SODIUM IODIDE (\(^{131}\text{I}\)) 74MBq & 925MBq SOLUTION FOR INJECTION
PL 00221/0113

UKPAR

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SODIUM IODIDE ($^{131}$I) 74MBq & 925MBq SOLUTION FOR INJECTION
PL 00221/0113

LAY SUMMARY

The Medicines Healthcare products Regulatory Agency granted GE Healthcare Limited a Marketing Authorisation (licence) for the medicinal product Sodium Iodide ($^{131}$I) 74MBq and 925MBq Solution for Injection, (PL 00221/0113).

These are prescription-only medicines (POM). Sodium Iodide ($^{131}$I) 74MBq and 925MBq Solution for Injection are “radiopharmaceutical” medicines. They contain an active ingredient called sodium [$^{131}$I] iodide. Sodium Iodide ($^{131}$I) 74MBq and 925MBq Solution for Injection are used to help identify and treat illness. Once injected it can be seen from the outside of the body with the aid of a special camera used in the scan. The scan can help the doctor see tumours in the thyroid glands and see how well a tumour is responding to treatment or if the tumour has spread to other parts of the body.

It can also be given to people to treat a thyroid tumour, an overactive thyroid or to treat goitre (swelling die to an enlarged thyroid). The use of Sodium [$^{131}$I] Iodide Injection in the treatment of an illness is often combined with surgical treatment and with medicines that inhibit the thyroid (antithyroidal agents).

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking product Sodium Iodide ($^{131}$I) 74MBq and 925MBq Solution for Injection, (PL 00221/0113) outweigh the risks; hence a Marketing Authorisation has been granted.
SODIUM IODIDE (\textsuperscript{131}I) 74MBq & 925MBq SOLUTION FOR INJECTION
PL 00221/0113

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 Sodium Iodide ($^{131}$I) 74MBq and 925MBq Solution for Injection, (PL 00221/0113) on 1st February 2010. These products are prescription-only medicines (POM).

These applications were made under Article 10a of Directive 2001/83/EC, so called well- established use, and as such these applications rely solely on bibliographic data with respect to the clinical aspects.

These products contain the active ingredient sodium $[^{131}\text{I}]$ iodide and are used for diagnostic and therapeutic purposes. Sodium $[^{131}\text{I}]$ iodide can be used as a “tracer” to study radioiodide 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. It is also used in the management of thyroid carcinoma; sodium $[^{131}\text{I}]$ iodide is used to identify thyroid remnant and metastases (after ablation). It is also used in thyroid scanning for benign conditions but only where circumstances do not allow for radiopharmaceuticals with more favourable dosimetry to be used.

Sodium $[^{131}\text{I}]$ iodide is also 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 [\(^{131}\text{I}\)] 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, sodium dihydrogen phosphate dihydrate, disodium hydrogen phosphate dodecahydrate, sodium chloride, sodium hydroxide and water for injections. All the ingredients within the body of the solution for injection comply with relevant Ph Eur. Appropriate justification for the inclusion of each excipient has been provided.

Satisfactory certificates of analysis have been provided for all excipients. None of the excipients used contain material of animal or human origin.
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 Type 1 neutral, clear 10 ml glass vial sealed with a polytetrafluoroethylene (PTFE) -faced butyl rubber closure with aluminium overseal. Each vial is packed within a radiation shielding container of lead metal and placed within a sealed metal tin. The pack size for 74 MBq ranges from 37 MBq to 740 MBq. The pack size 925 MBq ranges from 925 MBq to 9250 MBq.

Specifications and Certificates of Analysis for the primary packaging material have been provided and are satisfactory. All primary packaging is controlled to European Pharmacopoeia standards.

Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 31 days from the first activity reference date stated on the label, which is satisfactory. Storage conditions are “Store below 25oC. 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 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.
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 [\(^{131}\)I] 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 [\(^{131}\)I] 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.

Following injection, about 20% of blood iodide is extracted in a single passage through the thyroid gland. Peak thyroid accumulation occurs within 24 – 48 hours of dosing with about 50% of the maximum at 5 hours. This kinetic profile provides the rationale for the diagnostics procedures at 24 and 72 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.

2 INDICATIONS

Diagnostic 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 sodium [\(^{131}\)I] iodide can be performed but only where circumstances do not allow for radiopharmaceuticals with more favourable dosimetry to be used.

Therapeutic indications
Radioiodide thyroid therapy is indicated for:

- treatment of Grave’s 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.

