THERACAP$^{131}$ 37 MBq-5.55 GBq CAPSULES, HARD
PL 00221/0102

UKPAR

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LAY SUMMARY

The Medicines Healthcare products Regulatory Agency granted GE Healthcare Limited a Marketing Authorisation (licence) for the medicinal product THERACAP\(^{131}\) 37 MBq-5.55 GBq capsules, hard (PL 00221/0102).

This is a prescription-only medicine (POM). It is a “radiopharmaceutical” medicine. It contains an active ingredient called sodium \(^{[131]}\)I iodide and is used to treat tumours in the thyroid (a gland found in your neck), including if a tumour has spread to other parts of your body. It is used to treat an overactive thyroid (Grave’s disease) as well as treating goitres (swelling due to an enlarged thyroid).

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking product THERACAP\(^{131}\) 37 MBq-5.55 GBq capsules, hard, (PL 00221/0102) outweigh the risks; hence a Marketing Authorisation has been granted.
SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a marketing authorisation for the medicinal product THERACAP$^{131}$ I 37 MBq-5.55 GBq capsules, hard, PL 00221/0102) on 1st February 2010. This product is a prescription-only medicine (POM).

This application was made under Article 10a of Directive 2001/83/EC, so called well-established use, and as such this application relies solely on bibliographic data with respect to the clinical aspects.

This product contains the active ingredient sodium $[^{131}\text{I}]$ iodide and is used for therapeutic purposes. Sodium $[^{131}\text{I}]$ iodide is used to treat Grave’s disease, toxic multinodular goitre or autonomous nodules, papillary and follicular thyroid carcinoma including metastatic disease. Sodium $[^{131}\text{I}]$ iodide therapy is often combined with surgical intervention and with antithyroid medications.
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

INN: Sodium [\(^{131}\)I] iodide

CAS Number: 7790-26-3

Molecular formula: NAI

Relative molecular weight: 154

Physical form: iodide-131, as a solution of sodium iodide in NaOH, with or without 0.02-0.04M Na\(_2\)SO\(_4\), pH 9.0-13.0. No carrier needed.

Appearance: white odourless, deliquescent crystals or granules

Melting point: 651°C

Solubility: one gram is soluble in 0.5ml water, about 2ml alcohol or 1 ml glycerol. Soluble in acetone.

Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents, and these are supported by relevant certificates of analysis. No materials of animal or human origin are used in the production of the active substance.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Certificates of analysis have been provided for any working standards used. Batch analyses data are provided that comply with the proposed specification.

Suitable specifications for all materials used in the active substance packaging have been provided.

Appropriate stability data have been generated, from studies carried out in accordance with ICH conditions. A suitable shelf-life has been set, based on the stability data provided.

DRUG PRODUCT

Other ingredients
Other ingredients consist of pharmaceutical excipients, namely sodium thiosulphate pentahydrate, disodium phosphate dihydrate, sodium hydroxide and water for injections. All the ingredients within the body of the capsule comply with relevant Ph Eur. Appropriate justification for the inclusion of each excipient has been provided.

The capsule shell contains: gelatin, titanium dioxide (E171), yellow iron oxide (E172), sodium laurilsulphate, acetic acid and printing ink. The ingredients within the capsule shell and printing ink comply with relevant Ph Eur monographs. Satisfactory certificates of analysis have been provided for all excipients. With the exception of gelatin, none of the
excipients used contain material of animal or human origin. A satisfactory TSE certificate of suitability has been provided for the supplier of gelatine.

**Pharmaceutical Development**
Suitable pharmaceutical development data have been provided for this application.

**Manufacture**
A description and flow-chart of the manufacturing method has been provided. In-process controls are satisfactory based on process validation data and controls on the finished product. Process validation has been carried out on batches of the product. The results appear satisfactory.

**Finished product specification**
The finished product specification is satisfactory. Test methods have been described and adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

**Container Closure System**
The finished product is supplied in a polycarbonate cup with charcoal disc to absorb iodine-131. This cup is enclosed within a lead shield. Each pack contains a single capsule. Not all pack sizes may be marketed. Specifications and Certificates of Analysis for the primary packaging material have been provided. These are satisfactory. All primary packaging is controlled to European Pharmacopoeia standards and complies with guidelines concerning materials in contact with food.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 14 days from the first activity reference date stated on the label, which is satisfactory. Storage conditions are “Store below 25°C. Do not freeze.” and “Store in original container or in equivalent shielding.”

**Summary of Product Characteristics**
This is acceptable.

**Patient Information Leaflet**
A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups (“user testing”), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

**Label**
This is acceptable.

**Conclusion**
It is recommended that a Marketing Authorisation is granted for this application.
PRECLINICAL ASSESSMENT

NON-CLINICAL ASPECTS
The pharmacological, pharmacokinetic and toxicological properties of sodium $[^{131}\text{I}]$ iodide are well-known. As sodium $[^{131}\text{I}]$ iodide is a well-known active substance, no further studies are required and the applicant has provided none. An overview based on literature is thus appropriate.

NON-CLINICAL OVERVIEW
The non-clinical expert report has been written by an appropriately qualified person and is a suitable summary of the non-clinical aspects of the dossier.

EXCIPIENTS
The excipients are commonly used comply with their respective European Pharmacopoeiae.

ENVIRONMENTAL RISK ASSESSMENT
There is no environmental risk assessment statement included in the application. This is acceptable for a product which well-established.

SUMMARY OF PRODUCT CHARACTERISTICS
This is acceptable.

CONCLUSIONS
The applicant has provided an adequate review of the available non-clinical data. There were no new non-clinical data identified in the literature review that would change the risk-benefit analysis for sodium iodide.
CLINICAL ASSESSMENT

1 BACKGROUND
The application is submitted under Article 10a of the EC Directive 2001/83 (as amended), a so-called well-established use, or bibliographic, application.

