SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sodium iodide Na\(^{131}\)I, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium iodide Na\(^{131}\)I

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is used for diagnostic procedures of thyroid function (hyperthyroidism and hypothyroidism), to determine the localisation of thyroid tissue (including ectopy), its size, shape, functional characteristics of focal lesions such as cold (not trapping iodine) and warm (trapping iodine to the same extent as normal thyroid parenchyma) nodules. It is a basic radioscopie to detect metastatic lesions of differentiated tumours of the thyroid (following the surgical removal of the thyroid or radioisotopic ablaction).

Scintigraphy of thyroid gland and thyroid carcinoma metastases. In the therapy of: nodular goitre, hyperthyroidism in Graves-Basedow’s disease, autonomous thyroid nodules, Plummer’s disease. This medicinal product is used for the thyroid residue ablation after surgery of differentiated thyroid cancers and in the treatment of differentiated thyroid carcinoma metastases.

4.2 Posology and method of administration

Sodium iodide \(^{131}\)I, solution for injection is the formulation designed for the intravenous administration. The medicinal product can be administered directly to the patients in the various radioactivity doses, appropriate to the treatment and dependent on the purpose: the doses are different in the diagnostic and therapeutic procedures.

The recommended therapeutic dose is dependent on clinical assessment performed by medical team. This dose should be established individually for each patient. Taking into consideration dosimetric data of iodine \(^{131}\)I in therapy of metastases the dose of medicinal product should be predetermined, in order to maximise the therapeutic effect on the neoplastic tissue and limit the harmful influence on the surrounding tissues; however, at the same time minimize the risk of development of health complications.

The dose is established based on the dosimetric calculations considering: thyroid volume, effective half-life for \(^{131}\)I and empirically determined sensitivity of a pathological lesion to ionising radiation. It is assumed that the dose absorbed in case of immunogenic hyperfunction should range from 40 to 80 Gy, in case of autonomic nodules: 300 - 400 Gy and in neutral goitre: 150 Gy.

In the treatment of:

- hyperfunctional nodular goitre: 185 - 370 MBq;
- autonomic nodules: 740 - 925 MBq;
- Graves – Basedow’s disease: 185 - 555 differentiated thyroid tumours: 1850 - 9250 MBq.

The dose activity \(A\) (MBq) can be calculated using the formula below:

\[
A = (25 \times m \times 10^3) / (\text{F}_{\text{max}} \times T_{\text{eff}}) \text{ MBq}
\]

Where \(m\) is the mass of thyroid gland expressed in grams, calculated after scintigraphy performed by planimetric method:

\[
M = 0.214 \times 1.06 (\text{cm}^3)
\]

\(A\) = scintigram area of thyroid gland (in cm\(^2\))

\(D\) = the recommended value of absorbed dose, suitable for the individual case, expressed in Gy

\(\text{F}_{\text{max}}\) = maximal absorption of \(^{131}\)I expressed in %, obtained in absorption - wash out test of radioactive iodine from thyroid gland

\(T_{\text{eff}}\) = effective half-life, expressed in days, approximate results obtained from absorption - wash out test of radioactive iodine from thyroid gland.

The activity of a radiopharmaceutical administered to patients should always be considered in relation to its value in diagnosis and therapy. It is especially relevant to administration of ablative \(^{131}\)I dose which may cause serious side effects.

The dose administered for the treatment of hyperthyroidism is calculated from the knowledge of the 24 hours uptake value, the estimated thyroid mass and the effective half-life of \(^{131}\)I in the thyroid gland. The half-life of \(^{131}\)I is 6 days for a normal thyroid gland and is shorter in hypothyroidism.

4.3 Contraindications

No side effects and contraindications were observed after the administration of diagnostic doses of iodine-\(^{131}\)I. Radiotherapy should not be used in patients with renal failure. This radiopharmaceutical is also not recommended for use in patients under 40 years of age, pregnant women and breastfeeding mothers. There is a risk of hypothyroidism after administration of therapeutic doses in the treatment of benign thyroid gland diseases.

4.4 Special warnings and precautions for use

The radiopharmaceuticals may be used only by authorized persons. Safety precautions for careful handling this radiopharmaceutical should be observed. Ensure protection of the staff and patients against unnecessary exposure to ionising radiation. Permit to store and administer radiopharmaceuticals depends on specified local standards and regulations for radioactive materials. The solution with determined radioactivity can be administered directly to the patients. Patients exposed to the high doses of \(^{131}\)I need to be hospitalised because of the high radiological risk.