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

4 CLINICAL PHARMACOLOGY
The clinical pharmacology of Sodium \(^{131}\text{I}\) 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 \(^{131}\text{I}\) 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 \(^{131}\text{I}\) 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 of 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 Sodium Iodide ($^{131}$I) Injection 74 MBq/ml and 925 MBq/ml solution for injection is 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 $[^{131}]$ 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 $[^{131}]$ 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 $[^{131}]$ 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 $[^{131}]$ iodide is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.
SODIUM IODIDE (^{131}I) 74MBq & 925MBq SOLUTION FOR INJECTION
PL 00221/0113

STEPS TAKEN FOR ASSESSMENT

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<table>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 30&lt;sup&gt;th&lt;/sup&gt; 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&lt;sup&gt;th&lt;/sup&gt; 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&lt;sup&gt;th&lt;/sup&gt; December 2006 and 27&lt;sup&gt;th&lt;/sup&gt; June 2007.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 19&lt;sup&gt;th&lt;/sup&gt; April 2007 and 10&lt;sup&gt;th&lt;/sup&gt; September 2009 for the quality sections.</td>
</tr>
<tr>
<td>5</td>
<td>The applications were determined on 1&lt;sup&gt;st&lt;/sup&gt; February 2010.</td>
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SODIUM IODIDE (\(^{131}\text{I}\)) 74MBq & 925MBq SOLUTION FOR INJECTION
PL 00221/0113

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
Sodium Iodide (^131I) 74 MBq/ml and 925 MBq/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Sodium Iodide (^131I) Injection is a clear, colourless solution containing sodium[^131I]iodide:

37-740 MBq/vial (74 MBq/ml) at the activity reference date
0.925-9.25 GBq/vial (925 MBq/ml) at the activity reference date

The specific activity of the sodium[^131I]iodide is not less than 222 GBq/mg iodine at the activity reference date.

Iodine-131 is produced by fission of uranium-235 or by neutron bombardment of stable tellurium in a nuclear reactor. It decays by emission of gamma radiations of 365 keV (81.7%), 637 keV (7.2%) and 284 (6.1%) and beta radiations of maximal energy of 0.606 MeV to stable Xenon-131. Iodine-131 has a half-life of 8.02 days.

This medicinal product contains 5.92 mg/ml sodium. This needs to be taken into consideration for patients on a controlled sodium diet.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Solution for injection.

Clear, colourless solution.

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS

Diagnostic 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 sodium[^131I] iodide can be performed but only where circumstances do not allow for radiopharmaceuticals with more favourable dosimetry to be used.

Therapeutic indications
Radioiodide thyroid therapy is indicated for:
• treatment of Grave’s 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 POSOLOGY AND METHOD OF ADMINISTRATION

Diagnostic use
The recommended activities for an adult patient (70 kg) are as follows:
1. For the thyroid uptake studies: 0.2-3.7 MBq.
2. For post thyroid ablation (for metastases and thyroid remnant): a maximum dose 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 activity to be administered to a child and adolescent should be a fraction of the adult dose calculated from the body weight/surface area methods or according to the following equations:

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

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

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>
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<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>
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<td>24 kg</td>
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<td>0.53</td>
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<td>26 kg</td>
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<td>34 kg</td>
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<td>38 kg</td>
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<td>40 kg</td>
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<td>0.76</td>
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</table>

(Paediatric Task Group, European Association of Nuclear Medicines)

Therapeutic use

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, with cumulative activities of up to 5000 MBq. 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.

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.

The therapeutic activity to be administered to a child over 10 years and adolescent should be a fraction of the adult dose, calculated from body weight or surface area.

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

<table>
<thead>
<tr>
<th>Active substances</th>
<th>Withdrawal period prior to administration of sodium $^{[\text{I}]}$ 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>Phenybutazone</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
Use during pregnancy:
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.

Use during lactation:
Breast feeding should be discontinued after sodium $^{[\text{I}]}$ 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 $^{[\text{I}]}$ iodide:
Blood and the lymphatic system disorders
Bone marrow depression
Eye disorders
Sicca syndrome, endocrine ophthalmopathy, acquired dacryostenosis
Gastrointestinal disorders
Nausea, vomiting
Endocrine disorders
Hypothyroidism, aggravated hyperthyroidism, Basedow’s (Graves’) disease, hyperparathyroidism
Infections and infestations
Sialoadenitis
Neoplasms benign, malignant and unspecified (including cysts and polyps)
Gastric cancer, leukaemia, bladder and breast cancer
Immune system disorders
Hypersensitivity
Injury, poisoning and procedural complications
Radiation thyroiditis
Reproductive system and breast disorders
Impairment of fertility in man and woman
Congenital, familial and genetic disorders
Congenital thyroid disorders.

