IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0240/018/003
Case No: 2041908

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

GE Healthcare Limited

Amersham Place, **Little Chalfont**, **Buckinghamshire**, **HP7 9NA**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

SODIUM IODIDE [131I] Diagnostic Capsules

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **08/11/2007** until **12/04/2012**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Sodium Iodide [^{131}I] Diagnostic Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium [^{131}I] Iodide Diagnostic Capsules are presented as a white capsule. Each capsule contains 3.7MBq (100μCi) at the first reference date. At subsequent reference dates, at weekly intervals, the nominal activity per capsule is shown in the table below

Reference date	Days after first reference	Activity –MBq (μCi)
1	0	3.7 (100)
2	7	2.03 (54.9)
3	14	1.11 (30.0)
4	21	0.592 (16.0)
5	28	0.333 (9.0)

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 8.04days. It decays by emission of gamma radiations of 365KeV (81.2%), 637 KeV (7.3%) and 284 KeV (6.1%) and beta radiations of maximal energy of 606 KeV to stable Xenon 131.

For excipients see 6.1.

3 PHARMACEUTICAL FORM

Capsules

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Diagnostic indications

1. 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 dose can be used to calculate the activity required for radioiodine therapy.

2. In the management of thyroid carcinoma, sodium iodide is used to identify thyroid remnants and metastases (after ablation).

3. Thyroid scanning for benign conditions with iodine-131 can be performed but only when radiopharmaceuticals with more favourable dosimetry, eg iodine-123 or technetium-99m are not available.

4.2 Posology and method of administration

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

1. For thyroid uptake studies: 0.2 - 3.7 MBq

2. For post-thyroid ablation (for metastases and thyroid remnants): a maximum activity of 400 MBq

3. 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 acitivity to be administered to a child over 10 years and adolescent should be a fraction of the adult dose calculated from the body weight/surface area methods according to the following equations:

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

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

Correction factors given for guidance are proposed below.

Fraction of adult dose	
22 Kg = 0.50	42 Kg = 0.78
24 Kg = 0.53	44 Kg = 0.80
26 Kg = 0.56	46 Kg = 0.82
28 Kg = 0.58	48 Kg = 0.85
30 Kg = 0.62	50 Kg = 0.88
32 Kg = 0.65	52-54 Kg = 0.90
34 Kg = 0.68	56-58 Kg = 0.92
36 Kg = 0.71	60-62 Kg = 0.96
38 Kg = 0.73	64-66 Kg = 0.98
40 Kg = 0.76	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 iodine-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 H_2 antagonists or proton pump inhibitors is advised.

4.3 Contraindications

- Pregnancy
- For diagnostic purposes in children under 10 years of age.
- Thyroid scanning except in the follow-up of malignant disease or when iodine-123 or technetium-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 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 a relatively high radiation dose to most patients (see sections 4.8 and 5.4).

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, leukemia or mutations) in man with patients treated for diagnostic purpose with sodium [^{131}I] iodide.

4.5 Interaction with other medicinal products and other forms of interaction

Many pharmacological agents are known to interact with radioiodide. These may do so by a variety of mechanisms which can affect the protein binding, the pharmacokinetics or influence the dynamic effects of labelled iodide. It is therefore necessary to take a full drug history and ascertain whether any medications are required to be withheld prior to the administration of sodium [^{131}I] iodide. For example, antithyroid agents, carbimazole (or other imidazole derivatives such as propylthiouracil), salicylates, steroids, sodium nitroprusside, sodium sulfobromophtalein, perchlorate, miscellaneous agents (anticoagulants, anti-histamines, antiparasitics, penicillins, sulphonamides, tolbutamide, thiopental), are normally withheld for 1 week; phenylbutazone for 1-2 weeks; expectorants, vitamins for 2 weeks; natural or synthetic thyroid preparations (levothyroxine sodium, 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 of up to 1 year.

4.6 Pregnancy and lactation

Sodium iodide [^{131}I] 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 11-511mGy, and the foetal thyroid gland avidly concentrates iodine during the second and third trimesters).

When it is necessary to administer a radioactive medicinal product to women of childbearing potential, information should always be sought about pregnancy. Any
woman who has missed a period should be assumed to be pregnant until proven otherwise. Alternative techniques which do not involve ionising radiation should be considered. In the case of differentiated thyroid carcinoma diagnosed in pregnancy therefore, radioiodine treatment should be postponed until after the pregnancy has ended. Women receiving sodium iodide [^{131}I] 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 of activity in breast milk. Breast feeding should be discontinued indefinitely after sodium iodide [^{131}I] 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 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.

Exposure to ionising 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 diagnostic 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 [^{131}I], including nausea, vomiting and unspecified possible allergic phenomena. Nausea and vomiting are more frequent after administration by the oral route especially after therapeutic doses 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 agent, such as potassium perchlorate, the use of emetics and promoting a diuresis with frequent voiding of urine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: V09F X03
Iodide, in the amount used for diagnostic indications, is not known to have any pharmacological effect. More than 90% of the radiation effects resultfrom beta radiation which has a mean range of 0.5mm.

5.2 Pharmacokinetic properties

After oral administration sodium iodide [^{131}I] is absorbed rapidly from the upper gastrointestinal tract (90% in 60 minutes). The pharmacokinetics follow that of unlabelled iodide. After entering the bloodstream it is distributed in the extra thyroidal compartment. From here it is predominantly taken up by the thyroid or excreted renally. Small amounts of sodium iodide [^{131}I] are taken up by salivary glands, gastric mucosa and would also be localised 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 by the thyroid gland is about 6 days. Thus, after administration of sodium iodide [^{131}I], 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 compared with the normal food intake of iodine (40-500 µg/day) no acute toxicity is expected or observed.

There are no data available on the toxicity of repeated doses of sodium iodide nor on its effects on reproduction in animals or its mutagenic or carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium thiosulphate
Disodium dihydrate
Sodium hydroxide
Gelatin capsule:
Titanium dioxide (E171)
Gelatin

6.2 Incompatibilities

There are no known incompatibilities.

6.3 Shelf Life

The shelf life for this product is 6 weeks from the first activity reference date stated on the label.

6.4 Special precautions for storage

The product should be stored below 25^{o}C. Do not freeze

Storage should be in accordance with national regulations for radioactive material.

6.5 Nature and contents of container

The product is stored within a polystyrene container with a push-in cap made from polyurethane. The capsules are held in place by a foam wadding. This container is stored within a lead shield.

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

Adequate precautions must be taken to prevent contamination concerning the radioactivity eliminated by the patients.

All residues must be considered as radioactive waste and must be disposed of in conformity with the relevant national regulations.

7 MARKETING AUTHORISATION HOLDER

GE Healthcare Limited
Amersham Place
Little Chalfont
Buckinghamshire
HP7 9NA
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 240/18/3

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation 13th April 2007.

10 DATE OF REVISION OF THE TEXT

November 2007