1. NAME OF THE MEDICAL PRODUCT

**I-131-Sodium iodide injection for therapeutic purposes**

I-131-Sodium iodide containing sterile injection for intravenous application. Contains no added iodide carrier.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<table>
<thead>
<tr>
<th>Denomination of the components</th>
<th>Quantity per volume units</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Active ingredient</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natrium radioiodatum (131I)</td>
<td>18.5-37 MBq/ml</td>
<td>Local, lesion-specific radiation therapeutic effect</td>
</tr>
<tr>
<td></td>
<td>740-1850 MBq/ml</td>
<td></td>
</tr>
<tr>
<td>Phosphorus in the form of sodium phosphate</td>
<td>3.3 - 3.9 mg/ml</td>
<td>buffer</td>
</tr>
</tbody>
</table>

3. PHARMACEUTICAL FORM

Sterile, radioactive injection

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medical product is for RADIONUCLIDE THERAPY of the following diseases

a) Hyperthyreosis:
- Radionuclide therapy of the hyperfunction, decrease of the size of the thyroid.
  - Treatment of Basedow disease
  - Treatment of hyperfunction adenomas
  - Treatment of non-immunogen, diffuse goitre

b) Thyroid carcinoma:
- Radionuclide therapy treatment
  - Destruction of the remaining thyroid tissues after the operation of the thyroid (ablatio)
  - Treatment of recidives and metastases

4.2 Posology and mode of administration

a) Treatment of hyperthyreosis

The administerable activity is to be calculated from the recommended absorbed dose with the following formula. On the other hand an activity originating from and determined by other recommendations may also be administered.

Recommended absorbed dose values:
– For treatment of Basedow disease: 40-80 Gy
– For treatment of hyperfunction adenoma: 300-400 Gy
– For treatment of non-immunogen, diffuse goitre: 150-200 Gy

Activity to be administered: A (MBq)

\[ A (\text{MBq}) = \frac{25 \times M (\text{g}) \times D (\text{Gy})}{F_{\text{max}} (%) \times T_{\text{eff}} (\text{day})} \]

where M is the mass of the thyroid in grams, which is to be calculated from the scintigram by the planimetry method:

\[ M = 0.214 \times 1.06 \sqrt{A^3} \]

A = area of the thyroid scintigram in square centimetres (cm²)
D = recommended absorbed dose value for the relevant kind of disease type in Gy
Fmax = maximum I-131 uptake in %, obtained in the radioiodine uptake – wash-out examination
Teff = effective half life in days, coming from the result of the radioiodine uptake – wash-out examination.

Activity values applied for treatment of hyperthyreosis usually fall in the range of 50 MBq – 1 GBq.

b) Treatment of thyroid tumour:– In case of ablation following the operation of thyroid tumour: 1.8-3.7 GBq/patient.
– Before treating local recidives and metastases 370 MBq I-131 activity is administered and a total body exposure is taken after 48-72 hours. Depending upon the number and the expansion of the metastases the treatment is carried out by administering of 3.7-7.4 GBq I-131.

Mode of administration:
The general mode of administration is intravenous injection. In case of small activity per os (oral) administration is permitted, too.

4.3 Contraindications

RELATIVE CONTRAINDICATIONS
The use of the product is relatively contraindicated
– at the age below 18 years
except when the necessity and importance of the treatment prevails the risk originating from the radiation exposure.

ABSOLUTE CONTRAINDICATIONS
The use of the product is absolutely contraindicated
– in case of pregnant or lactating women,
– if the patient does not provide an oral or written consent of being treated by radionuclide therapy.

4.4 Special warnings and special precautions for use
The product is a radioisotope containing pharmaceutical. The rules for handling, transportation and storage of radioactive materials are applicable for the product. The pharmaceutical can only be applied by
properly qualified and trained personnel within designated clinical settings, which possess the appropriate government authorisation for the use and manipulation of radioisotopes. The treatment of hyperthyreosis can be carried out in ambulant way as well. Such in case the relevant international and national prescriptions and regulations should be taken into consideration concerning the patient’s way of living are to be kept (mode of traffic, urination, living with family members, etc.). The radionuclide therapy treatment of thyroid tumor can only be carried out in a designated health institute (hospital, clinic) with taking consideration of the relevant regulations.

4.5 Interactions with other medicinal products and other forms of interaction. Hindered I-131 uptake is disadvantageous both in case of thyroid scintigraphy and thyroid radionuclide therapy, therefore, introduction of inactive iodine is to be avoided. Such treatments are to be terminated prior to the administration of radioiodide according to the following table:

<table>
<thead>
<tr>
<th>Treatment with</th>
<th>Termination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metothyrin</td>
<td>4-7 days before I-131 administration</td>
</tr>
<tr>
<td>Triiodothyronine</td>
<td>2 weeks before I-131 administration</td>
</tr>
<tr>
<td>Thyroxine</td>
<td>1 month before I-131 administration</td>
</tr>
<tr>
<td>Steroids</td>
<td>1 week before I-131 administration</td>
</tr>
<tr>
<td>Salicilates</td>
<td>1 week before I-131 administration</td>
</tr>
</tbody>
</table>

he clearance of radioiodide from the thyroid – in case of necessity – can be slowed down with lithium-carbonate. Colchicin also reduces the radioiodide clearance rate.