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: diagnostic radiopharmaceuticals, thyroid, sodium iodide (\(^{131}\)I), ATC Code: V09FX03

Pharmacotherapeutic group: therapeutic radiopharmaceuticals, sodium iodide (\(^{131}\)I), ATC Code: V10XA01

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 0.5mm.

5.2 PHARMACOKINETIC PROPERTIES
Following injection, about 20% of blood iodide is extracted in a single passage through the thyroid gland. Peak thyroid accumulation occurs within 24 – 48 hours of dosing with about 50% of the maximum at 5 hours. This kinetic profile provides the rationale for the diagnostics procedures at 24 and 72 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
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
Sodium dihydrogen phosphate, dihydrate
Disodium hydrogen phosphate, dodecahydrate
Sodium chloride
Sodium hydroxide
Water for injections

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 31 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 original lead container or in equivalent shielding.

6.5 NATURE AND CONTENTS OF CONTAINER
The product is supplied in a Type 1 neutral, clear 10 ml glass vial sealed with a PTFE-faced butyl rubber closure and aluminium overseal.
Each vial is packed within a radiation shielding container of lead metal and placed within a sealed metal tin.

Pack size: 74 MBq - pack sizes range from 37 MBq to 740 MBq
925 MBq - pack sizes range from 925 MBq to 9250 MBq

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 00221/0113

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>Iodine-131</th>
<th>half life: 8.02 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorbed dose per unit activity administered (mGy/MBq)</td>
<td></td>
</tr>
<tr>
<td>Organ</td>
<td>Adult</td>
</tr>
<tr>
<td>-------------------</td>
<td>--------</td>
</tr>
<tr>
<td>Adrenals</td>
<td>3.7E-02</td>
</tr>
<tr>
<td>Bladder wall</td>
<td>6.1E-01</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td>3.2E-02</td>
</tr>
<tr>
<td>Breast</td>
<td>3.3E-02</td>
</tr>
<tr>
<td>Stomach wall</td>
<td>3.4E-02</td>
</tr>
<tr>
<td>Small intest</td>
<td>3.8E-02</td>
</tr>
<tr>
<td>ULI wall</td>
<td>3.7E-02</td>
</tr>
<tr>
<td>LLI wall</td>
<td>4.3E-02</td>
</tr>
<tr>
<td>Kidneys</td>
<td>6.5E-02</td>
</tr>
<tr>
<td>Liver</td>
<td>3.3E-02</td>
</tr>
<tr>
<td>Lungs</td>
<td>3.1E-02</td>
</tr>
<tr>
<td>Ovaries</td>
<td>4.2E-02</td>
</tr>
<tr>
<td>Pancreas</td>
<td>3.5E-02</td>
</tr>
<tr>
<td>Red marrow</td>
<td>3.5E-02</td>
</tr>
<tr>
<td>Spleen</td>
<td>3.4E-02</td>
</tr>
<tr>
<td>Testes</td>
<td>3.7E-02</td>
</tr>
<tr>
<td>Thyroid</td>
<td>2.9E-02</td>
</tr>
<tr>
<td>Uterus</td>
<td>5.4E-02</td>
</tr>
<tr>
<td>Other tissue</td>
<td>3.2E-02</td>
</tr>
<tr>
<td>Effective Dose Equivalent (mSv/MBq)</td>
<td>7.2E-02</td>
</tr>
</tbody>
</table>

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

The effective dose equivalent to an adult administered 3.7MBq with 0% thyroid uptake is 0.27mSv. The effective dose is 0.23mSv.

