The patients exposed to a high dose of radioisotope for radioactive materials. Safety precautions for careful handling this radiopharmaceutical should be observed. Ensure Radiopharmaceuticals may be used only by authorized persons in designated clinical settings. 4.4 Special warnings and precautions for use 4.3 Contraindications

The activity of the radiopharmaceutical administered to patients should always be considered in relation to its diagnostic value. In diagnostics, the oral administration of 1 - 4 MBq of sodium iodide (Na$^{131}$), "warm" (trapping iodine at a similar extent to normal thyroid parenchyma), "hot" (trapping iodine at a higher extent than normal thyroid parenchyma) nodules. It is the basic radiophosphate in the diagnosis of metastatic lesions of differentiated thyroid cancers (following the surgical removal of the thyroid or radioscintilation ablation).

4.2 Posology and method of administration

Sodium iodide Na$^{131}$ POLATOM, capsules for diagnostic use, is a preparation for oral administration. In diagnostics, the oral administration of 1 - 4 MBq of sodium iodide (Na$^{131}$) is recommended 24 hours prior to the scintigraphic examination of the thyroid.

The activity of the radiopharmaceutical administered to patients should always be considered in relation to its diagnostic value. 4.3 Contraindications

The preparation must not be administered to pregnant and breastfeeding women. Its use is not recommended in children under 10 years of age. 4.4 Special warnings and precautions for use

Radiotherapeutics may be used only by authorized persons in designated clinical settings. 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 patients exposed to a high dose of radiophosphate need to be hospitalized because of high radiological risk. 4.5 Interactions with other medicinal products and other forms of interaction

The uptake of the preparation by the thyroid may be inhibited by:

- excess iodine in patient's diet (e.g. multivitamin preparations)
- use of iodine-based contrasts (radiological examination)
- steroid hormones, thyroid hormones (triiodothyronine, thyroxine), bromides, nitrates, perchlorates, thiocyanates, thiourea derivatives (propylthiouracil, methimazole, methimazole, amiodarone).

Administration of TSH (thyroid-stimulating hormone) leads to an increase of iodine uptake by the 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 women who has had menstrual cycle disturbances. Any woman who has missed a period should be assumed to be pregnant until proven otherwise.

Examinations using radiopharmaceuticals in women of childbearing potential should be carried out during the first (about 10) days following the onset of menses. Pregnancy should be avoided for 1 year following the treatment.

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 reduce 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 low and therefore the frequency of these adverse effects is low. For most diagnostic nuclear medicine investigations the absorbed dose to the patient is less than 20 mSv.

For sodium iodide Na$^{131}$ POLATOM, capsules for diagnostic use, whose activity is 1 - 37 MBq, this level is usually slightly higher.

4.9 Overdose

The preparation is supplied as a known activity capsule, which facilitates control of the dose administered to the patient. However, in the event of overdose, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radioidine from the body by forced diuresis and administration of liquids.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic radiopharmaceutical ("I")

ATC code: V 06 F 03

5.2 Pharmacokinetic properties

$I^{131}$ accumulates in the thyroid gland, leading to the irradiation of this gland with $\beta$ and $\gamma$ particles. 90% of the whole radioactive dose is contributed by $\beta$ particles. $I^{131}$ radionuclide-based diagnostics is a valuable and widely used supplementary method of thyroid tissue evaluation. Its side effects are considered small, and serious complications occur rarely, so that the benefits of diagnostics exceed its potential risk.

After the administration of a capsule containing $Na^{131}$, the absorption of radiation in the patient’s body is considerably dependent on the functional state of the thyroid. In healthy volunteers the iodine thyroid uptake is rapid and complete.

When administered orally, the preparation is effectively absorbed from the gastrointestinal tract into the bloodstream. Within 60 minutes following the oral administration of a capsule, the concentration of iodine-$131$ in the blood reaches approximately 98% of maximum. The $I^{131}$ accumulates in the thyroid due to active transport through the gland's cell membranes. Iodine is then oxidized in the thyroid into iodine and is incorporated into thyroglobulin thyroid residues. Under normal conditions, every hour approximately 2% of free circulating radioactive iodine is absorbed in the thyroid gland.

Maximum iodine uptake in the thyroid occurs within 24 hours and is associated with the iodide concentration in the diet. The concentration of radioactive iodine in the thyroid depends on its ability to bind iodine and its tissue volume. A small percentage of iodide is also accumulated in the salivary glands and the stomach mucosa. Radioactive iodine is mainly excreted in urine, but small radioactivity doses are present in sweat and faeces. Radioactive iodine is secreted into the breast milk.

5.3 Preclinical safety data

With respect to the daily iodine consumption, the administered doses do not have any toxic effect on the human body. There is also no data on mutagenic or carcinogenic effects of sodium iodide.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium carbonate
Sodium bicarbonate
Disodium hydrogen phosphate dihydrate
Sodium thiosulphate pentahydrate
Hard gelatin capsules (bovine gelatin, dyes: titanium dioxide, quinoline yellow, indigotine, erythrosine, iron oxides).

6.2 Incompatibilities

The uptake of the $I^{131}$ by the thyroid may be affected by various pharmaceuticals which decrease the uptake. These are preparations containing iodides (Lugol’s solution etc.), iodine contrasts, antithyroid drugs (tapazoles, propylthiouracil), natural and synthetic thyroid preparations and $TcO_4$.$^-$, $Br_2$, $ClO_4^-$, $SCN$ ions.

