



SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

¹³¹I-sodium-iodide ThyroTop hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

4-7400 MBq sodium iodide (¹³¹I) per hard capsule

Excipients: disodium hydrogen phosphate dihydrate, sodium thiosulphate
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Colourless hard capsule

Radioactive pharmaceutical containing ¹³¹I-labelled sodium iodide active substance, for oral administration

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Indications **field: radionuclid therapy**

Design of therapy: ; determination of the thyroidal uptake of radioiodine and its saturation curve to design the individual patient dose of the radionuclide therapy in case of hyperthyroidism and thyroid carcinoma.

Treatment of hyperthyreosis

- Graves disease
- Hyperfunctioning adenoma
- Non immunogenic diffuse goiter
- Treatment of thyroid carcinoma
- Ablation of residual thyroid tissues following thyroid cancer surgery
- Treatment of recidivations and metastases

4.2 Posology and method of administration

Use of ¹³¹I-sodium-iodide ThyroTop capsule is contraindicated for children under 18 years of age except if the necessity and importance of obtaining the diagnostic information outweighs the risk associated with the radiation exposure.

Posology

a) For determination of individual patient dose in case of radionuclide therapy: capsule of 4MBq is recommended. The patient takes the capsule per os with some water.

Activity uptake is determined in 1-48 hours after administration at more points in order to get the percentage of maximal uptake.

b) Therapy of hyperthyroidism

Amount of activity to be administered is calculated by using the absorbed dose data and the percentage of maximal iodine uptake. (Or use activity amounts recommended by other sources).

Recommended dose values:

- Graves disease 40-80 Gy
- For treatment of hyperfunctioning adenomas 300-400 Gy
- For treatment of not immunogen diffuse goiter 150-200 Gy

There are two methods for determination of the activity of the ¹³¹I sodium iodide capsule to be administered.

1. Therapeutic activity is calculated after the administration of low activity solution by using the following equation:

$$A = \frac{M \cdot D \cdot 25}{F_{\max} \cdot T_{\text{eff}}}$$

M: mass of thyroid [g], $M = 0.214 \cdot 1.06 \cdot \sqrt{A^3}$

D: dose proposed dose

F_{max} : maximal thyroidal uptake [%]

T_{eff} : effective half life of radioiodine elimination from the thyroid

A: activity to be administered [MBq]

According to the other method diameters of the lobes are determined by means of scintigram and ultrasound. Mass of lobes of thyroid can be determined considering them ellipsoids.

c.) Treatment of thyroid carcinoma administration of capsules with following activities are recommended:

Ablation following thyroid carcinoma surgery: 1.8 – 3.7 GBq/patient

Before treatment of local recidivations and metastases 370 MBq ¹³¹I is administered.

48-72 hours after whole body image is taken. For treatment use 3.7-4.7 GBq ¹³¹I

activity depending on the number and size of metastases.

Method of administration

Required amount of activity is administered per os in one or maximum two capsules.

Swallowing of the capsule can be facilitated by drinking some water.

Method of examination

Monitoring can be performed by imaging with gamma scanner 1 – 48 hours after administration. To prepare thyroid scintigram usually front-view is used, but right and left anterior oblique imaging (LAO, RAO) can also be useful.

4.3 Contraindications

In case of radionuclid therapy of hyperthyreosis and thyroid carcinoma

- Hypersensitivity to active substance or to any of the excipients

and ascertain whether any medications are required to be withheld prior to the administration of ThyroTop hard capsules.

Treatment with the products listed below should be withheld for the proposed period

Preparation / Compound	Withheld prior to treatment
Thyroid staties (e.g. carbimazole, methimazole, propil.thiouracil)	2-5 days before therapy, / some days after therapy
saliylates, steroids, sodium nitroprusside, sodium sulfobromophthalein, anticoagulants, anti-histamines, antiparasitics, penicillins, sulphonamides, tolbutamide, thiopentone phenylbutazon	1 week
Iodine containing expectorants and vitamins	1-2 weeks
Thyroid hormone preparations	About 2 weeks
Amiodarone*, benzodiazepines, lithium	2-6 weeks
Iodine containing preparations for topical treatments	About 4 weeks
iodine containing contrast media	1-9 month
	1 year

* iodine uptake in thyroid tissue can be reduced for some month due to long half-life of iodine containing contrast media

Amiodaron

It has to explored if the patient had been treated with contrast media in the last year and

when.