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

<table>
<thead>
<tr>
<th>uptake: 0.5%</th>
<th>3.0 E-01</th>
<th>4.5 E-01</th>
<th>6.9 E-01</th>
<th>1.5 E+00</th>
<th>2.8 E+00</th>
</tr>
</thead>
<tbody>
<tr>
<td>uptake 1.0%</td>
<td>5.2 E-01</td>
<td>8.1 E-01</td>
<td>1.2 E+00</td>
<td>2.7 E+00</td>
<td>5.3 E+00</td>
</tr>
<tr>
<td>uptake 2.0%</td>
<td>9.7 E-01</td>
<td>1.5 E+00</td>
<td>2.4 E+00</td>
<td>5.3 E+00</td>
<td>1.0 E+01</td>
</tr>
</tbody>
</table>
### 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></td>
<td>3.6E-02</td>
<td>4.3E-02</td>
<td>7.1E-02</td>
<td>1.1E-01</td>
<td>2.2E-01</td>
</tr>
<tr>
<td>Bladder wall</td>
<td></td>
<td>5.2E-01</td>
<td>6.4E-01</td>
<td>9.8E-01</td>
<td>1.5E+00</td>
<td>2.9E+00</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td></td>
<td>4.7E-02</td>
<td>6.7E-02</td>
<td>9.4E-02</td>
<td>1.4E-01</td>
<td>2.4E-01</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td>4.3E-02</td>
<td>4.3E-02</td>
<td>8.1E-02</td>
<td>1.3E-01</td>
<td>2.5E-01</td>
</tr>
<tr>
<td>GI tract</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach wall</td>
<td></td>
<td>4.6E-01</td>
<td>5.8E-01</td>
<td>8.4E-01</td>
<td>1.5E+00</td>
<td>2.9E+00</td>
</tr>
<tr>
<td>Small intest</td>
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<td>2.8E-01</td>
<td>3.5E-01</td>
<td>6.2E-01</td>
<td>1.0E+00</td>
<td>2.0E+00</td>
</tr>
<tr>
<td>ULI wall</td>
<td></td>
<td>5.9E-02</td>
<td>6.5E-02</td>
<td>1.0E-01</td>
<td>1.6E-01</td>
<td>2.8E-01</td>
</tr>
<tr>
<td>LLI wall</td>
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<td>4.2E-02</td>
<td>5.3E-02</td>
<td>8.2E-02</td>
<td>1.3E-01</td>
<td>2.3E-01</td>
</tr>
<tr>
<td>Kidneys</td>
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<td>6.0E-02</td>
<td>7.5E-02</td>
<td>1.1E-01</td>
<td>1.7E-01</td>
<td>2.9E-01</td>
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<tr>
<td>Liver</td>
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<td>6.8E-02</td>
<td>1.1E-01</td>
<td>2.2E-01</td>
</tr>
<tr>
<td>Lungs</td>
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<td>5.3E-02</td>
<td>7.1E-02</td>
<td>1.2E-01</td>
<td>1.9E-01</td>
<td>3.3E-01</td>
</tr>
<tr>
<td>Ovaries</td>
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<td>5.9E-02</td>
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<td>1.4E-01</td>
<td>2.6E-01</td>
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<tr>
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<td>6.2E-02</td>
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<td>2.7E-01</td>
</tr>
<tr>
<td>Red marrow</td>
<td></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>
</tr>
<tr>
<td>Spleen</td>
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<td>5.1E-02</td>
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<td>1.2E-01</td>
<td>2.3E-01</td>
</tr>
<tr>
<td>Testes</td>
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<td>3.5E-02</td>
<td>5.8E-02</td>
<td>9.4E-02</td>
<td>1.8E-01</td>
</tr>
<tr>
<td>Thyroid</td>
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<td>1.1E+03</td>
<td>2.0E+03</td>
</tr>
<tr>
<td>Uterus</td>
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<td>1.1E-01</td>
<td>1.7E-01</td>
<td>3.1E-01</td>
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<tr>
<td>Other tissue</td>
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<td>6.5E-02</td>
<td>8.9E-02</td>
<td>1.4E-01</td>
<td>2.2E-01</td>
<td>4.0E-01</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 3.7MBq with 15% thyroid uptake is 24.42mSv.

### 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></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>
</tr>
<tr>
<td>Bladder wall</td>
<td></td>
<td>4.0E-01</td>
<td>5.0E-01</td>
<td>7.6E-01</td>
<td>1.2E+00</td>
<td>2.3E+00</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td></td>
<td>7.6E-02</td>
<td>1.2E-01</td>
<td>1.6E-01</td>
<td>2.3E-01</td>
<td>3.5E-01</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td>6.7E-02</td>
<td>6.6E-02</td>
<td>1.3E-01</td>
<td>2.2E-01</td>
<td>4.0E-01</td>
</tr>
<tr>
<td>GI tract</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach wall</td>
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<td>4.6E-01</td>
<td>5.9E-01</td>
<td>8.5E-01</td>
<td>1.5E+00</td>
<td>3.0E+00</td>
</tr>
<tr>
<td>Small intest</td>
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<td>2.8E-01</td>
<td>3.5E-01</td>
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<td>1.0E+00</td>
<td>2.0E+00</td>
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<tr>
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<td>1.7E-01</td>
<td>3.0E-01</td>
</tr>
<tr>
<td>LLI wall</td>
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<td>4.0E-02</td>
<td>5.1E-02</td>
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<td>1.3E-01</td>
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<tr>
<td>Kidneys</td>
<td></td>
<td>5.6E-02</td>
<td>7.2E-02</td>
<td>1.1E-01</td>
<td>1.7E-01</td>
<td>2.9E-01</td>
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<tr>
<td>Liver</td>
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<td>3.7E-02</td>
<td>4.9E-02</td>
<td>8.2E-02</td>
<td>1.4E-01</td>
<td>2.7E-01</td>
</tr>
<tr>
<td>Lungs</td>
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<td>9.0E-02</td>
<td>1.2E-01</td>
<td>2.1E-01</td>
<td>3.3E-01</td>
<td>5.6E-01</td>
</tr>
<tr>
<td>Ovaries</td>
<td></td>
<td>4.2E-02</td>
<td>5.7E-02</td>
<td>9.0E-02</td>
<td>1.4E-01</td>
<td>2.7E-01</td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
<td>5.4E-02</td>
<td>6.9E-02</td>
<td>1.1E-01</td>
<td>1.8E-01</td>
<td>3.2E-01</td>
</tr>
<tr>
<td>Red marrow</td>
<td></td>
<td>8.6E-02</td>
<td>1.2E-01</td>
<td>1.6E-01</td>
<td>2.2E-01</td>
<td>3.5E-01</td>
</tr>
<tr>
<td>Spleen</td>
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<td>1.5E-01</td>
<td>2.8E-01</td>
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<td>8.9E-02</td>
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<tr>
<td>Thyroid</td>
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<td>7.9E+02</td>
<td>1.2E+03</td>
<td>2.6E+03</td>
<td>4.7E+03</td>
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<tr>
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<td>1.0E-01</td>
<td>1.6E-01</td>
<td>3.0E-01</td>
</tr>
</tbody>
</table>
Other tissue 1.1E-01 1.6E-01 2.6E-01 4.1E-01 7.1E-01