Sodium $^{[131I]}$ Iodide has been used for a number of years to treat tumours in the thyroid, oversized thyroid (goiters) as well in the detection and diagnosis of tumours within the thyroid.

Sodium $^{[131I]}$ Iodide in the amount used for diagnostic and therapeutic 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.

After oral administration sodium $^{[131I]}$ iodide 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 I-131 iodide 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 up by the thyroid gland is about 6 days. Thus after administration of I-131 sodium iodide 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.

2 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.

Sodium $^{[131I]}$ iodide therapy is often combined with surgical intervention and with antithyroid medications.

The proposed indications are consistent with those licensed indications approved for other Sodium Iodide ($^{131I}$) products and are therefore satisfactory.

3 DOSE & DOSE SCHEDULE

The proposed posology is consistent with the text of section 4.2 of the SPC approved for other Sodium Iodide ($^{131I}$) products and are therefore satisfactory.

4 CLINICAL PHARMACOLOGY

The clinical pharmacology of Sodium $^{[131I]}$ Iodide has been documented in published papers. No new clinical pharmacology data are required and none are provided by the applicant. This is satisfactory.
5  **EFFICACY**  
The efficacy of Sodium $[^{131}I]$ Iodide has been documented in published papers. No new data are submitted and none are required for this type of application.

6  **SAFETY**  
The safety of Sodium $[^{131}I]$ Iodide has been documented in published papers. No new data are submitted and none are required for this type of application.

7  **EXPERT REPORTS**  
An adequate clinical overview written by an appropriately qualified expert has been provided.

8  **SUMMARY OF PRODUCT CHARACTERISTICS (SMPC), PATIENT INFORMATION LEAFLET AND LABELLING**  
The SmPC, PIL and labelling are medically satisfactory.

9  **APPLICATION FORM (MAA)**  
The MAA is medically satisfactory.

10  **RISK MANAGEMENT PLAN (RMP)**  
The marketing authorisation holder has provided adequate justification for not submitting a RMP. This is a bibliographic application for a well-known active substance with a well established safety profile. No specific risk minimisation activities are required. Routine pharmacovigilance as proposed by the applicant is considered to be sufficient.

11. **PHARMACOVIGILANCE SYSTEM**  
The pharmacovigilance system as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

12  **MEDICAL CONCLUSION**  
A marketing authorisation may be granted for this preparation.

13.  **RECOMMENDATIONS**  
The efficacy and safety of the product is satisfactory for the grant of a product licence.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of, THERACAP\textsuperscript{131} 37 MBq-5.55 GBq capsules, hard are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type.

EFFICACY
Sodium \([^{131}\text{I}]\) iodide is a well known therapeutic and diagnostic "tracer" and has been used for many years to help treat or identify certain illnesses such as tumours in the thyroid gland, and see how a tumour is responding to treatment or if the tumour has spread to other parts of the body.

Medicinal, diagnostic and therapeutic products containing sodium \([^{131}\text{I}]\) iodide have been available in the UK for much more than ten years. Their use is well established with recognised efficacy and acceptable safety.

The published literature supports the efficacy of sodium \([^{131}\text{I}]\) iodide and identifies no new safety issues or concerns. No new or unexpected safety concerns arise from this application.

PRODUCT LITERATURE
The approved SmPC, PIL and labelling are satisfactory.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with sodium iodide is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.
# STEPS TAKEN FOR ASSESSMENT

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 30\textsuperscript{th} April 1992.</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 27\textsuperscript{th} November 2006.</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the applications the MHRA requested further information relating to the quality dossiers on 19\textsuperscript{th} December 2006 and 27\textsuperscript{th} June 2007.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 19\textsuperscript{th} April 2007 and 10\textsuperscript{th} September 2009 for the quality sections.</td>
</tr>
<tr>
<td>5</td>
<td>The applications were determined on 1\textsuperscript{st} February 2010.</td>
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</table>
THERACAP$^{131}$ 37 MBq-5.55 GBq CAPSULES, HARD
PL 00221/0102

**STEPS TAKEN AFTER AUTHORISATION - SUMMARY**

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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</table>
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
THERACAP\(^{131}\) 37 MBq-5.55 GBq capsules, hard

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
THERACAP is presented as a single yellow capsule containing sodium \(^{[131]I}\)iodide in the following dosage range; 37-740 MBq in 37 MBq steps and 0.925-5.55 GBq in 185 MBq steps at the activity reference date. Each capsule contains a maximum of 20 µg of sodium iodide. The specific activity of the sodium \(^{[131]I}\)iodide is not less than 222 GBq/mg.

Iodine-131 is produced by fission of uranium-235 or by neutron bombardment of stable tellurium in a nuclear reactor. Iodine-131 has a half life of 8.02 days. It decays by emission of gamma radiations of 365 keV (81.7%), 637 keV (7.2%) and 284 keV (6.1%) and beta radiations of maximal energy of 606 keV to stable Xenon-131.

This medicinal product contains: 140 mg of sodium per capsule

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Capsule, hard.

Yellow gelatin capsule.

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.

Sodium \(^{[131]I}\)iodide therapy is often combined with surgical intervention and with antithyroid medications.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
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 is usually in the range of 200-800 MBq but repeated treatment may be necessary. The dose required depends on the diagnosis, the size of the gland, thyroid uptake and iodine clearance. Patients should be rendered euthyroid medically whenever possible before giving radioiodine treatment for hyperthyroidism.

• 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.