6.3 Shelf life

21 days from the production date.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of the container

Sodium iodide Na$^{131}$ POLATOM, capsules for diagnostic use, are supplied in the following types of immediate packages:

First type of container:
The Na$^{131}$ capsules with an activity of 1 - 4 MBq are supplied in the polypyrrole vials, sealed with the polyelethylene stoppers. Vials are placed in the shielding lead containers. A single vial can contain up to 10 capsules of the same radioactivity.

Second type of container:
The Na$^{131}$ capsules, with an activity of 1 - 37 MBq are supplied in the polypyrrole vials, sealed with stoppers equipped with charcoal filter, and placed in shielding lead containers. Each vial contains a single capsule. Each box is accompanied by a separate applicator for capsule administration.

6.6 Special precautions for disposal and other handling

This radiopharmaceutical may be received, used and administered only by authorized 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. Any unused product or waste should be disposed of in accordance with regulations for radioactive materials.

7. MARKETING AUTHORISATION HOLDER

National Centre for Nuclear Research
Andrzej Soltan 7, 05-400 Otwock, Poland
Phone: +48 22 7160700
Fax: +48 22 7160350
e-mail: polatom@polatom.pl

8. MARKETING AUTHORISATION NUMBER

19004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11. DOSIMETRY

Iodine $^{131}$I 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 $^{131}$I refers to intravenous administration, however the radioiodine tests of thyroid function are usually performed with oral administration. Since absorption of radioiodine 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.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Adults</th>
<th>15-years</th>
<th>10-years</th>
<th>5-years</th>
<th>1 year</th>
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<tbody>
<tr>
<td>Adrenals</td>
<td>0.037</td>
<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>
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<td>0.075</td>
<td>1.100</td>
<td>1.800</td>
<td>3.400</td>
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<tr>
<td>Bone surfaces</td>
<td>0.032</td>
<td>0.038</td>
<td>0.061</td>
<td>0.097</td>
<td>0.190</td>
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<tr>
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<td>0.033</td>
<td>0.052</td>
<td>0.085</td>
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<tr>
<td>Gastrointestinal tract</td>
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<tr>
<td>Stomach wall</td>
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<td>0.040</td>
<td>0.064</td>
<td>0.100</td>
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</tr>
<tr>
<td>Small intestine</td>
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<td>0.075</td>
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<td>0.220</td>
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<tr>
<td>ULI wall</td>
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<td>0.045</td>
<td>0.070</td>
<td>0.120</td>
<td>0.210</td>
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<tr>
<td>LLI wall</td>
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<td>0.052</td>
<td>0.082</td>
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<tr>
<td>Kidneys</td>
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<td>0.080</td>
<td>0.120</td>
<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>0.065</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>
<td>0.190</td>
</tr>
<tr>
<td>Ovaries</td>
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<td>0.054</td>
<td>0.084</td>
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<tr>
<td>Pancreas</td>
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<td>0.043</td>
<td>0.069</td>
<td>0.110</td>
<td>0.210</td>
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<tr>
<td>Red 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>
<td>0.065</td>
<td>0.100</td>
<td>0.200</td>
</tr>
<tr>
<td>Testes</td>
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<td>0.075</td>
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<td>0.230</td>
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<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>
<td>0.170</td>
<td>0.300</td>
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<tr>
<td>Other tissues</td>
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<td>0.039</td>
<td>0.062</td>
<td>0.100</td>
<td>0.190</td>
</tr>
<tr>
<td>Effective dose equivalent</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.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

The radiopharmaceutical is supplied as a capsule of ordered activity (the activity is determined at 12h on the day of calibration).

Instructions for opening the container with the radioactive product:

First type of container:
1. Tear off the upper cover of the shipping container (metal tin).
2. Remove the upper styrofoam inlay.
3. Take the capsule shielding container out.
4. Remove the upper cover of the lead shielding container.
5. Remove the plastic cap from the polypropylene vial inside the lead container.
6. Using a tweezers, take out the capsules separately from the vial.

Second type of container:
1. Tear off the upper cover of the shipping container (metal can).
2. Remove the upper styrofoam inlay.
3. Take the capsule shielding container out.
4. Tear the paper foil-mouthpiece wrapping and take out the mouthpiece.
5. Open the shielding container containing the capsule. To do this, hold the bottom part of the container and pull the upper part upwards. The insert containing the capsule should remain in the shielding container.
6. Connect the mouthpiece to the insert. To do this, press the mouthpiece into the insert containing the capsule. A snap fastener fixes two parts firmly together.
7. It is recommended to keep the capsule insert in the shielding container during the administration of the capsule. The patient holding the shielding container in his hands takes the mouthpiece opening in his mouth and then tilts it to get the capsule from the insert through the mouthpiece.
8. After the administration of the capsule, dispose of the mouthpiece and the insert. The shielding container should be returned to the manufacturer.
9. To disconnect the mouthpiece from the insert, put the insert with the mouthpiece in the shielding container, and then hold the container with your hand till the mouthpiece aside in order to disconnect it. During disconnecting the mouthpiece should not be damaged and if it remains clean, it can be used again.
10. To measure the capsule activity, take the mouthpiece fixed to the capsule insert with the gripping device of the dose calibrator and load in the dose calibrator. When the measurement is finished remove the mouthpiece fixed to the capsule insert and place it back in the shielding container. When transferring the capsule to another room the mouthpiece should be disconnected from the insert according to instructions in pt. 9. After disconnecting the mouthpiece, cover the shielding container with a lid.

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