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

<table>
<thead>
<tr>
<th></th>
<th>1.5E+01</th>
<th>2.4E+01</th>
<th>3.6E+01</th>
<th>7.8E+01</th>
<th>1.4E+02</th>
</tr>
</thead>
</table>

The effective dose equivalent (EDE) in an adult administered 3.7MBq with 35% thyroid uptake is 55.5mSv. The effective dose is 88.8mSv.

**Thyroid uptake 55%**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Absorbed dose per unit activity administered (mGy/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adult</td>
</tr>
<tr>
<td>Adrenals</td>
<td>4.9E-02</td>
</tr>
<tr>
<td>Bladder wall</td>
<td>2.9E-01</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td>1.1E-01</td>
</tr>
<tr>
<td>Breast</td>
<td>9.1E-02</td>
</tr>
<tr>
<td>Gl tract</td>
<td></td>
</tr>
<tr>
<td>Stomach wall</td>
<td>4.6E-01</td>
</tr>
<tr>
<td>Small intest</td>
<td>2.8E-01</td>
</tr>
<tr>
<td>ULI wall</td>
<td>5.8E-02</td>
</tr>
<tr>
<td>LLI wall</td>
<td>3.9E-02</td>
</tr>
<tr>
<td>Kidneys</td>
<td>5.1E-02</td>
</tr>
<tr>
<td>Liver</td>
<td>4.3E-02</td>
</tr>
<tr>
<td>Lungs</td>
<td>1.3E-01</td>
</tr>
<tr>
<td>Ovaries</td>
<td>4.1E-02</td>
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<tr>
<td>Pancreas</td>
<td>5.8E-02</td>
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<tr>
<td>Red marrow</td>
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<tr>
<td>Spleen</td>
<td>5.1E-02</td>
</tr>
<tr>
<td>Testes</td>
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<tr>
<td>Thyroid</td>
<td>7.9E+02</td>
</tr>
<tr>
<td>Uterus</td>
<td>4.6E-02</td>
</tr>
<tr>
<td>Other tissue</td>
<td>1.6E-01</td>
</tr>
</tbody>
</table>

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

<table>
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<tr>
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<th>2.4E+01</th>
<th>3.7E+01</th>
<th>5.6E+01</th>
<th>1.2E+02</th>
<th>2.2E+02</th>
</tr>
</thead>
</table>

For this product, the effective dose equivalent (EDE) to an adult with 55% thyroid uptake resulting from the administration of a 3.7MBq capsule is 88.8mSv.

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

This radiopharmaceutical 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 (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

2. What Sodium Iodide Injection is and what it is used for

This medicine is for diagnostic and therapeutic use. It is used both to help identify illness and treat illness.

Sodium Iodide Injection is a radio pharmaceutical medicine.

- It contains an active ingredient called 'sodium iodide'.
- Once injected it can be seen from outside your body by a special camera used in the scan.
- The scan can help your doctor see tumours in the thyroid glands, and to see how well a tumour is responding to treatment or if the tumour has spread to other parts of the body.

- Some other people are given this medicine to treat a thyroid tumour, an overactive thyroid or to treat goitre (swelling due to an enlarged thyroid).