The activity to be administered in children and adolescents should be a fraction of the adult dose calculated from the body weight/surface area methods according to the following equations:

\[
\text{Paediatric dose (MBq)} = \frac{\text{Adult dose (MBq)} \times \text{child weight (kg)}}{70}
\]
Correction factors given for guidance are proposed below.

<table>
<thead>
<tr>
<th>Fraction of adult dose</th>
<th>3 kg</th>
<th>4 kg</th>
<th>6 kg</th>
<th>8 kg</th>
<th>10 kg</th>
<th>12 kg</th>
<th>14 kg</th>
<th>16 kg</th>
<th>18 kg</th>
<th>20 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>22 kg</td>
<td>0.10</td>
<td>0.14</td>
<td>0.19</td>
<td>0.23</td>
<td>0.27</td>
<td>0.32</td>
<td>0.36</td>
<td>0.40</td>
<td>0.44</td>
<td>0.46</td>
</tr>
<tr>
<td>24 kg</td>
<td>0.50</td>
<td>0.53</td>
<td>0.56</td>
<td>0.58</td>
<td>0.62</td>
<td>0.65</td>
<td>0.68</td>
<td>0.71</td>
<td>0.73</td>
<td>0.76</td>
</tr>
<tr>
<td>26 kg</td>
<td>0.53</td>
<td>0.56</td>
<td>0.58</td>
<td>0.62</td>
<td>0.65</td>
<td>0.68</td>
<td>0.71</td>
<td>0.73</td>
<td>0.76</td>
<td>0.76</td>
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<tr>
<td>28 kg</td>
<td>0.50</td>
<td>0.53</td>
<td>0.56</td>
<td>0.58</td>
<td>0.62</td>
<td>0.65</td>
<td>0.68</td>
<td>0.71</td>
<td>0.73</td>
<td>0.76</td>
</tr>
<tr>
<td>42 kg</td>
<td>0.78</td>
<td>0.80</td>
<td>0.82</td>
<td>0.85</td>
<td>0.88</td>
<td>0.90</td>
<td>0.92</td>
<td>0.96</td>
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<td>44 kg</td>
<td>0.78</td>
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<td>0.85</td>
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<td>0.90</td>
<td>0.92</td>
<td>0.96</td>
<td>0.98</td>
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<tr>
<td>46 kg</td>
<td>0.80</td>
<td>0.82</td>
<td>0.85</td>
<td>0.88</td>
<td>0.90</td>
<td>0.92</td>
<td>0.96</td>
<td>0.98</td>
<td>0.99</td>
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<tr>
<td>48 kg</td>
<td>0.82</td>
<td>0.85</td>
<td>0.88</td>
<td>0.90</td>
<td>0.92</td>
<td>0.96</td>
<td>0.98</td>
<td>0.99</td>
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<tr>
<td>50 kg</td>
<td>0.85</td>
<td>0.88</td>
<td>0.90</td>
<td>0.92</td>
<td>0.96</td>
<td>0.98</td>
<td>0.99</td>
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<tr>
<td>52-54 kg</td>
<td>0.88</td>
<td>0.90</td>
<td>0.92</td>
<td>0.96</td>
<td>0.98</td>
<td>0.99</td>
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<tr>
<td>56-58 kg</td>
<td>0.90</td>
<td>0.92</td>
<td>0.96</td>
<td>0.98</td>
<td>0.99</td>
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<tr>
<td>60-62 kg</td>
<td>0.92</td>
<td>0.96</td>
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<td>0.99</td>
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<tr>
<td>64-66 kg</td>
<td>0.96</td>
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<tr>
<td>68 kg</td>
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</table>

(Paediatric Task Group, European Association of Nuclear Medicines (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 sodium $^{[131]}$iodide 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.

After high doses used e.g. for the treatment of thyroid carcinoma, patients should be encouraged to increase oral fluids to have frequent bladder emptying to reduce bladder radiation.

4.3 CONTRAINDICATIONS

- Hypersensitivity to the active substance or to any of the excipients
- 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 is 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

The possibility of hypersensitivity including anaphylactic/anaphylactoid reactions should always be considered. Advanced life support facilities should be readily available.

This medicinal product contains 140 mg of sodium in each capsule. To be taken into consideration by patients on a controlled sodium diet.

The administration of high dose radioiodine may result in significant environmental hazard. Suitable precautions should be taken concerning the activity eliminated by the patients in order to avoid any contamination.
The therapeutic administration of sodium $[^{131}\text{I}]$iodide in patients with significant renal impairment requires special attention with regards to administered activity. Sperm banking should be considered for young men who have extensive disease and therefore may need high radioiodine therapeutic doses.

Contraception for 6 months (for patients with benign thyroid conditions) or 12 months (for patients with thyroid cancer) is recommended for both sexes after therapeutic administration of sodium $[^{131}\text{I}]$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.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

A full drug history should be taken and relevant medication including the ones mentioned below should be withheld prior to the administration of sodium $[^{131}\text{I}]$iodide.

<table>
<thead>
<tr>
<th>Active substances</th>
<th>Withdrawal period prior to administration of sodium $[^{131}\text{I}]$iodine.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithyroid agents (e.g. carbimazole, methimazole, propyluracil, perchlorate)</td>
<td>2 – 5 days before until several days after administration.</td>
</tr>
<tr>
<td>Salicylates, steroids, sodium nitroprusside, sodium sulfobromophthalein, anticoagulants, antihistamines, antiparasitics, penicillins, sulphonamides, tolbutamide, thiopental</td>
<td>1 week.</td>
</tr>
<tr>
<td>Phenylbutazone</td>
<td>1-2 weeks.</td>
</tr>
<tr>
<td>Containing iodine expectorants and vitamins</td>
<td>approx. 2 weeks.</td>
</tr>
<tr>
<td>Thyroid hormone preparations</td>
<td>2-6 weeks.</td>
</tr>
<tr>
<td>Amiodarone*, benzodiazepines, lithium</td>
<td>approx. 4 weeks.</td>
</tr>
<tr>
<td>Containing iodine preparations for topical use</td>
<td>1–9 months.</td>
</tr>
<tr>
<td>Containing iodine contrast media</td>
<td>up to 1 year.</td>
</tr>
</tbody>
</table>

* Due to the long half-life of amiodarone, iodine uptake in the thyroid tissue can be decreased for several months.