4.6 Pregnancy and lactation

Use of the product is absolutely contraindicated in case of pregnancy and lactation.

Sodium (¹³¹I) iodide is contraindicated during established or suspected pregnancy or when pregnancy has not been excluded.

When it is necessary to administer radioactive medicinal products to women of childbearing potential, information should always be sought about pregnancy. Any woman who has missed a period should be assumed pregnant until proven otherwise. Alternative techniques which do not involve ionising radiation should be considered.

During treatment of pregnant women with radionuclides the foetus is also exposed to radiation. Absorbed dose after radioiodine treatment is between 10,8 – 599.4 mGy. Absorbed dose higher than 0.5 mGy is considered potential risk to the foetus.

Moreover, iodine accumulates in foetal thyroid in second and third trimester. Therefore in the case of differentiated thyroid carcinoma diagnosed in pregnancy radioiodine treatment should be postponed until after the pregnancy has ended.

Women treated with ¹³¹I-sodium iodide are advised to avoid being pregnant in the following 12 month.

¹³¹I sodium iodide is excreted into the breast milk

Before administering a radioactive medicinal product to a mother who is breast feeding, consideration should be given as to whether the treatment could be reasonably delayed until the mother has ceased breast feeding. After ¹³¹I sodium iodide treatment, lactation must be ceased for undetermined period. If the treatment is inevitable, lactation must be discontinued prior to the therapy. Moreover, contact between mother and infant should be avoided for minimum on week.

4.7 Effects on ability to drive and use machines

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

In occurrence of unexpected adverse reactions driving and/or working with machines should be reconsidered.

4.8 Undesirable effects

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary effects. The radiation dose resulting from therapeutic exposure may result in higher incidence of cancer and mutations. In all cases it is necessary to make sure that the risks associated with the radiation are lower than those of the disease.

The absorbed radiation dose after therapeutic doses of sodium (¹³¹I) iodide is higher than 20 mSv.

Post-marketing experience

The reporting rate of adverse reactions is classified as very common (>1/10), common (>1/100-<1/10), uncommon (>1/1000, <1/100), rare (>1/10000, <1/1,000), very rare (<1/10000, including individual cases).

Nausea, vomiting can occur after administration of high activities. Precaution should be taken in order to avoid the contamination.

Allergic reactions after administration of ¹³¹I-sodium iodide have been reported very rare.

Use of the product should be avoided after such reactions. Adequate devices and

medicaments should be available in case of emergency.

After use of sodium (¹³¹I) iodide capsules undesirable effects listed in the table below have been observed.

General disorders and administration site conditions	Pain oedema of the face, peripheral and generalized oedema
Gastrointestinal disorders	Nausea, vomiting, abdominal pain
Skin and subcutaneous tissue disorders	Skin exanthem, itching, urticaria, angioneurotic oedema
Nervous system disorders	Skin redness
Respiratory, thoracic and mediastinal disorders	Angina
Exocrine disorders	Salivary gland inflammation

Adverse reactions detailed below are consequences of radiation exposure

Short-term effects

Therapeutic quantities of sodium (¹³¹I) iodide may temporarily increase existing Graves disease.

Gastrointestinal disturbances may occur in the first hours to days after administration due to high levels of radioactivity. This can however easily be prevented or counteracted by means of symptomatic treatment.

After treatment with high level radioactivity 1-3 days after administration transient thyroiditis and tracheitis may occur which can be accompanied by constriction of trachea particularly in case of persistent tracheal stenosis.