Your doctor or nurse will tell you anything else you need to know about how Sodium Iodide Injection works.

The use of Sodium Iodide Injection for treatment of an illness is often combined with surgical treatment and with medicines that inhibit the thyroid (antithyroidal agents).
2. Before you are given Sodium Iodide Injection

You should not be given Sodium Iodide Injection:
- If you are allergic (hypersensitive) to the active ingredient or any other ingredient (listed in Section 6).
- If you are pregnant or think you might be pregnant.
- If you are breast-feeding.
- If you have a scan of benign thyroid tumours.

Do not have Sodium Iodide injection if any of the above apply to you. If you are not sure talk to your doctor or nurse.

Take special care with Sodium Iodide Injection:
Check with your doctor or nurse before having Sodium Iodide Injection:
- If the person who will be given this medicine is a child or adolescent.
- If you have missed your last period.
- If you are breast-feeding.
- If you are on a low sodium diet.

Taking other medicines:
Please tell your doctor 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 Sodium Iodide Injection works.

Before you are given Sodium Iodide injection 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 parasite infections such as thiabendazole, rifampicin or amphotericin B.
- Penicillins.
- Medicines called 'sulphonamides' such as sulphasalazine (used for rheumatoid arthritis and some bowel problems), sumatriptan (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 diabetics.
• 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 hospitals 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 Sodium Iodide Injection.

Having Sodium Iodide Injection with food and drink
• Your doctor may recommend a low iodine diet.
• After been given Sodium Iodide Injection you may be asked to drink more liquids.

Pregnancy and breast-feeding
You should not be given Sodium Iodide Injection if you are pregnant or think that you may be pregnant. This is because it may affect the baby.

You may be told by your doctor not to become pregnant for at least 6 months after being given Sodium Iodide Injection.

Do not breast-feed if you are given Sodium Iodide Injection. 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 Sodium Iodide Injection. If it is not possible to wait your doctor will ask you to:
• stop breast-feeding, and
• use formula feed for your child, and
• express (remove) breast milk and throw away the milk.
Your doctor will let you know when you can start breast-feeding again.
Driving and using machines
Ask your doctor if you can drive or use machines after you have been given Sodium Iodide Injection.

Important information Sodium Iodide injection
When Sodium Iodide injection is used you are exposed to radioactivity.
- Your doctor will always consider the possible risks and benefits before you are given the medicine.
- Ask your doctor if you have any questions.

3. How Sodium Iodide Injection is given
Sodium Iodide Injection will be given to you by a specially trained and qualified person.

- Sodium Iodide Injection will always be used in a hospital or clinic.
- They will tell you anything you need to know for its safe use. Your doctor will decide the dose that is best for you.

The usual dose is:
- One single injection before a scan. Scans may be taken after 4 hrs and up to 72 hrs after injection.
- The number of doses and length of treatment will depend on your condition.
- Ask your doctor if you have any questions.

6. Possible side effects
Like all medicines, Sodium Iodide Injection can cause side effects, although not everybody gets them. The side effects will depend on whether you are being given this medicine to scan (diagnose) or treat a condition. Side effects from Sodium Iodide Injection may occur soon after receiving the product (early side effects) or some time after receiving the product (late side effects). You are only at risk of the late side effects if you have been given this product to treat a condition.

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 of your nearest hospital.

Other early side effects include:
- feeling sick (nausea)
- being sick (vomiting).
If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

If you are receiving this product as treatment for a condition you may also experience the following early
**Side effects that your doctor may be able to prevent or treat**

- diarrhoea
- pain around your stomach area (abdominal pain)
- swelling (inflammation) of your thyroid
- swelling of your windpipe (trachea), which may cause difficulty in 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 Sodium Iodide Injection. Symptoms could include increased appetite, palpitations, feeling restless (anxiety), weight loss or sweating.

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

**Late side effects (within weeks, months or years):**

- your parathyroid may become underactive (hypoparathyroidism).

  Signs may include 'pins and needles', weakness, muscle spasms, muscle twitches or cramps all over, tingling, vibrating, burning and numbness; trouble concentrating, feeling dizzy or irritable, sensitivity to noise, muscles that stop working properly (muscle paralysis) or fits (seizures).

High doses of Sodium Iodide Injection or repeat treatments within 6 months of the first treatment may lead to a reduction in the ability of your bone marrow to make blood cells. This can cause bruising and bleeding problems. In many cases patients recover fully. Very rarely, in severe cases, this may cause death.

Patients who have received Sodium Iodide Injection appear to be more at risk of developing stomach cancer and if high doses have been received, leukaemia. There may also be a small increase in the 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.

