablation).
- Thyroid scanning for benign conditions with I-131 can be performed but only when radiopharmaceuticals with more favourable dosimetry, e.g. I-123 or Tc-99m, are not available.

## 4.2 Posology and method of administration

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

- For the thyroid uptake studies: 0.2-3.7 MBq
- For post thyroid ablation (for metastases and thyroid remnant): a maximum activity of 400 MBq
- For thyroid imaging: 7.4-11 MBq

Scans are usually performed at 4 hours, and then again at 18 - 24 hours (for scintigraphy also at 72 hours). The diagnostic activity to be administered to a child over 10 years and adolescents should be a fraction of the adult dose calculated from the body weight/surface area methods according to the following equations:

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

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

Correction factors given for guidance are proposed below.

22 kg = 0.50	24 kg = 0.53	26 kg = 0.56	28 kg = 0.58	30 kg = 0.62
32 kg = 0.65	34 kg = 0.68	36 kg = 0.71	38 kg = 0.73	40 kg = 0.76
42 kg = 0.78	44 kg = 0.80	46 kg = 0.82	48 kg = 0.85	50 kg = 0.88
52-54 kg = 0.90	56-58 kg = 0.92	60-62 kg = 0.96	64-66 kg = 0.98	68 kg = 0.99

(Paediatric Task Group, EANM)

The capsule is administered orally together with a drink. It should be swallowed whole. In patients with suspected gastrointestinal disease, great care should be taken when administering I-131 capsules. 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.

## 4.3 Contraindications

- Pregnancy.
- For diagnostic purpose at children under 10 years of age.
- Thyroid scanning except in the follow-up of malignant disease or when
- I-123 or Tc-99m are not available.
- Patients with dysphagia, oesophageal stricture, active gastritis, gastric erosions and peptic ulcer.
- Patients with suspected reduced gastrointestinal motility.

## 4.4 Special warnings and precautions for use

Radiopharmaceuticals may be received, used and administered only by authorized persons, in a designated clinical setting. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the local competent official organization.

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 a relatively high radiation dose to most patients (*see section 4.8, Undesirable Effects and 11, Dosimetry*). Suitable precautions should be taken concerning the activity eliminated by the patients in order to avoid any contaminations. I-131 for diagnostic studies is not to be used in children under 10 years of age and is not suitable for administration to children over 10 years old and adolescents unless exceptional circumstances prevail, due to a 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 Iodide (I-131).

#### **4.5 Interaction with other medicinal products and other forms of interaction**

Many pharmacological agents are known to interact with radioiodine. 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 antithyroid agents, carbimazole (or other imidazole derivatives such as propylthiouracil), salicylates, steroids, sodium nitroprusside, sodium sulfobromophthalein, perchlorate, miscellaneous agents (anticoagulants, anti-histamines, antiparasitics, penicillins, sulphonamides, tolbutamide thiopentone), are normally withheld for 1 week; phenylbutazone for 1 - 2 weeks; expectorants, vitamins for 2 weeks; natural or synthetic thyroid preparations (sodium thyroxine, sodium liothyronine, thyroid extract) for 2 - 3 weeks; amiodarone, benzodiazepines, lithium for 4 weeks; topical iodides for 1 - 9 months; and for intravenous contrast agents, oral cholecystographic agents, iodine containing contrast media for a period up to 1 year.

#### **4.6 Pregnancy and lactation**

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 agent is likely to be in the range of 11 - 511 mGy, and the foetal thyroid gland avidly concentrates iodine during the second and third trimesters). 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 ionizing radiation should be considered. Women receiving sodium iodide I-131 should be advised NOT to become pregnant within four months of administration.

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 indefinitely after sodium iodide I-131 administration.

#### **4.7 Effects on ability to drive and use machines**

No effects on the ability to drive or to operate machinery are to be expected after use of the drug.

#### **4.8 Undesirable effects**

For each patient, exposure to ionizing 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 reasonably achievable bearing in mind the need to obtain the intended diagnostic or therapeutic result.

Exposure to ionizing radiation is linked with cancer induction and a potential for development of hereditary effects. For diagnostic nuclear medicine investigations the current evidence suggests that these adverse effects will occur with low frequency because of the low radiation doses incurred.

For most diagnostic investigations using a nuclear medicine procedure the radiation dose delivered (EDE) is less than 20 mSv. These levels are usually exceeded for this compound.

Some cases of adverse reactions have been reported following the administration of sodium iodide I-131, including nausea, vomiting and unspecified possible allergic phenomena. Nausea and vomiting are more frequent after administration by oral route and the risks of contamination following the occurrence of vomiting have to be considered.

## 4.9 Overdose

This agent is intended for use by competent personnel within a hospital setting. As such the risk of overdose is theoretical. The risks relate to the inadvertent administration of excess radioactivity. High radiation exposure through overdose can be reduced by means of administration of thyroid blocking agents, such as potassium perchlorate, the use of emetics and promoting a diuresis with frequent voiding of urine.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Iodide in the amount used for diagnostic indications, is not known to have any pharmacological effect. More than 90% of the radiation effects result from beta radiation which has a mean range of 0.5 mm.

### 5.2 Pharmacokinetic properties

After oral administration sodium iodide I-131 is absorbed rapidly from the upper gastrointestinal tract (90% in 60 minutes). The pharmacokinetics follow 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 renally. 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 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. Urinary excretion is 37 - 75%, faecal excretion is about 10% with almost negligible excretion in sweat.

### 5.3 Preclinical safety data

Because of the small quantities of substance administered (< 0.1 mcg/day for diagnostic) compared with the normal food intake of iodine (40 - 500 mcg/day) no acute toxicity is to be expected or observed. There is 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

Anhydrous disodium phosphate  
Sodium thiosulphate  
Sodium carbonate decahydrate  
Sodium hydrogen carbonate  
Water for injections  
Gelatin  
Colouring materials (titanium dioxide, azorubin, quinoline yellow, indigo carmine).

### 6.2 Incompatibilities

None known.

### 6.3 Shelf Life

Sodium Iodide ( $^{131}\text{I}$ ) Capsule D expires 4 weeks after activity reference date and time.

## 6.4 Special precautions for storage

The preparation should be stored below 25°C (room temperature) either within its original lead shield or within shielding of appropriate thickness. Storage should be in accordance with national regulations for radioactive material.

## 6.5 Nature and contents of container

10 capsules in a 10 ml glass vial (Type 1 Ph. Eur) closed with a chlorobutyl rubber stopper and an aluminium seal cap.

## 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

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

## 7 MARKETING AUTHORISATION HOLDER

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

## 8 MARKETING AUTHORISATION NUMBER

PA 0690/006/001

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 29 June 2001

Date of last renewal: 29 June 2006

## 10 DATE OF REVISION OF THE TEXT

November 2008

## 11 DOSIMETRY

Tabulated radiation dosimetry as reported in ICRP publication n° 53 (1987) 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.

### IODIDE

**Thyroid blocked, uptake 0%**

<sup>131</sup>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 intest	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 05%:	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 intest	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+0	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 intest	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 intest	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. The administration of radio pharmaceuticals creates risks for other persons from external radiation or contamination from spills of urine, vomiting, etc. Adequate precautions must be taken to prevent contamination concerning the radioactivity eliminated by the patients. Radiation protection precautions in accordance with national regulations must therefore be taken. All residues must be considered as radioactive waste and must be disposed of in conformity with the relevant national regulations.