Sialadenitis may occur along with swelling, pain in salivary gland, partial loss of taste and dry mouth

The incidence varies between 10% (with precautions) and 60 % (without precautions). Sialadenitis is reversible, spontaneously or supported by anti-inflammatory drug treatments. Cases have also occasionally been described of dose-dependent persistent loss of taste and dry mouth, followed by tooth loss. The radiation exposure of the salivary glands should be reduced by stimulating saliva excretion by acidic substances. Lacrimary glands disturbances may occur in 25% of the cases and results in Sjögren-s syndrome. This effect transient but may persist for years in some cases.

In patient having lung metastases radiation –induced pneumonia and pulmonary fibrosis have been reported.

Graves's ophthalmopathy may develop or already existing case may worsen (15-30% of the cases without corticoid treatment)

High levels of uptake of radioiodine in the tissues may induce local pain, discomfort, oedema.

In the treatment of metastasizing thyroid carcinomas with CNS involvement, the possibility of local cerebral oedema and/or an increasing existing cerebral oedema must also be taken into consideration.

Long-term effects

As a long-term effect of earlier radioiodine therapy of hyperthyroidism, dose dependent hypothyroidism may occur weeks or years after treatment. These cases require suitable timed checks, and thyroid hormones replacement. Hypothyroidism usually not develop until 6-12 weeks after treatment; occurrence: 2-70%. Transitional parathyroid gland insufficiency may occur after radioiodine administration. These case must be followed and treat with repositio therapy. As late consequence reversible or very rarely irreversible bone marrow depression may occur after administration of 5000 MBq (one time) or repeated administration in a 6 month range. Isolated thrombopenia or anaemia may aggravate this, and can lead death. Transitional leucocytosis have often been observed but leucopenia occurred very rarely.

Functional disorder of salivary and lacrimary glands resulting in sicca syndrome can be develop one month or even after two years after treatment.

Epiphora resulting from nasolacrimal duct occlusion has been occurred in case of 3% of the patients, usually 3-16 month after treatment.

Salivary gland cancer development after radioiodine induced salivary gland inflammation has been reported in the literature.

Incidence of gastric cancer is higher in patients treated with radioiodine, according to an epidemiologic study.

Incidence of leukaemia as well as bladder and breast cancer are higher after administration of higher doses used in case of thyroid cancer.

Radiotherapy of thyroid carcinoma can lead to an impairment of fertility in man and woman. A dose-dependent, reversible impairment of spermatogenesis has been proven above 1850 MBq; clinically relevant effects including oligospermia and azoospermia, and increased serum FSH values have been described after use of more than 3700 MBq.

4.9 Overdose

No case of overdose has been reported.

Administration of higher activities than prescribed is unnecessary and must be avoided in order to avoid the excess absorbed radiation dose of the patient and his/her environment. Administration of higher activities than needed may cause hypothyreosis.

In case of incidental overdose the actual absorbed radiation dose must be calculated by using the data of the dosimetric table of Chapter 11. Necessity and method of further treatment should be concluded based on these results.

Radiation exposure due to overdose can be reduced by thyroid blocking agents e.g. potassium –perchlorate, vomitory or frequent urination.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotheapeutic group: Therapeutic radiopharmaceuticals; Iodide (¹³¹I)

compounds, ATC code: V10X A 01

The pharmacologically active substance of the capsule is iodine-131 as ¹³¹I-sodium iodide, which enriches in thyroid. Due to its long retention time it decays mainly here leading to selective irradiation of the organ. The small quantity of ¹³¹I-sodium iodide administered during therapy does not produce any pharmacodynamic effects. More than 90% of the radiation effect of iodine-131 are based on the emitted beta-radiation

with a medium irradiation range in the tissue of 0.5 mm which induces dose-dependent reduction of the function and cell division and destruction of the thyroid cells. Due to

reduction of the function and cell division and destruction of the thyroid cells. Due to the short range and practically no storage of ¹³¹I-sodium iodide outside of the thyroid, radiation exposure outside of the thyroid is negligible.

In case of radioactive iodine intake, amount of iodine entering the body is not more than 20 µg. This is 2.4 – 4.9 % of the optimal daily iodine requirement of the human body.