4.6 PREGNANCY AND LACTATION

Sodium $[^{131}\text{I}]$ iodide 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 11-511 mGy, and the foetal thyroid gland avidly concentrates iodine during the second and third trimesters. When it is necessary to administer radioactive products 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, radiiodine treatment should be postponed until after the pregnancy has ended. Women receiving sodium $[^{131}\text{I}]$ iodide should be advised not to become pregnant within four months of administration.

Breast feeding should be discontinued after sodium $[^{131}\text{I}]$ iodide administration. For radioprotection reasons following therapeutic doses, it is recommended to avoid close contact between mother and child for at least one week.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effect on the ability to drive or use machines have been performed.

4.8 UNDESIRABLE EFFECTS

The following undesirable effects are recognised for sodium $[^{131}\text{I}]$iodide:
4.9 OVERDOSE
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
Pharmacotherapeutic group: therapeu tic radiopharmaceuticals, sodium $[^{131}I]$iodine, ATC Code: V10XA01

Iodide, in the amount used for therapeutic 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 $[^{131}I]$iodide is absorbed rapidly from the upper gastrointestinal tract (90% in 60 minutes). The pharmacokinetics follow that of unlabelled iodide. From the extra thyroidal compartment it is predominantly taken up by the thyroid or excreted renally. Small amounts of sodium $[^{131}I]$iodide are taken up by salivary glands, gastric mucosa and would also be localised in breast milk, the placenta and choroids 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 $[^{131}I]$iodide, 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
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, pentahydrate
Disodium phosphate dihydrate
Sodium hydroxide
Water for injections

Capsule:
Gelatin
Yellow iron oxide (E172)
Titanium dioxide (E171)
Sodium laurilsulfate
Acetic acid
Printing ink

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

6.3 SHELF LIFE
The shelf life for this product is 14 days from the activity reference date stated on the label.

6.4 SPECIAL PRECAUTIONS FOR STORAGE
Store below 25°C. Do not freeze.

Store in the original lead container or in equivalent shielding

6.5 NATURE AND CONTENTS OF CONTAINER
Each capsule is contained within a polycarbonate cup with a charcoal disc to absorb iodine-131. This cup is enclosed within a lead shield.

Pack sizes: 37-740 MBq in 37 MBq steps and 0.925-5.55 GBq in 185 MBq steps. Each pack contains a single capsule.

Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
Normal safety precautions for handling radioactive materials should be observed. After use, all materials associated with the preparation and administration of radiopharmaceuticals, including any unused product and its container, should be decontaminated or treated as radioactive waste and disposed of in accordance with the conditions specified by the local competent authority. Contaminated material must be disposed of as radioactive waste via an authorised route.

7 MARKETING AUTHORISATION HOLDER
GE Healthcare Limited
Amersham Place
Little Chalfont
Buckinghamshire HP7 9NA
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 00221/0102

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
01/02/2010

10 DATE OF REVISION OF THE TEXT
01/02/2010
11 DOSIMETRY (IF APPLICABLE)

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 wall increase by about 30% for iodine-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 effective dose equivalent (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 tables below show the dosimetry as calculated according to the Publication 53 of the ICRP (International Commission on Radiological Protection, Radiation Dose to Patients from Radiopharmaceuticals, Pergamon Press 1987).

IODIDE
Thyroid blocked, uptake 0%

<table>
<thead>
<tr>
<th>Absorbed dose per unit activity administered (mGy/MBq)</th>
<th>Adult</th>
<th>15 Year</th>
<th>10 Year</th>
<th>5 Year</th>
<th>1 Year</th>
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</thead>
<tbody>
<tr>
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<td>Bone surfaces</td>
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<td>3.3E-02</td>
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<td>GI tract</td>
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<td>Kidneys</td>
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<td>3.1E-01</td>
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<td>Ovaries</td>
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<td>2.0E-01</td>
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<td>1.1E-01</td>
<td>1.7E-01</td>
<td>3.0E-01</td>
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<td>Effective Dose Equivalent (mSv/MBq)</td>
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<td>4.0E-01</td>
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</tbody>
</table>
Bladder wall contributes to 50.8% of the effective dose equivalent. The effective dose equivalent to an adult administered 5.55 GBq with 0% thyroid uptake is 399.6 mSv.

Incomplete blockage:
Effective dose equivalent (mSv/MBq) with little uptake in the thyroid.

<table>
<thead>
<tr>
<th>Uptake</th>
<th>Absorbed Dose per Unit Activity Administered (mGy/MBq)</th>
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</thead>
<tbody>
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<td>0.5%</td>
<td>3.0 E-01 4.5 E-01 6.9 E-01 1.5 E+00 2.8 E+00</td>
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<td>2.0%</td>
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Thyroid uptake 15%