4.5 Interactions with other medicinal products and other forms of interactions

Various factors affect the absorption of iodine in thyroid gland. High iodine concentrations in blood cause decrease of iodine absorption in thyroid gland. The increase of iodine concentration in blood can be caused by the diet, performed radiographic procedures with contrast agent containing iodine (radiodiagnostic of gall bladder or kidneys) or using the expectorant medicines. The cause of low absorption rate in thyroid gland can also be many other medicines (perchlorates, rhodanates, chlorides, iodides, etc.), that imitate chemical action of iodine in physiological functions of thyroid gland. Other factors reducing the absorption in thyroid gland are: methimazols (Tapazole) and PTU, that interfere with iodine conversion to organic compounds. Glucocorticosteroids, progesterone, T3 and T4 also reduce the iodine absorption in thyroid gland, while administration of TSH leads to increase of iodine absorption in thyroid gland.

Taking into account all these factors, the physician should be aware of the previous treatment history of the patient.

4.6 Pregnancy and lactation

When it is necessary to administer radiopharmaceuticals to women of childbearing potential, information should always be sought about pregnancy. Pregnancy should be excluded in any women who has had menstrual cycle disturbances. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. Breastfeeding should be interrupted following administration of the first dose of radiopharmaceutical product due to potential risk for the child. It can be restarted when radiation dose potentially received by the child during breastfeeding and contact with mother is within the range of approved standards. Where uncertainty exists it is important to minimize the radiation exposure during examinations.

Alternative techniques which do not involve ionising radiation should be considered.

4.7 Effects on ability to drive and use machines

The radiopharmaceutical has no influence on ability to drive and use machines.

4.8 Undesirable effects

The exposure to radiation should be substantiated by benefits resulting from the performed test. The administered radioactivity should be adjusted in order to achieve the desired diagnostic effect and possibly lower the radiation dose to the patient. The exposure to ionising radiation is linked with the risk of cancer induction and potential for hereditary defects. For diagnostic nuclear medicine investigations the current statistical evidence suggests that the radiation doses related to the examinations are very low and therefore the frequency of these adverse effects is low. As a result of administration of this radiopharmaceutical, decrease of bone marrow function and/ or hypothyroidism can be observed.

4.9 Overdose

The radiation dose resulting from administration of a radiopharmaceutical should always be substantiated by its diagnostic and therapeutic value. This is especially relevant to administration of an ablative \(^{131}\)I dose which may cause serious side effects.

The medicinal product is supplied in vials, which enable the physician calculation of the dose administered for the treatment of hyperthyroidism.
5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic and therapeutic radiopharmaceutical

ATC code: V 09F X03, V 10X A01

Iodine 131I is accumulated in the thyroid gland, leading to irradiation of thyroid gland with β and γ particles, whereas 90% of radioactivity consists of β particles. Uptake of iodine from the blood serum into the thyroid gland is the active form of transport through the membrane of thyroid gland cells.

The therapy based on isotope 131I is a useful and widely used supplementary method of treatment of thyroid gland cancer. Side effects are assessed as mild, and serious complications are rare, so that the benefits of therapy exceed its potential risk. After 131I preparation is administered, the absorption of radiation in patient’s body is to a considerable degree dependent on the functional status of thyroid gland. In healthy volunteers iodine thyroid uptake is prompt and complete.

5.2 Pharmacokinetic properties

Radioactive iodine is eliminated mainly in the urine, but small radioactivity doses are present in sweat and faeces. Radioactive iodine is secreted into the breast milk. Thyroid takes up iodine from the blood serum via the active transport through the thyroid gland cells membrane. There the iodide is oxidized to iodine and then built into the thyroxyl residues of thyroglobulin. Under normal conditions, every hour approximately 2% of free circulating radioactive iodine is absorbed in the thyroid gland. Maximum iodine uptake in the thyroid gland appears within 24 hours and is associated with the iodide concentration in the diet.

The concentration of radioactive iodine in the thyroid gland depends on its ability to bind iodine and its volume. A small percentage of iodide is also accumulated in the salivary glands and the stomach mucosa.

5.3 Preclinical safety data

LD₅₀ value was assessed using a Thompson-Well method and it is 718 mg/kg of b.w.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- sodium carbonate
- sodium bicarbonate
- sodium thiosulphate pentahydrate
- sodium chloride
- water for injection

6.2 Incompatibilities

Some medicinal products, that decrease the ability of thyroid gland to take up iodide, can affect the distribution of iodine 131I in the thyroid gland. These are preparations containing iodide ions (Lugol’s solution etc.), contrast agents, antithyroid drugs (Tapazole, propylthiouracil) natural and synthetic thyroid preparations and anions: TO₄, Br⁻, CIO₄, SCN⁻.

6.3 Shelf life

28 days from the production date.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Sodium iodide NaI solution for injection is supplied in the 10 ml multi-dose glass vial. The vial is sealed with the rubber stopper and aluminium cap, placed in the lead shielding container.

6.6 Special precautions for disposal and other handling

This radiopharmaceutical may be received, used and administered only by authorised persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of the local competent official organizations. Radiopharmaceuticals should be prepared by the user in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken, complying with the requirements for pharmaceuticals. Unused product or radioactive waste should be disposed of in accordance with regulations for radioactive materials.