Therefore, the chemical concentration of the active ingredient of the drug product is negligible. Gamma radiation of ¹³¹I provides the diagnostic information and beta particles absorbing in the tissue are responsible for the therapeutic effect.

Excretion of radioactive iodine occurs via the urine.

5.2 Pharmacokinetic properties

Orally applied ¹³¹I-sodium iodide is quickly absorbed in the upper gastrointestinal tract (90 % within 60 min). Absorption is influenced by stomach emptying. Absorbtion is

increased with hyperthyroidism and decreased with hypothyroidism.

In studies of the solubility of ¹³¹I-sodium iodide hard capsules it was proven that the dissolution took place within 5-12 minutes and the radioactivity was distributed homogeneously on the surface of the gastric mucosa. Studies of the serum activity showed that after a fast rise over 10-20 minutes the equilibrium was reached approximately after 40 minutes. After oral administration of a ¹³¹I-sodium iodide the equilibrium was reached at the same time.

The pharmacokinetics is similar to that of non-radioactive, stable iodine. After entrance into the bloodstream iodine-131 distributes in the extrathyroidal compartment. From there it is absorbed mainly by the thyroid, which extracts approx. 20% of the iodide during one passage, or it is renally eliminated. The uptake of the iodine into the thyroid reaches its maximum within 24-48 hours; 50% of the maximum peak are reached within five hours.

The uptake is influenced by a number of factors: age of the patient, volume of the thyroid, kidney clearance, amount of the circulating iodide and other medicinal products (see section 4.5. Interaction with other medicinal products and other forms of interaction). Normally iodine clearance of the thyroid takes 5-50 ml/min, rises under iodine deficiency up to 100ml/min and under hyperthyroidism up to 1,000 ml/min, while it can decrease down to 2-5 ml/min under overloading conditions. Iodine accumulates also in the kidneys; small quantities are taken up by the salivary glands and gastric mucosa and are detectable also in breast milk, in the placenta and the plexus chorioideus.

The iodide taken up to the thyroid follows the well-known metabolism of the thyroid hormones where it is integrated into organic compounds from which the thyroid hormones are synthesised. The effective radioactive half-life of iodine-131 in the plasma is about 12 hours, while it is about six days when stored in the thyroid.

Therefore, after administration of ¹³¹I-sodium iodide about 40% of the activity exhibit an effective radioactive half-life of 0.4 days while the remaining 60% have an effective radioactive half-life of eight days. 37-75% of iodine-131 is eliminated via the kidneys and only a small portion with faeces; elimination via the sweat glands is negligible. Urine excretion is characterised by renal clearance, which amounts to approx. 3% of iodine passage through the kidneys and is relatively constant from individual to individual. It is lower in hypothyrosis and malfunctions of the kidneys and higher in hyperthyroidism.

Mean urine excretion in healthy volunteers (24-hour urine was examined) amounted to 2.8 mg/kg in men and 2.7 mg/kg in women. In euthyroid patients with normal kidney function, 50-75% of the applied activity were excreted with the urine within 48 hours.

5.3 Preclinical safety data

LD₅₀ value, which expresses the acute toxicity of I-131 introduced orally into the body, is 1000 mg/kg body weight for mice and 760 mg/kg body weight for dogs. Since the maximum iodine content of the highest possible dose administered to a patient (7.4 GBq) cannot exceed 20 µg, this is at most 2.4-4.9% of the optimum iodine intake.

Therefore, it is obvious that the product is safe in regard of iodine intake.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each capsule contains:

Disodium hydrogen phosphate dihydrate, sodium thiosulphate, gelatine capsule shell

6.2 Incompatibilities

This medicinal product is incompatible to moisture, water and liquids since these substances moistens and softens the capsule, which can bring about the opening of the capsule, spreading of its load and radioactive contamination.

This product must not be mixed with acids; radioactive iodine takes volatile form in acidic medium, contaminating the environment.

Radioactive iodine is in the capsule in iodide form (oxidation number is -1). Oxidising agents (e.g. acids) oxidise iodide to elemental iodine (oxidation number is 0), iodate (oxidation number is +5) or periodate (oxidation number: +7). These compounds having oxidation number other than -1, are radiochemical impurities of the product and their formation must be avoided.

