GE Healthcare

TECHNICAL LEAFLET

THERACAP 131™

IBS.600PX

14944851 IBS600P-SG0120-LFT

Formulation

Gelatin capsules containing sodium iodide [^{131} I] solution absorbed onto an inert carrier, consisting of disodium phosphate anhydrous, colloidal anhydrous silica and maize starch.

Each capsule contains a maximum of 20 µg of sodium iodide.

Iodine-131 is produced by fission of uranium-235 or by neutron bombardment of stable tellurium in a nuclear reactor. Iodine-131 has a half-life of 8.02 days. It decays by emission of gamma radiations of 365 keV (81.7%), 637 keV (7.2%) and 284 keV (6.1%) and beta radiations of maximal energy of 606 keV to stable Xenon-131.

Excipient(s) with known effect:
One hard capsule contains not more than 50 mg of sodium.

Applications

THERACAP^{131} can be used in place of sodium iodide [^{131} I] solution for radioiodine therapy. [8] This includes treatment of hyperthyroidism [1] in cases where surgery is contraindicated and the elimination of residual thyroid activity after thyroidectomy in cases of thyroid carcinoma. [2] [9]

Pharmacology

After oral administration of the capsules, sodium iodide [^{131} I] is absorbed rapidly into the bloodstream and concentrates in the thyroid, where it is incorporated into hormones which are stored in the intrafollicular colloid. The therapeutic effect depends upon the beta emission and the range over which these particles are effective. This is approximately 400-2000 µm which considerably exceeds the follicular diameter (15 µm). Consequently both the cytoplasm and nucleus are irradiated, as are adjacent follicles. Various workers have investigated the effects of radioiodine therapy and it is apparent that irradiated cells continue to contribute to biochemical function of the gland but lose the ability to undergo mitotic cell division [3]. Thus the total gland mass is steadily reduced.

Dosage

1. **Thyrotoxicosis**

Patients should be rendered euthyroid medically whenever possible before giving radioiodine treatment for hyperthyroidism.

In order to obtain an estimate of thyroid size and iodide uptake, a diagnostic dose of approximately 0.185 MBq (5µCi) is administered first. This is followed by the appropriate therapeutic dose, usually in the range 185-555 MBq (5-15 mCi).

2. **Ablation of normal thyroid function**
0.925-1.85 GBq (25-50 mCi).

3. **Thyroid carcinoma**
For total thyroid ablation following thyroidectomy, 2.22-3.7 GBq (60-100 mCi) repeated after an interval if necessary.

Radioactivity

The activity of the capsules at 1200 GMT on each day before (-), on, and after the activity reference date, can be calculated by multiplying the factor in Table 1 by the nominal activity on the reference day.

Table 1

Day	Factor	Day	Factor
-6	1.677	5	0.650
-5	1.539	6	0.596
-4	1.412	7	0.547
-3	1.295	8	0.502
-2	1.188	9	0.460
-1	1.090	10	0.422
0	1.000	11	0.387
1	0.917	12	0.355
2	0.842	13	0.326
3	0.772	14	0.299
4	0.708		

Radiation dosimetry

The absorbed radiation doses to patients following administration of iodine-131 depend markedly on the functional state of the thyroid gland. In Table 2 radiation dose estimates are presented for three thyroidal functional states as defined by Riggs [4]. The estimates for the euthyroid condition correspond to normal thyroid function. The estimates for hyperthyroidism correspond to a moderately 'severe' hyperthyroid condition. In the case of hypothyroidism, the patient's medical treatment regime immediately prior to administration will have a profound effect on the degree of iodine uptake. The organ doses given in the table correspond to the complete absence of functional thyroid tissue.