4.6 Application during pregnancy and lactation
Application of the product during pregnancy and lactation is contraindicated.

4.7 Effect of the product on ability to drive and on working in circumstances of significant accident risk The product has no direct influence on ability of car driving or working in hazardous circumstances. In occurrence of unexpected side effects the ability to drive and the aptitude to work amidst accident risk are to be reconsidered.

4.8 Undesirable effects
Occurrence of undesirable effects and symptoms is unexpected.

4.9 Overdose
There is no information available about any actually occurred overdose. Administration of higher activity than prescribed results in unnecessary absorbed radiation dose on the patient and her/his environment, which is to be avoided.
Administration of higher activity than necessary may cause hypothyreosis. In occurrence of an eventual overdose the effective absorbed radiation dose is to be calculated with using the dosimetry table of the section 5.4 and the decision about the necessity and mode of further treatments are to be made based on the result.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Iodine is a microelement of vital importance, which is inevitably necessary to the synthesis of the metabolism regulating thyroid hormones. 90% of I-131-sodium-iodide introduced into the body gets to the blood within an hour and 100% of it within 4 hours. From the circulation system it runs to the thyroid, appears in the salivary glands, the placenta and it is excreted by the plexus chorioideus and the mucous membrane of the stomach. In case of lactating women it appears in the milk as well.

In normal case the body takes up approximately 100-500 µg iodine per day with the food, the optimum quantity is 150-300 µg per day (1). Adults’ minimum daily requirement is 100 µg. approximately 10-60% (mostly 20-30%) of the introduced iodine quantity concentrates in the adults’ thyroid of 20 g weight in average, where it is built in the thyroid hormones and their precursors. The iodine concentration of the thyroid depends upon how extensively the satisfaction of the iodine demand is supported by the iodination of the foodstuffs. In Hungary 414 ± 280 µg/g thyroid value is common. The specific activity of I-131 is at least 1 GBq/µg, therefore, even in case of administering the maximum recommended therapy dose (7.4 GBq) only 7.4 µg is introduced into the body. Comparing this value to the normal iodine intake data it is obvious that the therapy is not carried out by the pharmacokinetic effect of the chemical iodine quantity but it is the consequence of the energy and transmitted to the tissue during the absorption of the beta-particles emitted by I-131 nuclide, which is devoted to the destruction of the thyroid cells. In normal case radioiodine washes out from the body with the urine.

5.2 Pharmacokinetic properties

90% of I-131-sodium-iodide introduced into the body per os gets to the bloodstream within an hour and 100% of it within 4 hours.

The kinetics of the radioiodine uptake in the thyroid highly depends on the degree of the iodine supply of the area where the patient lives. For the normal case:

In places of medium degree of iodine supply 20 ± 9% of the activity appears in the thyroid 2 hours after administration. After 6 hours 32 ±
12% is taken up, while the maximum activity (43 ± 11%) after 24 hours. Only 40 ± 10% is the uptake 48 hours subsequent to the administration. In case of patients with iodine deficiency the uptake is extensive and fast: 80% after 12-18 hours. No wash out can be observed during the first 24 hours. In hyperthyreosis, due to the increased hormone production, both the uptake and the wash out are faster: The uptake can reach 80% within 2-6 hours from the introduction, while the wash out is 50% and then 70% after 24 and 48 hours, respectively. In hypothyreosis and in acute inflamed condition of the thyroid the uptake is of small extent and rate: hardly reaches 20% after 48 hours. The biological half life of the wash out of I-131 from the body is 4 days in normal case, 1-3 days in hyperthyreosis.

The absorbed dose values caused by the introduced I-131-sodium-iodide in function of the maximum uptake in the thyroid are shown in the following table:

<table>
<thead>
<tr>
<th>Organ</th>
<th>Absorbed dose values in case of uptake of different degree in the thyroid mGy/MBq</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5%</td>
</tr>
<tr>
<td>Thyroid</td>
<td>70.2</td>
</tr>
<tr>
<td>Liver</td>
<td>0.054</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.038</td>
</tr>
<tr>
<td>Testes</td>
<td>0.022</td>
</tr>
<tr>
<td>Red bone marrow</td>
<td>0.038</td>
</tr>
<tr>
<td>Stomach wall</td>
<td>0.378</td>
</tr>
<tr>
<td>Whole body</td>
<td>0.065</td>
</tr>
</tbody>
</table>

The I-131 product can contain radionuclide impurities only in quantity less than 0.1%.

6.2 Incompatibilities

Above all, the product is incompatible with acids because in their presence radiiodide is converted into a volatile form (radical or elemental iodine), which – getting to the air – may cause a widespread radioactive contamination in the environment.

Furthermore, the product is incompatible with oxidising agents since they oxidise the present radiiodide (oxidation degree: -1) into elementary radiiodine (oxidation degree: 0), moreover, iodate (oxidation degree: +5) and periodate (oxidation degree: +7) ions may appear. Such components count as radiochemical impurities of the product, their formation is to be avoided.

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6.3 Shelf life
21 days from the day of production.

6.4 Special precautions for storage
The product is to be stored at room temperature (15-25°C); free from acidic vapours and oxidative agents; using appropriate radiation shielding. Storage conditions should be in accordance with the national regulations on radioactive materials.