<table>
<thead>
<tr>
<th>Organ</th>
<th>Absorbed dose per unit activity administered (mGy/MBq)</th>
<th>Adult</th>
<th>15 Year</th>
<th>10 Year</th>
<th>5 Year</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenals</td>
<td>3.6E-02</td>
<td>4.3E-02</td>
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<td>Bladder wall</td>
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<td>9.8E-01</td>
<td>1.5E+00</td>
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<tr>
<td>Bone surfaces</td>
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<td>G1 tract</td>
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<tr>
<td>Small intest</td>
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<td>1.0E+00</td>
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<td>1.3E-01</td>
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<tr>
<td>Kidneys</td>
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<td>1.1E-01</td>
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<td>1.0E-01</td>
<td>1.5E-01</td>
<td>2.7E-01</td>
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</tr>
<tr>
<td>Red marrow</td>
<td>5.4E-02</td>
<td>7.4E-02</td>
<td>9.9E-02</td>
<td>1.4E-01</td>
<td>2.4E-01</td>
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</tr>
<tr>
<td>Spleen</td>
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<td>5.1E-02</td>
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<td>9.4E-02</td>
<td>1.8E-01</td>
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</tr>
<tr>
<td>Thyroid</td>
<td>2.1E+02</td>
<td>3.4E+02</td>
<td>5.1E+02</td>
<td>1.1E+03</td>
<td>2.0E+03</td>
<td></td>
</tr>
<tr>
<td>Uterus</td>
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<td>3.1E-01</td>
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<tr>
<td>Other tissue</td>
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<td>1.4E-01</td>
<td>2.2E-01</td>
<td>4.0E-01</td>
<td></td>
</tr>
</tbody>
</table>

Effective Dose Equivalent (mSv/MBq) 6.6E+00 1.0E+01 1.5E+01 3.4E+01 6.2E+01

The effective dose equivalent (EDE) in an adult administered 5.55 GBq with 15% thyroid uptake is 36,630 mSv.

Thyroid uptake 35%

<table>
<thead>
<tr>
<th>Organ</th>
<th>Absorbed dose per unit activity administered (mGy/MBq)</th>
<th>Adult</th>
<th>15 Year</th>
<th>10 Year</th>
<th>5 Year</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenals</td>
<td>4.2E-02</td>
<td>5.0E-02</td>
<td>8.7E-02</td>
<td>1.4E-01</td>
<td>2.8E-01</td>
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</tr>
<tr>
<td>Bladder wall</td>
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<td>7.6E-01</td>
<td>1.2E+00</td>
<td>2.3E+00</td>
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<tr>
<td>Bone surfaces</td>
<td>7.6E-02</td>
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<td>1.6E-01</td>
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<tr>
<td>Breast</td>
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<td>1.3E-01</td>
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<td>4.0E-01</td>
<td></td>
</tr>
</tbody>
</table>
The effective dose equivalent (EDE) in an adult administered 5.55 GBq with 35% thyroid uptake is 83,250 mSv

<table>
<thead>
<tr>
<th>GI tract</th>
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</thead>
<tbody>
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<td>2.0E+00</td>
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<tr>
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<td>3.3E-01</td>
<td>5.6E-01</td>
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<tr>
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<td>4.7E+03</td>
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<td>1.6E-01</td>
<td>3.0E-01</td>
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<tr>
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<td>1.6E-01</td>
<td>2.6E-01</td>
<td>4.1E-01</td>
<td>7.1E-01</td>
</tr>
</tbody>
</table>

| Effective Dose Equivalent (mSv/MBq) | 1.5E+01 | 2.4E+01 | 3.6E+01 | 7.8E+01 | 1.4E+02 |
Thyroid uptake 55%

<table>
<thead>
<tr>
<th>Organ</th>
<th>Absorbed dose per unit activity administered (mGy/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenals</td>
<td>4.9E-02, 5.8E-02, 1.1E-01, 1.7E-01, 3.4E-01</td>
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</tr>
<tr>
<td>Bone surfaces</td>
<td>1.1E-01, 1.7E-01, 2.2E-01, 3.2E-01, 4.8E-01</td>
</tr>
<tr>
<td>Breast</td>
<td>9.1E-02, 8.9E-02, 1.9E-01, 3.1E-01, 5.6E-01</td>
</tr>
<tr>
<td>GI tract</td>
<td></td>
</tr>
<tr>
<td>Stomach wall</td>
<td>4.6E-01, 5.9E-01, 8.6E-01, 1.5E-00, 3.0E+00</td>
</tr>
<tr>
<td>Small intest</td>
<td>2.8E-01, 3.5E-01, 6.2E-01, 1.0E+00, 2.0E+00</td>
</tr>
<tr>
<td>ULI wall</td>
<td>5.8E-02, 6.7E-02, 1.1E-01, 1.8E-01, 3.2E-01</td>
</tr>
<tr>
<td>LLI wall</td>
<td>3.9E-02, 4.9E-02, 7.8E-02, 1.3E-01, 2.4E-01</td>
</tr>
<tr>
<td>Kidneys</td>
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<td>Uterus</td>
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</table>

**Effective Dose Equivalent (mSv/MBq)**

- **2.4E+01**
- **3.7E+01**
- **5.6E+01**
- **1.2E+02**
- **2.2E+02**

For this product, the effective dose equivalent (EDE) to an adult with 55% thyroid uptake resulting from the administration of a 5.55GBq capsule is 133,200mSv.

12 **INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)**

This radiopharmaceutical may be received, used and administered only by authorised persons, in designated clinical setting. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the local competent official organisation. (see section 6.6).

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

1. What Theracap is and what it is used for
   - Theracap is a "radio-pharmaceutical" medicine.
   - It contains an active ingredient called "sodium iodeide".
   - It is used to treat tumours in the thyroid (a gland found in your neck), including if a tumour has spread to other parts of your body.
   - It can be used to treat an overactive thyroid (Graves' disease).
   - Some other people are given this medicine to treat goitre (swelling due to an enlarged thyroid). Your doctor will tell you anything else you need to know about how Theracap works.