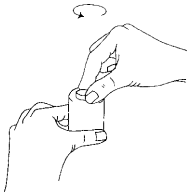
Table 2
Absorbed radiation dose estimates to various body organs for three defined thyroid functional states

Organ	Absorbed dose per 37MBq (1mCi) Iodine-131 administered					
	Euthyroid		Hyperthyroidism		Hypothyroidism	
	mGy	rads	mGy	rads	mGy	rads
Thyroid	19000	1900	33000	3300		see text
Ovaries	2.0	0.2	3.0	0.3	2.0	0.2
Whole Body	10.0	1.0	17.0	1.7	2.0	0.2
Bladder	14.0	1.4	11.0	1.1	19.0	1.9

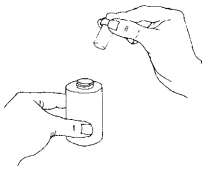
Procedure for use:
The following procedure should be used when the product is being administered to the patient:

Step 1 Check the activity and reference date on the lead pot label.

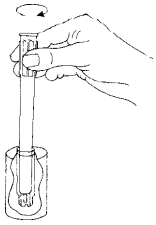
Step 2 Immediately before calibration or administration, unscrew cap anti-clockwise.



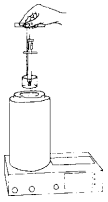
Step 3 Remove cap and plug unit



Step 4 Locate the THERACAP^{131} applicator on top of capsule holder. Turn clockwise until light resistance is felt (approximately 1 1/2 full turns). The capsule holder is now attached to the applicator.



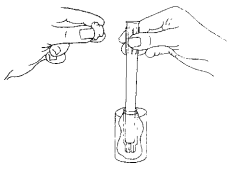
Step 5 Confirm activity of capsule by placing the THERACAP^{131} applicator in a calibrated ion chamber.



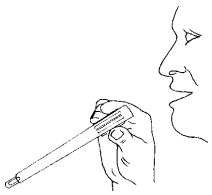
Step 6 Return the capsule to the lead container by reversing the preparation procedure.

Step 7 When ready to administer the capsule to the patient, repeat steps 2, 3 and 4.

Step 8 Ask the patient to remove the plastic cap from the ribbed end of the applicator using a simple pulling action.



Step 9 The capsule can now be swallowed by the patient presenting the open end of the THERACAP^{131} applicator to his/her bottom lip and gently tilting upwards allowing the capsule to fall freely into the mouth.



Step 10 The patient is asked to take a small lukewarm drink prior to and with the capsule (and asked not to bite through the capsule). After swallowing, follow with another drink.

Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- For diagnostic purposes in children under 10 years of age.
- Pregnancy [5] and breast-feeding.
- Patients with dysphagia, oesophageal stricture, oesophageal stenosis, oesophagus diverticulum, active gastritis, gastric erosions and peptic ulcer.
- Patients with suspected reduced gastrointestinal motility.
- It should be avoided in persons with kidney insufficiency.

Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions

If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification

For each patient, the radiation exposure must be justifiable by the likely benefit. The activity to be administered should in every case be as low as reasonably achievable to obtain the required therapeutic effect.

There is little evidence of an increased incidence of cancer, leukaemia or mutations in patients after treatment with radioiodine for benign thyroid diseases, despite its extensive use. In the treatment

of malignant thyroid diseases, in a study conducted on patients with doses of sodium iodide (^{131}I) higher than 3700 MBq a higher incidence of bladder cancer was reported. Another study reported a slight increase in leukaemia in patients receiving very high doses. Therefore, total cumulative doses greater than 26000 MBq are not recommended.

Gonadal function in males

The use of the sperm bank could be considered to compensate a potential reversible damage of gonadal function in males due to the high therapeutic dose of radioiodine, in the cases of patients with extensive disease.

Patients with renal impairment

Careful consideration of the benefit/risk balance in these patients is required since an increased radiation exposure is possible. In these patients it may be necessary to adjust the posology.

Patient preparation

Patients should be encouraged to increase oral fluids and urged to void as often as possible to reduce bladder radiation, especially after high activities e.g. for the treatment of thyroid carcinoma. Patients with bladder voiding problems should be catheterised after administration of high activities of radioiodine.

To reduce colon radiation exposure, mild laxatives (but not stool softeners which do not stimulate the bowel) may be necessary in patients having less than one bowel movement a day.

