The dose recommended in treatment of: thyroid nodular goitre, hyperthyroidism in the Graves-Basedow's disease, autonomic nodule and the Plummer's disease. It is used for the thyroid residue ablation after surgery of differentiated thyroid tumours and in the treatment of metastases of iodine-accumulating differentiated thyroid cancers.

4.1 Therapeutic indications

The preparation is used in the treatment of: thyroid nodular goitre, hyperthyroidism in the Graves-Basedow's disease, autonomic nodule and the Plummer's disease. It is used for the thyroid residue ablation after surgery of differentiated thyroid tumours and in the treatment of metastases of iodine-accumulating differentiated thyroid cancers.

4.2 Posology and method of administration

Sodium iodide Na\(^{131}\)I POLATOM, capsules for therapeutic use with varying radioactivity is a preparation for oral administration.

The recommended therapeutic dose is dependent on clinical assessment performed by medical team. This dose should be established individually for each patient. The dose is established based on the dosimetric calculations considering: tissue volume, effective half-life for iodine-131 in therapy of metastases, the use of medical product should be predetermined, in order to maximize 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 activity of the radiopharmaceutical administered to patients should always be considered in relation to its therapeutic value. It is especially relevant to administration of ablative \(\text{I}^{131}\) 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 \(\text{I}^{131}\) in the thyroid gland.

4.3 Contraindications

The preparation must not be administered to pregnant and breastfeeding women. In diagnostics, the preparation can be used in children under 10 years of age. Another contraindication is impossibility to administer the capsules orally (swallowing disorders, uncooperative patient). In such cases other forms of sodium iodide \(\text{Na}^{131}\)I should be used.

4.4 Special warnings and precautions for use

Radiopharmaceuticals 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. Expose to radiation should be substantiated by benefits resulting from the treatment. The administered radioactivity should be adjusted in order to achieve the desired therapeutic effect and possibly reduce the radiation dose to the patient. The exposure to ionising radiation is linked with the risk of potential hereditary defects. The patients exposed to high doses of \(\text{I}^{131}\)I 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 contrast agents (radiological examination)
- steroid hormones, thyroid hormones (iodothyronines, thyroxine), bromides, nitrates, perchlorates, thionamides, iodides (Lugol's solution), sulphonamides, thiourea derivatives (propylthiouracil, methythioracil), imidazole derivatives, amiodarone.

Administration of exogenic TSH (thyroid-stimulating hormone) leads to an increase in the thyroid uptake of \(\text{I}^{131}\)I radionuclide by the thyroid may be affected by various pharmaceuticals which inhibit or stimulate the sodium iodide transport system at its apical or basolateral membrane.

4.6 Pregnancy and lactation

The preparation is not allowed to be administered to pregnant and breastfeeding women. 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 women who has missed a period should be assumed to be pregnant until proven otherwise. Pregnancy should be avoided for 1 year following the treatment. Breastfeeding should be interrupted following administration of the first dose of radiopharmaceutical 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 treatment. Treatment should be stopped breastfeeding for a period appropriate to the activity administered and the retention of the preparation in the patient's body.

4.7 Effects on the ability to drive and use machines

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

4.8 Undesirable effects

Some of the undesirable effects occurring within the first few hours following the administration of the preparation at high doses are: thyroid inflammation, pain in the salivary glands, mouth dryness, incomplete Sjogren syndrome - mainly dryness of the oral mucosa, nausea, occasional vomiting, sore throat.

The late undesirable effects, occurring several weeks or months after the administration of the preparation (not earlier than in the 6th – 12th week) are thrombocytopenia and anemia. Temporary leucopenia is also a common symptom. Sodium iodide (Na\(^{131}\)I) can often induce hypothyroidism.

Thyroid cancer radiotherapy may cause a decrease in fertility in men and women.

The exposure to ionising radiation is linked with the risk of cancer induction (when high activities are used) and potential for hereditary defects.

Epidemiological data suggests an increased chance of stomach and breast cancers in patients treated with sodium iodide (Na\(^{131}\)I).

4.9 Overdose

The preparation is supplied as a capsule of known radioactivity, 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 radiodine from the body for forced diuresis and administration of fluids.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Radiopharmaceuticals are classified as therapeutic radiopharmaceuticals (\(\text{Na}^{131}\)I). The absorption of radiopharmaceutical in the patient's body is considerably dependent on the functional state of the thyroid. In healthy volunteers the iodine thyroid uptake is prompt 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 \(\text{Na}^{131}\)I accumulates in the thyroid due to active transportation through the gland's cell membranes. Iodine is then oxidized in the thyroid into iodine and incorporated into thyroidglobulin 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 iodides is also accumulated in the salivary glands and the stomach mucosa.

Radioactive iodine is mainly excreted in urine, but small radioiodine doses are present in sweat and feces. 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. PHARMACOLOGICAL PARTICULARS

6.1 List of excipients

Sodium carbonate

Sodium bicarbonate

Disodium hydrogen phosphate dihydrate

Sodium carbonate

6.2 Incompatibilities

The uptake of \(\text{I}^{131}\)I radionuclide by the thyroid may be affected by various pharmaceuticals which decrease the uptake. These are preparations containing iodides (Lugol's solution etc.), iodine compounds, and antithyroid drugs (thioglycolates, propylthiouracil), natural and synthetic thyroid preparations and T3, T4, T3/T4, T3/T4/THYROID ANIMALS.

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 container

Gelatin capsules for therapeutic use are provided in two types of direct packaging: a glass vial with a certificate of radiopharmaceutical activity and a separate polypropylene applicator (\(\text{Na}^{131}\)I) to breastfeeding women, they should be advised not to breastfeed 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 treatment. Treatment should be stopped breastfeeding for a period appropriate to the activity administered and the retention of the preparation in the patient's body.

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6.6 Special precautions for disposal and other handling

This radiopharmaceutical may be reused, received 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 AUTHORITY HOLDER
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Tel.: +48 22 7186700
Fax: +48 22 7186350
e-mail: polatom@polatom.pl

8. MARKETING AUTHORIZATION NUMBER
R6268

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF APPROVAL/REVISION OF THE TEXT
23.12.2011

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 iodine 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 $^{131}I$, the effects of circulating organic iodine and recycled iodide are to increase the self-doses to bodies other then thyroid, GI tract and bladder.

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12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMaceuticalS

The radiopharmaceutical is supplied as a capsule of ordered radioactivity (the activity is determined by the shielding container).

Instructions for opening the container with the radioactive product using the applicator TYPE A:

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. 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 hand takes the mouthpiece opening in his mouth and then lifts 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 mouthpiece into the shielding container, then hold the container with your hand till the mouthpiece aside in order to disconnect it.
10. In order to measure the capsule activity, take the mouthpiece fixed to the capsule insert with the gripping device of the dose calibrator and load it 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.

Instructions for opening the container with the radioactive product using the applicator TYPE B:

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. 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, screw in 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 hand takes the mouthpiece opening in his mouth and then lifts 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 mouthpiece into the shielding container, then hold the container with your hand screw off the mouthpiece in order to disconnect it.
10. In order to measure the capsule activity, take the mouthpiece fixed to the capsule insert with the gripping device of the dose calibrator and load it 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.