7. MARKETING AUTHORISATION HOLDER

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Phone: +48 22 7180700
Fax: +48 22 7180350
e-mail: polatom@polatom.pl

8. MARKETING AUTHORISATION NUMBER(S)

RO071

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION


The absorbed dose per activity unit, administered to patient [mGy/MBq]

<table>
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<tr>
<th>Organ</th>
<th>Adult</th>
<th>15 years</th>
<th>10 years</th>
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<tr>
<td>Adrenals</td>
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<td>0.042</td>
<td>0.067</td>
<td>0.110</td>
<td>0.200</td>
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<tr>
<td>Bladder wall</td>
<td>0.610</td>
<td>0.750</td>
<td>1.100</td>
<td>1.800</td>
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<td>Bone surfaces</td>
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<td>0.061</td>
<td>0.097</td>
<td>0.190</td>
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<td>Breast</td>
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<td>0.033</td>
<td>0.052</td>
<td>0.085</td>
<td>0.170</td>
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<tr>
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<tr>
<td>Stomach wall</td>
<td>0.034</td>
<td>0.040</td>
<td>0.064</td>
<td>0.100</td>
<td>0.190</td>
</tr>
<tr>
<td>Small intestine</td>
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<td>0.047</td>
<td>0.075</td>
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<td>LLI wall</td>
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<td>0.045</td>
<td>0.070</td>
<td>0.120</td>
<td>0.210</td>
</tr>
<tr>
<td>LLI wall</td>
<td>0.043</td>
<td>0.052</td>
<td>0.082</td>
<td>0.130</td>
<td>0.230</td>
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<tr>
<td>Kidneys</td>
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<td>0.080</td>
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<td>0.170</td>
<td>0.310</td>
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<tr>
<td>Liver</td>
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<td>0.040</td>
<td>0.085</td>
<td>0.100</td>
<td>0.200</td>
</tr>
<tr>
<td>Lungs</td>
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<td>0.038</td>
<td>0.060</td>
<td>0.096</td>
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<tr>
<td>Ovaries</td>
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<tr>
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<td>0.210</td>
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<tr>
<td>Bone marrow</td>
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<td>0.042</td>
<td>0.065</td>
<td>0.100</td>
<td>0.190</td>
</tr>
<tr>
<td>Spleen</td>
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<td>0.040</td>
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<td>0.100</td>
<td>0.200</td>
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<tr>
<td>Testes</td>
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<td>0.075</td>
<td>0.120</td>
<td>0.230</td>
</tr>
<tr>
<td>Thyroid</td>
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<td>0.038</td>
<td>0.063</td>
<td>0.100</td>
<td>0.200</td>
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<tr>
<td>Uterus</td>
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<td>0.067</td>
<td>0.110</td>
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<td>0.300</td>
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<tr>
<td>Other tissue</td>
<td>0.032</td>
<td>0.039</td>
<td>0.082</td>
<td>0.100</td>
<td>0.190</td>
</tr>
</tbody>
</table>

Effective dose equivalent [mSv/MBq]

<p>| | | | | | |</p>
<table>
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<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Bladder wall</td>
<td>0.072</td>
<td>0.088</td>
<td>0.140</td>
<td>0.210</td>
<td>0.400</td>
</tr>
</tbody>
</table>

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

10. DATE OF REVISION OF THE TEXT OF SUMMARY OF PRODUCT CHARACTERISTICS

04.10.2013

11. DOSIMETRY

Iodine 131I disintegrates by emitting gamma radiation with the most significant gamma photon of energy 0.365 MeV and half-life of 8.02 days. The radioactive dose absorbed by a patient depends on the ability of the thyroid gland to take up iodine and on the thyroid blockers.

The model which is used to calculate the doses of 131I refers to intravenous administration, however the radiiodine tests of thyroid function are usually performed with oral administration. Since absorption of radiodiode is rapid and complete, the intravenous model is applicable in this case also, but there is a further radiation dose to the stomach in addition to that due to iodide in gastric and salivary secretions.

Assuming a mean residence time in the stomach of 0.5 h, the absorbed dose to the stomach wall is increased by about 30% when compared with intravenous model. Changes in absorption by other organs and tissues are very small.

The model for the case of a blocked thyroid is the same, except that there is no specific uptake in any organ or tissue. A uniform distribution is assumed, together with an excretion half-time of 8 h.

For a 55% thyroid uptake of 131I, the effects of circulating organic iodine and recycled iodide are to increase the self doses to body organs other than thyroid, GI tract and bladder.

After the administration of iodine radiouclide, the dose absorbed by the thyroid gland depends on its ability to take up iodine as it is stated in ICRP 53: Annals of the ICRP, Radiation dose to Patients from Radiopharmaceuticals. Vol.18 No.1-4, 1987, p.259-278.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

The radiopharmaceutical product is supplied as a ready for use solution for injection. Regulations for safety of work at exposure to ionising radiation should be strictly observed during administration of radiopharmaceutical.