6.3 Shelf life

21 days from the manufacturing date.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original packaging. Comply with the regulations for radiation safety. Keep away from moisture, acid fumes and oxidative agents.

6.5 Nature and contents of container

Low activity capsules

Low activity ¹³¹I capsules are supplied in vials. 1 to 10 capsules can be packed into one vial. Vials are closed with rubber stopper and aluminium cap. The vial containing the low activity ¹³¹I-sodium iodide capsules are placed into KT-1 lead container, containing paper insert and a plastic foam insert. Not more than 3 vials in lead container are allowed to put into one tin container. Finally the tin container is closed with a tear-off cover.

High activity capsules

High activity ¹³¹I-sodium-iodide capsules are placed into lead container with wall thickness of 15-38 mm, in which a plastic insert with screwed cap (inner diameter 9.5 mm, height 32 mm) has been fixed. Bottom part of the insert is fixed in the bottom of the lead container while the upper part of the capsule is fixed in the upper part of the lead container. The packaging always contains one capsule.

The labelled lead container is packed into a labelled tin container which is closed with a tear-off cover. (Type 'A' packaging)

4-7400 MBq at the date of calibration

Content of packaging:

Hard capsule. The ordered quantity of capsules.

6.6 Special precautions for disposal and other handling

Opening procedure of packaging of low activity capsules

- Tear off the cover of the tin container
- Remove the upper part of the foam insert
- Lift the lead container containing the capsule out from the metal can and put it on the working area in vertical position. Manipulate behind an appropriate radiation shielding
- Remove the upper part of the lead container to open it
- Hold the vial with forceps and remove the aluminium cap of the glass vial by using a decapper
- Remove the rubber stopper of the glass vial with forceps
- Now the capsules can be easily taken out from the vial

Opening procedure of packaging of high activity capsules

- Tear off the cover of the tin container
- Remove the upper part of the foam insert
- If there is a protective lead container in the metal container, lift it out from the metal can
- Lift the lead container containing the capsule out from the metal can or the protective lead container and put it on the working area
- There are two ways of opening the lead container for two different purposes:
 - activity control with closed plastic insert without taking out the capsule or
 - opening the plastic insert with the same movement for taking out the capsule

Opening of lead container for activity measurement

- Manipulate behind an appropriate radiation shielding
- Hold the lower part of the lead container firmly with one hand and pull apart the upper part towards axial direction
- The plastic insert will remain fixed in the upper part of the lead container but the lead shielding will not cover its lower part. In this position the activity measurement can be performed by a laboratory activity measuring unit (dose calibrator) without taking out the capsule from the vial.

After measuring, close the lead container.

Opening of lead container and insert at the same time

- Hold the container in vertical position.
- Screwing the upper part of the lead container counter-clockwise. Both lead container and plastic insert will open.
- The upper part of the plastic insert remains in the upper part of the lead container, while the lower part of the vial, containing the capsule, remains in the lower part of the lead container.
- The capsule can be easily taken out or the lower part of the lead container can be given to the patient in order to get the capsule

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

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBERS(S)

OGYI-T-9681/01, OGYI-T-9681/04

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16 August 1995 / 18 December 2009

10. DATE OF REVISION OF THE TEXT

18 December 2009

11. DOSIMETRY

Tabulated radiation dosimetry, as reported in ICRP publication No 53 (1987) and ICRP publication No 60 (1990) are reported. The ICRP model refers to intravenous administration. Since absorption of radioiodine is rapid and complete, this model is applicable in case of oral administration also but there is a further radiation dose to the stomach 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 increase by about 30 % for [¹³¹I].

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 EDE (Effective dose equivalent) 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.