To avoid sialoadenitis that may occur after high dose radioiodine administration, the patient should be advised to take sweets or drinks containing citric acid (lemon juice, vitamin C) to stimulate saliva excretion before therapy. Other pharmacological protection measures may be used additionally.

Iodide overload from food or medicinal treatment should be investigated before administration of iodide. A low iodine diet prior to therapy is recommended to enhance uptake into functioning thyroid tissue.

Thyroid replacement should be stopped prior to radioiodine administration for thyroid carcinoma to ensure adequate uptake. It is recommended to stop triiodothyronine treatment for a period of 14 days and to stop thyroxine treatment for a period of 6 weeks. They should be restarted two days after treatment.

Carbimazole and propylthiouracil should be stopped 1 week prior to treatment of hyperthyroidism and restarted several days after treatment.

Hyponatraemia: Serious manifestations of hyponatraemia have been reported after sodium iodide (^{131}I) therapy in elderly patients who have undergone total thyroidectomy. Risk factors include older age, female sex, use of thiazide diuretics and hyponatraemia at the start of sodium iodide (^{131}I) therapy. Regular serum electrolytes measurements shall be considered for these patients.

The radioiodine treatment of Graves' disease should be performed under concomitant treatment of corticosteroids, particularly when endocrine ophthalmopathy is present.

In patients with suspected gastrointestinal disease, great care should be taken when administering sodium iodide (^{131}I) capsules. Concomitant use of H2-antagonists or proton pump inhibitors is advised.

After the procedure

Close contact with infants and pregnant women should be restricted for at least one week after therapeutic doses.

In case of vomiting, the risk of contamination has to be considered.

Patients receiving therapy of the thyroid should be re-examined at appropriate intervals.

Specific warnings

This medicinal product contains 50 mg of sodium per capsule, equivalent to 2.5% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Interaction with other medicinal products and other forms of interaction

Many pharmacologically active substances interact with radioiodide. Various interaction mechanisms exist which can affect the protein binding, the pharmacokinetics or the dynamic effects of labelled iodide. As a consequence, it should be considered that the thyroid uptake might be reduced. Therefore, a full drug history should be taken and relevant medicinal products are required to be withheld prior to the administration of sodium iodide (^{131}I).

For example, the treatment with the following substances should be discontinued:

Active substances	**Withdrawal period before administration of sodium iodide (^{131}I).**
Antithyroid medicinal products (e.g. carbimazole, methimazole, propyluracil), perchlorate	1 week before starting treatment till several days after
Salicylates, corticosteroids, sodium nitroprusside, sodium sulfobromophthalein, anticoagulants, antihistamines, antiparasitics, penicillins, sulphonamides, tolbutamide, thiopental	1 week.
Phenylbutazone	1 to 2 weeks.
Containing iodine expectorants and vitamins	approximately 2 weeks.
Thyroid hormone preparations	Triiodothyronine 2 weeks Thyroxine 6 weeks.
Benzodiazepines, lithium	Approximately 4 weeks.
Amiodarone *	3 to 6 months

Containing iodine preparations for topical use	1 to 9 months.
Water-soluble iodine-containing contrast media	6 to 8 weeks
Lipo-soluble iodine-containing contrast media	up to 6 months

* Due to the long half-life of amiodarone, iodine uptake in the thyroid tissue can be decreased for several months.

Fertility, pregnancy and lactation

Women of childbearing potential

When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient. Women receiving sodium iodide (^{131}I) should be advised not to become pregnant within 6-12 months after administration.

Contraception in males and females

Contraception for 6 months (for patients with benign thyroid conditions) or 12 months (for patients with thyroid cancer) is recommended for both sexes after therapeutic administration of sodium iodide (^{131}I).

Men should not father a child for a time period of 6 months after radioiodine treatment to allow the replacement of irradiated by non-irradiated spermatozoa. Sperm banking should be considered for men who have extensive disease and therefore may need high sodium iodide (^{131}I) therapeutic doses.