2. Before you are given Theracap
   You should not be given Theracap:
   - If you are allergic (hypersensitive) to the active ingredient or any other ingredient listed in Section 8.
   - If you are pregnant or think you might be pregnant.
   - If you are unable to swallow normally.
   - If you have digestive or stomach problems.
   - If it is possible that you have slow movement of food along your gut (reduced gastrointestinal motility). Do not have Theracap if any of the above apply to you. If you are not sure talk to your doctor or nurse.

Read all of this leaflet carefully before you are given Theracap.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

In this leaflet:
1. What Theracap is and what it is used for
2. Before you are given Theracap
3. How Theracap is given
4. Possible side effects
5. How to store Theracap
6. Further information
Take special care with Theracap
Check with your doctor or nurse before having Theracap:
• If the person who will be given this medicine is a child or adolescent.
• If you have missed your last period.
• If you are on a low sodium diet.

Taking other medicines
Please tell your doctor or nurse if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This includes herbal medicines. This is because some medicines can affect the way Theracap works.

Before you are given Theracap tell your doctor or nurse if you are taking any of the types of medicine below.
• Medicines used for an overactive or underactive thyroid such as carbimazole, propylthiouracil, levothyroxine sodium, sodium iodothyronine or thyroid extract.
• Salicylates such as aspirin.
• Steroids such as prednisolone or methylprednisolone.
• Medicines used to thin the blood such as warfarin or heparin.
• Antihistamines such as chlorpheniramine or cetirizine.
• Medicines used for parasitic infections such as thiabendazole, rifampicin or amphotericin B.
• Penicillins.
• Medicines called ‘sulphonamides’ such as sulphadiazine used for rheumatoid arthritis and some bowel problems, sumitriptan (used for migraine or probenecid (used for gout).
• Medicines called ‘benzodiazepines’, which are sedatives or are used to help you sleep, such as temazepam, nitrazepam or diazepam.
• ‘Expectorants’, used in cough and cold remedies, such as guaifenesin.
• Vitamins.
• Lithium, used for mental health problems.
• Tolbutamide, used for diabetes.
• Thiopental, an anaesthetic used in hospital.
• Phenytoin, used for pain and arthritis.
• Amiodarone, used for an uneven heart beat.
• Liquids or ointments that contain iodine.
• Sodium nitroprusside, used in hospital to lower blood pressure.
• Sodium sulfobromophthalein, used in hospital to check how well your liver is working.
• Perchlorate, a medicine given before certain types of scan.
• Medicines used in hospital for x-rays or scans of the gallbladder.
• Medicines that contain iodine used in hospital for x-rays or scans.

If you are not sure if any of the above apply to you, talk to your doctor or nurse before having Theracap.
Having Theracap with food and drink

- Your doctor may recommend a low iodine diet.
- After taking Theracap you may be asked to drink more liquids.
- You may be asked to eat sweets or have drinks that contain citric acid, such as orange juice, to help produce saliva and stop swelling of your salivary glands.

Pregnancy and breast-feeding

You should not be given Theracap if you are pregnant or think that you may be pregnant. This is because it may affect the baby.

You will be told by your doctor not to become pregnant for at least 6 months after being given Theracap.

Do not breast-feed if you are given Theracap. This is because small amounts of radioactivity will pass into the mother's milk. If you are breast-feeding, your doctor may wait until you have finished breast-feeding before giving you Theracap. If it is not possible to wait your doctor will ask you to:

- stop breast-feeding, and
- use formula food for your child, and
- express (remove) breast milk and throw away the milk.

Your doctor will let you know when you can start breastfeeding again.

Driving and using machines

Ask your doctor if you can drive or use machines after you have been given Theracap.

Important information about Theracap

When Theracap is used you are exposed to radioactivity.

- Your doctor will always consider the possible risks and benefits before you are given the medicine.
- Your doctor will have to ask you if you have any questions.

3. How Theracap is given

Theracap will be given to you by a specially trained and qualified person.

- Theracap will always be used in a hospital or clinic.

- They will tell you anything you need to know for its safe use.
- You will be asked to take Theracap with some liquid. It should be swallowed whole.
- If it is possible that you have problems with taking and digesting food (gastrointestinal disease) you may be asked to take some other medicines, to help the capsule get to your stomach.

Your doctor will decide the dose that is best for you.

The usual dose is:

- The number of doses and length of treatment will depend on your condition.
- Ask your doctor if you have any questions.
Possible side effects

Like all medicines, Theracap can cause side effects, although not everybody gets them. Side effects from Theracap may occur soon after receiving the product (early side effects) or some time after receiving the product (late side effects).

Early side effects (within hours, days or weeks):

Allergic reactions
If you have an allergic reaction when you are in hospital or a clinic, tell the doctor or nurse straightaway. The signs may include:
- skin rash or itching or flushing
- swelling of the face
- difficulty in breathing.

If any of these side effects happen after you leave the hospital or clinic, go straight to the casualty department of your nearest hospital.

Other early side effects include:
- feeling sick (nausea)
- being sick (vomiting)
- diarrhoea
- pain around your stomach area (abdominal pain)
- swelling (inflammation) of your thyroid
- swelling of your windpipe (trachea), which may cause difficulty breathing
- swelling of your salivary glands, which may cause pain, some loss of taste and a dry mouth.

Occasionally this can be severe, and cause a permanent loss of taste and dry mouth. This has caused some patients to lose teeth.

- pain, discomfort and swelling in the thyroid area (your neck)
- if your thyroid is overactive (hyperthyroidism) your symptoms may get worse for a short time after being given Theracap.
  Symptoms could include increased appetite, palpitations, feeling restless (anxiety), weight loss or swelling.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

Early side effects that your doctor may be able to prevent or treat
Your doctor may give you other medicines to help stop side effects such as:
- feeling sick (nausea)
- being sick (vomiting)
- diarrhoea
- pain around your stomach area (abdominal pain)
- swelling of your salivary glands.
Late side effects (within weeks, months or years):

- Your thyroid may become underactive (hypothyroidism). Signs may include feeling tired or a loss of energy (lethargy), muscle weakness, cramps, feeling the cold, a slow heart rate, dry flaky skin, hair loss, a deep and husky voice or weight gain.