Mainly the thyroid is affected by the radiation. The radiation exposure of other organs is usually only in the range of some thousandths of that of the thyroid. It also depends on the supply of stable iodine with food (uptake of radioactive iodine increases up to 90 % in iodine deficiency areas, drops down to 5 % in iodine-rich areas). Further, it

depends on the thyroid function (euthyrosis, hyperthyrosis or hypothyrosis) and whether there is iodine-storing tissue in the body (e.g. after thyroidectomy), presence of iodine-storing metastases or whether the thyroid was blocked. Thus the radiation exposure of all other organs is higher or lower depending on the iodine level in the thyroid.

Radiation exposure (Thyroid blocked, uptake 0 %)

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	Adult	15 years	10 years	5 years	1 year
Adrenal glands	0.037	0.042	0.067	0.11	0.2
* Bladder wall	0.61	0.75	1.1	1.8	3.4
Bone surfaces	0.032	0.038	0.061	0.097	0.19
Breast	0.033	0.033	0.052	0.085	0.17
GI-tract					
Stomach wall	0.034	0.04	0.064	0.1	0.19
Small intestine	0.038	0.047	0.075	0.12	0.22
Wall of upper large intestine	0.037	0.045	0.07	0.12	0.21
Wall of lower large intestine	0.043	0.052	0.082	0.13	0.23
intestine					
intestine	0.065	0.08	0.12	0.17	0.31
Kidneys	0.033	0.04	0.065	0.1	0.2
Liver	0.031	0.038	0.06	0.096	0.19
Lungs	0.042	0.054	0.084	0.13	0.24
Ovaries	0.035	0.043	0.069	0.11	0.21
Pancreas	0.035	0.042	0.065	0.10	0.19
Red marrow	0.034	0.040	0.065	0.10	0.20
Spleen	0.037	0.045	0.075	0.12	0.23
Testes	0.029	0.038	0.063	0.10	0.20
Thyroid	0.054	0.067	0.11	0.17	0.30
Uterus	0.032	0.039	0.062	0.10	0.19
Other tissues	0.064	0.081	0.126	0.198	0.374
Effective dose equivalent (mSv/MBq)					
*Bladder wall contributes to 47.6 % of the effective dose.					

Partial blocking:

Effective dose equivalent (mSv/MBq) at small uptake in the thyroid.

Uptake	0.5 %	0.79	1.20	2.60	4.90
Uptake 1.0 %	0.90	1.42	2.10	4.70	9.30
Uptake 2.0 %	1.60	2.6	4.20	9.30	17

Thyroid uptake: 1.5 %

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	0.036	0.043	0.071	0.11	0.22
* Bladder wall	0.52	0.64	0.98	1.5	2.9
Bone surfaces	0.047	0.067	0.094	0.14	0.24
Breast	0.043	0.043	0.081	0.13	0.25
GI-tract					
Stomach wall	0.46	0.58	0.84	1.5	2.9
Small intestine	0.28	0.35	0.62	1.0	2.0
Wall of upper large intestine	0.059	0.065	0.10	0.16	0.28
intestine					
Wall of lower large intestine	0.042	0.053	0.082	0.13	0.23
intestine					
Kidneys	0.060	0.075	0.11	0.17	0.29
Liver	0.032	0.041	0.068	0.11	0.22
Lungs	0.053	0.071	0.12	0.19	0.33
Ovaries	0.043	0.059	0.092	0.14	0.26
Pancreas	0.052	0.062	0.10	0.15	0.27
Red marrow	0.054	0.074	0.099	0.14	0.24
Spleen	0.042	0.051	0.081	0.12	0.23
Testes	0.028	0.035	0.058	0.094	0.18
Thyroid	2.10	3.40	5.10	11.00	20.00
Uterus	0.054	0.068	0.11	0.17	0.31
Other tissue	0.065	0.089	0.14	0.22	0.40
Effective dose equivalent (mSv/MBq)	11.1	17.9	26.8	58.7	107

Thyroid uptake: 3.5 %

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	0.042	0.050	0.087	0.14	0.28
* Bladder wall	0.40	0.50	0.76	1.2	2.3
Bone surfaces	0.076	0.12	0.16	0.23	0.35
Breast	0.067	0.066	0.13	0.22	0.40
GI-tract					
Stomach wall	0.46	0.59	0.85	1.5	3.0
Small intestine	0.28	0.35	0.62	1.0	2.0
Wall of upper large intestine	0.058	0.065	0.10	0.17	0.30
intestine					
Wall of lower large intestine	0.040	0.051	0.080	0.13	0.24
intestine					
Kidneys	0.056	0.072	0.11	0.17	0.29