5. **How to store Sodium Iodide Injection**

Sodium Iodide Injection is kept out of the reach and sight of children.
6. Further Information

What Sodium Iodide Injection contains

- The active ingredient is sodium iodide (131I). Each ml of Sodium Iodide (131I) injection contains 74 MBq (Megabecquerel – the unit in which radioactivity is measured) or 925 MBq of sodium iodide (131I) at a fixed time.
- The other ingredients are sodium thiosulfate, disodium hydrogen phosphate, sodium dihydrogen phosphate, sodium chloride and water for injections.

What Sodium Iodide Injection looks like and contents of the pack

Sodium iodide injection is supplied as a single clear glass vial containing a solution for injection.

Marketing Authorisation Holder

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

Manufacturer

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

1. Name of the medicinal product

Sodium iodide (131I) Injection 74 MBq/ml and 925 MBq/ml solution for injection

2. Qualitative and quantitative composition

Sodium iodide (131I) injection is a clear, colourless solution containing sodium (131I) iodide.

- 37 MBq/1 ml (0.01 MBq/ml) at the expiry date reference date (June 2025).

The specific activity of the sodium (131I) iodide is not less than 202 MBq/g at the expiry date reference date. Iodine-131 is produced by the nuclear reaction of stable tellurium in a nuclear reactor. Iodine-131 has a half-life of 8.02 days. It decays by emission of gamma radiation of 66 keV (3.17 %), 364 keV (72.2%) and 2.64 MeV (6.1%) and beta radiation of maximal energy of 650 keV to stable xenon-131.

This medicinal product contains 500 mg/L sodium. This needs to be taken into consideration for patients on a controlled sodium diet.

For a full list of excipients, see section 6.1.
UKPAR Sodium Iodide (131I) 74 MBq & 925 MBq Solution for Injections PL 00221/0113

3 PHARMACOLOGICAL FORM
Solution for injection.
Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Diagnostic indications
Sodium iodide may be given as a “trace” dose to study radioactive iodine. An examination of the thyroid uptake and effective half-life obtained within 24 hours can be used to calculate the activity required for radiiodine therapy.

In the management of thyroid carcinoma, sodium iodide is used to identify thyroid remnant and metastases before iodine 131.

Thyroid scanning for benign conditions with sodium 131 can be performed but only where circumstances do not allow for radioiodine methods with more favourable dosimetry to be used.

Therapeutic indications
Radioactive iodine therapy is indicated for:
- treatment of Graves’ disease toxic multinodular goiter or autonomous nodules
- treatment of papillary and follicular thyroid carcinoma including metastatic disease.

Sodium 131 therapy is often combined with surgical intervention and with other thyroid medications.

4.2 Precautions and method of administration
Diagnostic use
The recommended activities for an adult patient (70 kg) are as follows:

1. For the thyroid uptake study: 0.2 - 0.4 MBq
2. For post thyroid ablation (for metastasis and thyroid remnant): minimum dose of 0.3 MBq.

Therapeutic use
The diagnostic activity to be administered to a child and adolescent should be a fraction of the adult dose calculated from the body weight/height area methods according to the following equations:

Radioiodine MBq = adult dose MBq x weight (kg) / 70 kg

Radioiodine MBq = adult dose MBq x height (cm) / 168 cm

Connections for adults given for guidance are proposed below:

<table>
<thead>
<tr>
<th>Fraction of adult dose</th>
<th>5 kg</th>
<th>10 kg</th>
<th>15 kg</th>
<th>20 kg</th>
<th>30 kg</th>
<th>40 kg</th>
<th>50 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.10</td>
<td>0.14</td>
<td>0.15</td>
<td>0.16</td>
<td>0.17</td>
<td>0.18</td>
<td>0.19</td>
<td>0.20</td>
</tr>
<tr>
<td>0.20</td>
<td>0.21</td>
<td>0.22</td>
<td>0.23</td>
<td>0.24</td>
<td>0.25</td>
<td>0.26</td>
<td>0.27</td>
</tr>
<tr>
<td>0.05</td>
<td>0.06</td>
<td>0.07</td>
<td>0.08</td>
<td>0.09</td>
<td>0.10</td>
<td>0.11</td>
<td>0.12</td>
</tr>
<tr>
<td>0.02</td>
<td>0.03</td>
<td>0.04</td>
<td>0.05</td>
<td>0.06</td>
<td>0.07</td>
<td>0.08</td>
<td>0.09</td>
</tr>
<tr>
<td>0.01</td>
<td>0.01</td>
<td>0.02</td>
<td>0.03</td>
<td>0.04</td>
<td>0.05</td>
<td>0.06</td>
<td>0.07</td>
</tr>
</tbody>
</table>

For the thyroid ablation and treatment of metastases
The administered activity following a test dose in the range of 18.5 - 37 MBq, it depends on the patient’s size and radioiodine uptake. The subsequent treatment for metastases administered activity is in the range of 370 - 1110 MBq.