- Your parathyroid may become underactive (hypoparathyroidism). Signs may include ‘pins and needles’, weakness, muscle spasms, muscle twitches or cramps all over, tingling, vibrating, burning, numbness, trouble concentrating, feeling dizzy or irritable, sensitivity to noise, muscles that stop working properly (muscle paralysis) or fits (seizures).

Other late side effects include:

- High doses of Theracap or repeat treatments within 6 months of your first treatment may lower the ability of your bone marrow to make blood cells. Signs of this may include bruising more easily and bleeding for longer. In many cases people recover fully. Very rarely, in severe cases, this may cause death.

- Patients who have had Theracap may be more at risk of developing stomach cancer and if high doses have been used, blood cancer (leukaemia). There may also be a small increase in your risk of developing bladder and breast cancers.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

Late side effects that your doctor may be able to prevent or treat:

The following can be treated with medicines from your doctor:

- Underactive thyroid (hypothyroidism)
- Underactive parathyroid (hypoparathyroidism).

5. How to store Theracap

Theracap is kept out of the reach and sight of children.

The product label includes the correct storage conditions and the expiry date for the batch. Hospital staff will ensure that the product is stored and disposed of correctly and not used after the expiry date stated on the label.

6. Further information

What Theracap contains:

The active ingredient is sodium iodide ($^{131}$I). Each capsule of Theracap contains 37 MBq-5.55 GBq (Megabecquerel & Gigabecquerel – the units in which radioactivity is measured) of sodium iodide ($^{131}$I) at a fixed time.

- The other ingredients are sodium thiosulphate, disodium hydrogen...
orthophosphate, sodium hydroxide and a capsule (containing yellow iron oxide, titanium dioxide and gelatin).

What Theracap looks like and contents of the pack
Theracap is supplied as a single hard capsule in a plastic cup.

Marketing Authorisation Holder
GE Healthcare Limited
Amersham Place
Little Chalfont
Buckinghamshire HP7 8NA
United Kingdom

Manufacturer
GE Healthcare Buchler GmbH & Co. KG
Gieselweg 1
D-38110 Braunschweig
Germany

This leaflet was last approved in MM/WW.

Marketing Authorisations
UK: 002210102

PACKET LEAFLET: INFORMATION FOR THE HEALTHCARE PROFESSIONAL

THERACAP®
37 MBq-5.55 GBq capsules, hard
for therapeutic use.

Sodium [131] Iodide
IB5600P

1. NAME OF MEDICINAL PRODUCT
Theracap®
37 MBq-5.55 GBq capsules, hard
for therapeutic use.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Theracap is presented as a single yellow capsule containing sodium [131] Iodide in the following dosage range: 27 MBq - 5.55 GBq. Each capsule contains 185 MBq ± 15% of the activity reference dose. Each capsule contains a maximum of 20 μg of sodium iodide. The specific activity of the sodium [131] Iodide is not less than 222 GBq/g.

Sodium [131] Iodide is produced by fission of uranium-235 or by neutron bombardment of stable tellurium in a nuclear reactor. Sodium [131] Iodide has a half-life of 8.1 days. It decays by emission of gamma radiation of 365 keV (80.7%), 60.7 keV (7.2%) and 260 keV (1.1%) and beta radiation of maximal energy of 696 keV to stable xenon-131.

The medicinal product contains: 1.16 mg of sodium iodide per capsule. For a full list of excipients, see section 6.1.
UKPAR THERACAP131 37 MBq-5.55 GBq capsules, hard PL 00221/0102

3 PHARMACEUTICAL FORM
Capsule, hard.
Yellow gelatin capsule.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Radioactive iodine therapy is indicated for:
- Treatment of Graves’ disease, toxic multinodular goitre or autonomous nodules.
- Treatment of papillary and follicular thyroid carcinoma including metastatic disease.
Sodium[131I]iodide therapy is often combined with surgical intervention and with antithyroid medications.

4.2 Dosage and method of administration
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 is usually in the range of 200-600 MBq, but repeated treatment may be necessary. The dose required depends on the diagnosis, the size of the thyroid gland and iodine content. Patients should be rendered euthyroid medically whenever possible before giving radioactive treatment for hyperthyroidism.

4.3 Contraindications
- Hyperthyroidism to the active substance or to any of the excipients.
- Pregnancy.
- For diagnostic purposes in children under 10 years of age.
- Thyroid carcinoma in the follow-up of malignant disease and with bone 123 or technetium 99m no uptake.
- Patients with oesophageal, oesophagogastric or gastric ulcer.
- Patients with suspected reduced gastrointestinal motility.

4.4 Special warnings and special precautions for use
The possibility of hyperthyroidism including worsening of symptoms or stimulation of the thyroid is to be considered. Adequate supportive facilities should be readily available.

This medicinal product contains 140 mg of sodium in each capsule. To be avoided in patients on a controlled sodium intake.

The administration of high dose iodine may result in significant environmental hazard. Suitable precautions should be taken concerning the activity eliminated by the patients in order to avoid any contamination.

The therapeutic administration of sodium [131I]iodide imprisons with significant renal impairment requires special attention with regards to administered activity.
Sperm banking should be considered for young men who have extensive disease and therefore may need high medical or therapeutic doses.

For each patient exposed to ionizing radiation, the extent of the dosage should be justified on the basis of likely benefit. The activity achieved 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.