Liver	0.037	0.049	0.082	0.14	0.27
Lungs	0.090	0.12	0.21	0.33	0.56
Ovaries	0.042	0.057	0.090	0.14	0.27
Pancreas	0.054	0.069	0.11	0.18	0.32
Red marrow	0.086	0.12	0.16	0.22	0.35
Spleen	0.046	0.059	0.096	0.15	0.28
Testes	0.026	0.032	0.054	0.089	0.18
Thyroid	500	790	1200	2600	4700
Uterus	0.050	0.063	0.10	0.16	0.30
Other tissue	0.11	0.16	0.26	0.41	0.71
Effective dose equivalent (mSv/MBq)	25.6	41.5	62.3	137	248

Thyroid uptake: 5.5 %

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	0.049	0.058	0.11	0.17	0.34
* Bladder wall	0.29	0.36	0.54	0.85	1.6
Bone surfaces	0.11	0.17	0.22	0.32	0.48
Breast	0.091	0.089	0.19	0.31	0.56
GI-tract					
Stomach wall	0.46	0.59	0.86	1.5	3.0
Small intestine	0.28	0.35	0.62	1.0	2.0
Wall of upper large intestine	0.058	0.067	0.11	0.18	0.32
intestine					
Wall of lower large intestine	0.039	0.049	0.078	0.13	0.24
intestine					
Kidneys	0.051	0.068	0.10	0.17	0.29
Liver	0.043	0.058	0.097	0.17	0.33
Lungs	0.13	0.18	0.30	0.48	0.80
Ovaries	0.041	0.056	0.090	0.15	0.27
Pancreas	0.058	0.076	0.13	0.21	0.38
Red marrow	0.12	0.18	0.22	0.29	0.46
Spleen	0.051	0.068	0.11	0.17	0.33
Testes	0.026	0.031	0.052	0.087	0.17
Thyroid	790	1200	1900	4100	7400
Uterus	0.046	0.060	0.099	0.16	0.30
Other tissue	0.16	0.24	0.37	0.59	1.0
Effective dose equivalent (mSv/MBq)	40.2	65.0	100	214	391

INSTRUCTIONS FOR PREPARATION OF

RADIOPHARMACEUTICALS

Method of control of the drug

Radioiodine compounds being present in form other than iodide are determined by paper chromatography.

Radiochemical purity test

Dissolve the capsule in 10 ml 1% sodium-hydrogen-carbonate solution. This is the analytical sample.

Preparation of test solution

A solution is prepared with the next composition: 1 g/l potassium iodide, 2 g/l

potassium iodate and 10 g/l sodium-hydrogen-carbonate. Same volume is introduced from the analytical sample.

Reference solution:

0.1 g potassium iodide and 0.2 g potassium iodate are dissolved in 10 ml distilled

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:

1. What ThyroTop is and what it is used for
2. Before you use ThyroTop
3. How to use ThyroTop
4. Possible side effects
5. How to store ThyroTop
6. Further information

1. WHAT THYROTOP IS AND WHAT IT IS USED FOR

¹³¹I-sodium iodide ThyroTop hard capsule is a radioactive medicine, which can be used for

determination of thyroidal uptake of radioiodine and its saturation curve, to design the individual patient dose of radionuclide therapy, treatment of hyperfunction in case of hyperthyroidism, reducing the size of thyroid, therapy of thyroid carcinoma. This medicine can be used only in nuclear medicine departments.

The capsule itself is colourless and contains white powder. After oral administration of the capsule, ¹³¹I-sodium iodide gets into the blood stream and reaches the thyroid, the salivary glands, placenta, gastric mucosa and plexus choroideus (and breast milk in case of lactation).