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 irritation.

The therapeutic activity to be administered to a child over 10 years and adolescents should be a fraction of the adult dose calculated from body weight or surface area.

4.3 Contraindications
- Hypersensitivity to the active substance or any of the excipients.
- Pregnancy.
- For diagnostic purposes in children under 10 years of age.
- Thyroid scintigraphy for follow-up of malignancy when radionuclides 123I or technetium-99m is not available.

4.4 Special warnings and precautions for use
The possibility of hyperactivity including anxiety and psychosomatic reactions should always be considered. Adequate life support facilities should be readily available.
4.5 Interactions with other medicinal products and other forms of interaction

A full list today, should be taken as relevant interactions including the ones mentioned below, should be avoided prior to the administration of sodium [131I] iodide.

Active substances

<table>
<thead>
<tr>
<th>Substance</th>
<th>Withdrawal period prior to administration of sodium [131I] iodide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithyroid agents (e.g., methimazole, propylthiouracil)</td>
<td>7 - 10 days before sodium [131I] iodide administration.</td>
</tr>
<tr>
<td>Radioactive iodine ( {\text{iodine}^{131}} )</td>
<td>24 weeks.</td>
</tr>
</tbody>
</table>

4.6 Pregnancy and lactation

Use during pregnancy:

The absorbed dose to the uterus for this agent is likely to be in the range 11.5 - 111.5 MBq, and the fetal thyroid gland ovary concentrates iodine during the second and third trimesters.

Use during lactation:

Breast feeding should be discontinued after sodium [131I] iodide administration for adopthyroid or thyrotoxic cases, i.e., to avoid close contact between mother and infant for at least one week.

4.7 Effects on ability to drive or 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 [131I] iodide:

Bone marrow depression

Hypothyroidism, myocardial infarction, edema, digestive upset, nausea, vomiting.
6 PHARMACOLOGICAL PROPERTIES

6.1 Pharmacodynamic properties:

Pharmacotherapeutic group: diagnostic radiopharmaceuticals, thyroid, sodium iodide (131I), ATC Code: V03FA03.

Pharmacodynamic action: therapeutic radiopharmaceuticals, sodium iodide (131I), ATC Code: V03FA01.

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.

Pharmacokinetic properties:

Following injection, about 30% of the iodine is excreted in a single passage through the thyroid gland. Peak thyroid accumulation occurs within 24 - 48 hours of dosing in 6-16% of the remaining radioactivity. The iodine profile is the rationale for the diagnostic procedures at 24 and 12 hours after dosing.

The effective half-life of radioiodine in plasma is in the order of 1.7 hours, whereas that for radioiodine taken by the thyroid gland is about 6 days.

6.3 Preclinical safety data:

No acute toxicity is expected or observed.

6.4 Special precautions for storage

Store below 25°C. Do not freeze.

Store in original glass container or in equivalent shielding.

6.5 Nature and contents of container:

The product is supplied in a Type I neutral, clear glass vial sealed with a 3M Eva-Dur/Eva-Sol/STP liner and aluminum outer seal.

Each vial is packed within a radiation shielding container of lead metal and placed within a sealed metal tin.

Pack size: 1 vial - pack sizes range from 37 MBq to 740 MBq

375 MBq - pack sizes range from 205 MBq to 410 MBq

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling:

Normal radiation 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 as 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.
### Thyroid uptake 9%

<table>
<thead>
<tr>
<th>Gender</th>
<th>Absorbed dose (per unit activity of labelled iodide)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adult</td>
</tr>
<tr>
<td>All ages</td>
<td>0.02%</td>
</tr>
<tr>
<td>Male</td>
<td>0.02%</td>
</tr>
<tr>
<td>Female</td>
<td>0.01%</td>
</tr>
</tbody>
</table>

### 12 INSTRUCTIONS FOR PREPARATION OF RADIPHARMACEUTICALS

This radiopharmaceutical 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 (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.

### 13 OTHER INFORMATION

**Manufacturer**

GE Healthcare Buciller GmbH & Co. KG
Gieseweg 1
D-38120 Braunschweig
Germany
Sodium Iodide $^{131}$I Injection 925 MBq/ml

**IBS25P**

Primary Label (Vial)

Sodium Iodide $^{131}$I Injection 925 MBq/ml

**IBS25P**

Secondary Label (Lead Pot)