4.6 Pregnancy and lactation

Use during pregnancy:
The radiation dose to the fetus for this agent is likely to be in the range of 0.1-1.1 mSv and the fetal thyroid gland will not become functional until the second and third trimesters.

Use during lactation:
Breast feeding should be discontinued after the last dose of iodine-131 (I-131) is administered. For non-lactating women and also for lactating women following therapeutic doses, it is recommended to avoid close contact between mother and child for at least one week.

4.7 Effects on ability to drive or use machines

No studies on the effect of the ability to drive or use machines have been performed.

4.8 Undesirable effects

The following undesirable effects are recognised for iodine-131 (I-131):

Blood and the lymphatic system disorders
- Bone marrow depression
- Erythrocyte disorders
- Sickle-cell disease

Skin disorders
- Erythema, pruritus, paronychia, dermatitis

Endocrine disorders
- Hyperthyroidism, hypothyroidism
- Thyroiditis
- Adrenal insufficiency
- Diabetes mellitus

Reproductive system disorders
- Amenorrhea
- Menorrhagia

Neurological disorders
- Headache
- Dizziness

Injuries, poisoning and procedural complications
- Radiation injuries
- Congenital heart defects
- Congenital malformations
- Congenital malformations
- Congenital malformations

4.9 Overdose

High radiation exposure through ingestion can be reduced by means of administration of thyroglobulin-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

Pharmacotherapeutic group: therapeutic radiopharmaceuticals, sodium [131I]Iodide. AFC Code: V30401

Iodide, inhaled, must be used for therapeutic indications, not administered to have any pharmacological effect.

More than 90% of the radiation effect is from beta radiation which has a mean range of 0.5 mm.

5.2 Pharmacokinetic properties

After oral administration sodium [131I]iodide is absorbed rapidly from the upper gastrointestinal tract by 60% in 60 minutes. The pharmacokinetics follow those of unlabelled iodide. From the extra thyroidal compartment it is predominantly taken up by the thyroid or excreted renally. Small amounts of sodium [131I]iodide are taken up by salivary glands, gastric mucous and would also be localised in breast milk, the placenta and choroid plexus.

Following injection, about 20% of blood iodide is extracted in a single passage through the thyroid gland. Peak thyroidal accumulation occurs within 24 - 48 hours of dosing with about 60% of the maximum at 5 hours. This kinetic profile provides the rationale for the diagnostic procedures at 24 and 36 hours after dosing.

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.

5.3 Preclinical safety data

Acute toxicity is expected or observed. There are no data available on the toxicity of repeated doses of sodium iodide or on its effect on reproduction in animals or its mutagenic or carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium thiosulphate, pentaerythritol
Sodium phosphate, dibasic
Sodium hydroxide
Water for injection.

6.2 Incompatibilities

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

6.3 Shelf life

The shelf life for this product is 3.5 days from the date of manufacture as stated on the label.

6.4 Special precautions for storage

Store below 25°C. Do not freeze.

Store in the original lead container or in equivalent shielding.

6.5 Nature and contents of container

Each capsule is contained within a polycarbonate cup with a cardboard disc to absorb moisture. The cup is encased within a lead shield.

Pack size: 17-140 MBq in 37 MBq steps and 4.9-5.55 GBq in 1.85 GBq steps. Each pack contains a single capsule.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Normal safety precautions for handling radioactive materials should be observed. After use, all materials associated with the preparation and administration of radiopharmaceuticals, including the unused product and its container, should be disassembled or treated as radioactive waste and disposed of in accordance with the conditions specified by the local competent authority. Contaminated material must be disposed of as radioactive waste via an authorised route.

7. MARKETING AUTHORISATION HOLDER

GE Healthcare Limited
Amersham Place
Lechlade
Buckinghamshire HP7 9NA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL 00221/0102

9. DATE OF FIRST AUTHORIZATON/RENEWAL OF AUTHORISATION

Date of first authorisation: 02/04/2007
Date of last renewal: 02/04/2012

10. DATE OF REVIEW OF THE TEXT

MM/YY
11. DOSIMETRY

The ICRP model refers to intravenous administration. Since absorption of radiopharmaceutical is rapid and complete, this model is applicable in cases of oral administration also but there is a further radiation dose to the stomach wall in addition to that due to gastric and small bowel evacuation. Assuming that the mean residence time in the stomach is 5.0 hr, the absorbed dose to the stomach wall increases by about 30% for oral-111m.

The dose is specific to organs, which may need the target organ therapy, can be influenced significantly by physiological changes induced by the medical process.

As part of the risks assessment it is advised that the effective dose equivalent (ED) and/or radiation dose to individual target organs be calculated prior to intervention. The activity might be adjusted according to tissue mass, biological half-life, and the "in-vivo" factor which takes into account the physiological status of the patient (including iodine depletion and the underlying pathology).

The tables below show the dosimetry as calculated according to Publication 50 of the ICRP (International Commission on Radiological Protection). Radiation Dose to Patients from Radiopharmaceuticals. Pergamon Press 1987.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Adult</th>
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<th>Elder</th>
<th>Sex</th>
<th>Effective dose (Sv)</th>
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12. INSTRUCTIONS FOR PREPARATION OF RADIONUCLIDE PHARMACEUTICALS

The radiopharmaceutical may be received used and administered only by authorized persons, in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of the local competent official organization (see section 6.5).

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spills of radioactivity. Radiation protection measures (in accordance with national regulations) must therefore be taken.

13. OTHER INFORMATION

Manufacturer:
GS Healthcare GmbH & Co. KG
Glasdor 1
D-34223 Korschenbroich
Germany

<table>
<thead>
<tr>
<th>Name</th>
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LABELLING

THERACAP®
I35600P
Secondary Label (Tin)