2. BEFORE YOU USE THYROTOP

Do not take ThyroTop

- if you are allergic (hypersensitive) to sodium (¹³¹I) iodide or any of the other ingredients of ThyroTop, for example, to gelatine
- if you are pregnant, or breastfeeding
- if you are under 18 years of age
- if you do not consent to the nuclear medicine examination

Taking other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Hindered radioiodine uptake of thyroid is a problem in case of thyroid scintigraphy as well as in case of radionuclide therapy of thyroid. That is why administration of inactive iodines should be avoided:

Treatment with Methoxyrin, triiodothyronine and thyroxine should be withheld 4-7 days, 2 weeks, and 1 month, respectively prior to radioiodine administration. Steroid and salicylate should be discontinued 1 week before radioiodide administration. Clearance of radioiodide from thyroid can be delayed by administration of lithium carbonate or colchicin.

Taking ThyroTop with food and drink

Swallowing of the hard capsule can be facilitated by drinking some water.

Pregnancy and breast-feeding

Ask your doctor for advice before taking any medicine.

Thyrotop must not be used during pregnancy and breastfeeding.

Driving and using machines

You may drive or operate machines

In occurrence of unexpected adverse reactions driving and/or working with machines should be reconsidered.

Important information about some of the ingredients of ThyroTop

ThyroTop reduces the whole body rabsorbed adiation dose in order to achieve better therapeutic effect against benign and malign formations.

If you have any further questions on the use of this product, ask your doctor.

3. HOW TO USE THYROTOP

You should take the capsule orally.

Your doctor will decide the amount of the administered activity, considering your condition.

What should you do if you received overdose of the medicinal product?

Since you will be given ThyroTop by a doctor under strictly controlled conditions there is only little chance of overdose. In case you get a capsule of greater activity than you should, your doctor determines the absorbed radiation dose and will provide the appropriate treatment. Pharmaceutical overdose is not possible; trials proved no pharmaceutical damaging after administration of excess of capsules.

ThyroTop can be handled, used and administered only by people specialized for handling of radioactive materials and waste. These people give you instructions about the precautions and warnings. Comply with their instructions.

4. POSSIBLE SIDE EFFECTS

Like all medicines, ThyroTop can cause side effects, although not everybody gets them.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary effects. However these effects are hardly expected regarding the applied amount of activity.

Allergic reactions after administration of ¹³¹I-sodium iodide have been reported very rare (less than one of 10000 patients).

Other possible side effects: pain, oedema in face, peripheral and generalized angioneurotic oedema, skin redness, angina, salivary gland inflammation, oedema, nausea, vomiting, abdominal pain, skin exanthem, itching, urticaria,

About side effects related to the absorbed radiation dose in case of radioiodine therapy ask your doctor.

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 THYROTOP

Keep out of the reach and sight of children and people who are not authorized to handle, use or transport this product!

Hospital staff will ensure that the product is stored correctly and not used after expiry date stated on the label.

Store below 25 °C, in the original package.

Expiry date and storage condition requirements are stated on the packaging.

6. FURTHER INFORMATION

What ThyroTop contains

- The active substance is sodium (¹³¹I) iodide. One capsule contains 4 – 7400 MBq of sodium (¹³¹I) iodide.
- The other ingredients are disodium hydrogen phosphate dihydrate, sodium thiosulphate, gelatine capsule shells.

What ThyroTop looks like and contents of the pack

Colourless hard capsule

Packaging

Low activity capsules

Low activity ¹³¹I capsules are supplied in vials. 1 to 10 capsules can be packed into one vial. Vials are closed with rubber stopper and aluminium cap.

The vial containing the low activity ¹³¹I-sodium iodide capsules are placed into lead container, containing paper insert and a plastic foam insert. Not more than 3 vials in lead container are allowed to put into one tin container.

High activity capsules

High activity ¹³¹I-sodium-iodide capsules are placed into lead container with in which a plastic insert with screwed cap has been fixed. The packaging always contains one capsule.

The labelled lead container is packed into a labelled tin container.

Marketing Authorisation Holder and Manufacturer

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