Pregnancy

The use of sodium iodide (^{131}I) is contraindicated during established or suspected pregnancy or when pregnancy has not been excluded because transplacental passage of sodium iodide (^{131}I) can cause severe and possibly irreversible hypothyroidism in neonates (the absorbed dose to the uterus for this medicinal product is likely to be in the range 11-511 mGy, and the foetal thyroid gland avidly concentrates iodine during the second and third trimesters) (see **Contraindications**).

If a differentiated thyroid carcinoma is diagnosed during pregnancy, sodium iodide (^{131}I) treatment should be postponed until after the childbirth.

Breastfeeding

Before administering radiopharmaceuticals to a mother who is breastfeeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding, and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk.

If the administration is considered necessary, breast-feeding must be discontinued at least 8 weeks before sodium iodide (^{131}I) administration and should not be resumed (see **Contraindications**).

For radioprotection reasons following therapeutic doses, it is recommended to avoid close contact between mother and infants for at least one week.

Fertility

After radioiodine therapy of thyroid carcinoma, a dose dependent impairment of fertility may occur in men and women. Depending on the activity dose, a reversible impairment of the spermatogenesis could occur in doses above 1850 MBq. Clinical relevant effects including oligospermia and azoospermia and elevated serum FSH serum levels have been described after administration greater than 3700 MBq.

Effects on ability to drive and use machines

Unknown.

Undesirable Effects

Summary of the safety profile

The frequencies of reported adverse reactions were derived from the medical literature. The safety profile of sodium iodide (^{131}I) differs widely according to the doses administered, while the doses to be administered are dependent on the type of treatment (i.e. treatment of benign or malignant disease). Moreover, the safety profile depends on the cumulative doses administered and the dosing intervals which are used. Therefore, the reported adverse reactions were grouped by their occurrence in treatment of benign or malignant disease.

Frequently occurring adverse reactions are: hypothyroidism [6] [7], transient hyperthyroidism, salivary and lacrimal gland disorders, and radiation local effects. In cancer treatment additionally, gastro-intestinal adverse reactions and bone marrow suppression may frequently occur.

Tabulated list of adverse reactions

The following tables include reported adverse reactions sorted by system organ classes. Symptoms, which are rather secondary to a group-syndrome (e.g. Sicca syndrome) are subsumed in parenthesis

behind the respective syndrome.

The following table presents how the frequencies are reflected in this section:

Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (frequency cannot be estimated from the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Adverse reactions after treatment of benign disease

System organ class	**Adverse reaction**	**Frequency**
Immune system disorders	Hypersensitivity including anaphylactoid reaction	Not known
Endocrine disorders	Permanent hypothyroidism, hypothyroidism	Very common
	Transient hyperthyroidism	Common
	Thyrotoxic crisis, thyroiditis, hypoparathyroidism (blood calcium decreased, tetany)	Not known
Eye disorders	Endocrine ophthalmopathy (in Graves' disease)	Very common
	Sicca syndrome	Not known
Respiratory, thoracic and mediastinal disorders	Vocal cord paralysis	Very rare
Gastrointestinal disorders	Sialoadenitis	Common
Hepatobiliary disorders	Hepatic function abnormal	Frequency not known**
Skin and subcutaneous tissue disorders	Iodide induced acne	Not known
Congenital, familial and genetic disorders	Congenital hypothyroidism	Not known

General disorders and administration site conditions	Local swelling	Not known

Adverse reactions after treatment of malignant disease

System organ class	**Adverse reaction**	**Frequency**
Neoplasms benign, malignant and unspecified (including cysts and polyps)	Leukaemia	Uncommon
	Solid cancers, bladder cancer, colon cancer, gastric cancer, breast cancer	Not known:
Blood and the lymphatic system disorders	Erythrocytopenia, bone marrow failure	Very common
	Leukopenia, thrombocytopenia,	Common
	Aplastic anemia, permanent or severe bone marrow suppression	Not known
Immune system disorders	Hypersensitivity including anaphylactoid reaction	Not known
Endocrine disorders	Thyrotoxic crisis, transient hyperthyroidism	Rare
	Thyroiditis (transient leukocytosis), hypoparathyroidism (blood calcium decreased, tetany), hypothyroidism, hyperparathyroidism	Not known
Nervous system disorders	Parosmia, anosmia	Very common
	Brain oedema	Not known
Eye disorders	Sicca syndrome (conjunctivitis, dry eyes, nasal dryness)	Very common
	Nasolacrimal duct obstruction (lacrimation increased)	Common

Respiratory, thoracic and mediastinal disorders	Dyspnoea	Common
	Throat constriction*, Pulmonary fibrosis, respiratory distress, obstructive airways disorder, pneumonia, tracheitis, vocal cord dysfunction (vocal cord paralysis, dysphonia, hoarseness), oropharyngeal pain, stridor	Not known
Gastrointestinal disorders	Sialoadenitis *(*dry mouth, salivary gland pain, salivary gland enlargement, dental caries, tooth loss), radiation sickness syndrome, nausea, ageusia, anosmia, dysgeusia, decreased appetite	Very common
	Vomiting	Common
	Gastritis, dysphagia	Not known
Hepatobiliary disorders	Hepatic function abnormal	Frequency not known**
Renal and urinary disorders	Radiation cystitis	Not known
Reproductive system and breast disorders	Ovarian failure, menstrual disorder	Very common
	Azoospermia, oligospermia, decreased fertility male	Not known
Congenital, familial and genetic disorders	Congenital hypothyroidism	Not known
General disorders and administration site conditions	Flu-like illness, headache, fatigue, neck pain Local swelling	Very common Common

* especially in existing tracheal stenosis

** this effect may be seen with other similar products but has not been observed with Theracap[131]

Overdose

This product must be used by authorised personnel in a hospital setting. The risk of overdose is therefore theoretical. In the event of administration of a radiation overdose, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by frequent micturition and by forced diuresis and frequent bladder voiding. Additionally, the blockade of the thyroid gland should be recommended (e.g. with potassium perchlorate) in order to reduce the radiation exposure of the thyroid gland. To reduce the uptake of sodium iodide (^{131}I), emetics can be given.

Special Precautions for handling

1.3% of iodine (^{131}I) decays via xenon (^{131m}Xe) (half-life 12 days) and a small amount of xenon (^{131m}Xe) activity may be present in the packaging as a result of diffusion. It is therefore recommended that the transport container be opened in a ventilated enclosure and that, after removal of the capsule, the packaging materials are allowed to stand overnight before disposal to permit the release of absorbed xenon (^{131m}Xe).

In addition, there can be limited leakage of volatile iodine-131 activity from the capsule. The container incorporates a small disc of charcoal in the lid which serves to absorb the iodine that escapes from the capsule. The charcoal disc may become contaminated with up to 1.3 MBq (35 μCi) of iodine-131. As a consequence of the charcoal disc, only very small amounts of iodine-131 (typically less than 1.85 kBq (50 nCi) may be present in the packaging.

Nuclear data

Iodine-131 has a half-life of 8.02 days (193 hours). Its predominant mode of decay is by the emission of gamma rays of energy 0.364 MeV in 81.8% of disintegrations and by a beta transition with an endpoint energy of 0.606 MeV in 89.7% of disintegrations.

1.3% of iodine-131 decays via xenon-131 (half-life 12 days).

The dose rate for iodine-131 in air due to gamma and X-ray radiation, at one metre from a point source containing one gigabecquerel is 5.7x10-2 mSv/hr.

References

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Presentation

Each capsule is presented within a polycarbonate container with a charcoal disc to absorb iodine-131. This container is enclosed within a lead shield.

Storage

Store at 15-25°C.

Availability

Capsules are available in the following sizes:
37-740 MBq in 37 MBq intervals
(1-20 mCi in 1 mCi intervals)
0.925-5.55 GBq in 185 MBq intervals
(25-150 mCi in 5 mCi intervals)

Manufacturer

GE Healthcare Buchler GmbH & Co. KG
Gieselweg 1
D-38110 Braunschweig
Germany

Expiry

The product should not be used later than 14 days after the reference date.

Date of preparation

September 2021

Licence Number in Singapore

SIN11923P

GE Healthcare Limited

HP8 4SP, UK

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