PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

Pr HICON®

Sodium Iodide (I 131)

Kit for the preparation of Sodium Iodide I 131 Solution and Capsules, USP

For Compounding of Oral Dosage Form

Therapeutic Radiopharmaceutical

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

HICON® (Sodium Iodide; I 131) is indicated for:

- The treatment of hyperthyroidism (diffuse toxic goiter and single or multiple toxic nodular goiter).
- The treatment of recurrent hyperthyroidism after surgery.
- The therapy of some thyroid carcinomas such as functioning metastatic papillary or follicular carcinoma of the thyroid.

1.1 Pediatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use (Section 9.1.3 *Warnings and Precautions*).

1.2 Geriatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatric use (Section 9.1.4 *Warnings and Precautions*).

2 CONTRAINDICATIONS

HICON® is contraindicated in:

- Patients with vomiting and diarrhea (Section 10 *Adverse Reactions*).
- Pregnancy (Section 9.1.1 *Warnings and Precautions*).
- Lactation (Section 9.1.2 *Warnings and Precautions*).
- Patients receiving concurrent anti-thyroid therapy (Section 9 *Warnings and Precautions* and Section 11.3 *Drug Interactions*).

HICON® is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. Although iodide is not considered an allergen, hypersensitivity reactions may occur in relation with excipients or chemical component of the capsule, such as sodium thiosulfate (Section 10 *Adverse Reactions*).

For a complete listing, see the Dosage Forms, Composition and Packaging section of the product monograph.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- Radiopharmaceuticals should be used only by those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans (Section 4 *Dosage and Administration*).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

The concentrated Sodium Iodide I 131 Solution USP provided with HICON® must not be used for direct administration to patients. It must be diluted and prepared as described in this section.

HICON® is a radioactive drug. Handle with appropriate safety measures to minimize radiation exposure to the patient and healthcare workers:

- Use only by, or under the direction of, physicians who are qualified by specific training and experience in the safe use and handling of radioactive materials, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radiopharmaceuticals.
- Use waterproof gloves when handling and administering the product.
- Maintain adequate shielding during the life of the product.
- Measure patient dose with a suitable radioactivity calibration system immediately prior to administration.

4.2 Dosage

Individualization of Therapy
The recommended dose for orally administered sodium iodide I 131 capsules or solution is based on the thyroid gland uptake as well as the size of the gland. Thyroidal uptake and size should be determined by the physician prior to treatment and may be useful in calculating the therapeutic dose to be administered to the individual patient.

Hyperthyroidism:	148 - 370 Megabecquerels (MBq) (4 - 10 milliCuries; mCi). Certain disorders such as toxic nodular goiter may require larger doses. Anti-thyroid drugs should be discontinued for 3 - 4 days prior to the administration of the dose and withheld for 7 - 14 days afterwards.
Thyroid Carcinoma:	3.7 - 5.55 Gigabecquerels (GBq) (100 - 150 mCi) for ablation of normal thyroid tissue; 3.7 - 7.4 GBq (100 - 200 mCi) for subsequent treatments.

4.3 Administration

- Do not directly administer the concentrated sodium iodide I 131 solution provided with HICON® to patients. The concentrated sodium iodide I 131 solution must be diluted and prepared prior to administration (Section 4.5 *Dosage and Administration*).
- Obtain a pregnancy test in females of reproductive potential prior to administration to verify the absence of pregnancy (Section 2 Contraindications and Section 9.1.1 *Warnings and Precautions*).
- Instruct patients to fast at least 2 hours before and 2 hours after administration to ensure absorption.
- Instruct patients to hydrate before and after administration of sodium iodide I 131 and to void frequently to enhance urinary elimination of the radioiodide that is not absorbed by the thyroid gland (Section 9 *Warnings and Precautions*).

- Instruct patients to maintain a low-iodide diet two weeks prior to radioiodide administration and continue for several days during the uptake or imaging process (Section 9 *Warnings and Precautions* and Section 11.4 *Drug Interactions*).
- Instruct patients to discontinue the anti-thyroid therapy three days before administration of sodium iodide I 131 (Section 9 *Warnings and Precautions* and Section 11.3 *Drug Interactions*).
- For patients with a history of renal impairment, evaluate renal function for therapeutic planning and consider dosimetry (Section 9 *Warnings and Precautions*).
- Obtain a complete blood count within one month of therapy. If patients show leukopenia or thrombocytopenia, dosimetry should be used to determine a safe sodium iodide I 131 activity, while delivering less than 2 Gy to the bone marrow (Section 9 *Warnings and Precautions*).

4.4 Instructions for Preparation and Use

Drug Handling

1. Use aseptic technique and wear waterproof gloves throughout the entire handling and administration procedure.

2. Make all transfers of radioactive solutions with an adequately shielded syringe and maintain adequate shielding around the vial during the useful life of the radioactive product.

Preparation of Dilute Sodium Iodide I 131 Solution USP

1. Using the calibration date and radionuclidic concentration on the label of the product vial, calculate the required volume to produce the necessary dose in MBq or mCi.

2. Using a shielded syringe, remove the required volume.

3. Using the shielded syringe, transfer the required volume to a suitably shielded receiving vial.

4. Add diluent solution to the receiving vial to produce a final dose of the desired volume.

5. The recommended diluent is Purified Water USP containing 0.2% Sodium Thiosulfate USP as a reducing agent. Acidic diluents should not be used as they may cause the pH to drop below 7.5 and stimulate the volatilization of Iodine I-131 hydriodic acid.

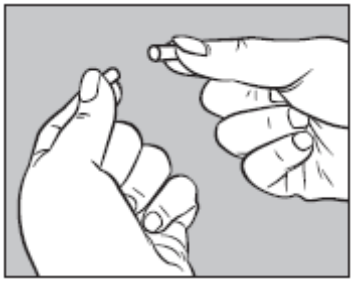
6. Present the dose in a shielded container for administration to the patient with a straw.

Preparation of Sodium Iodide I 131 Capsules USP

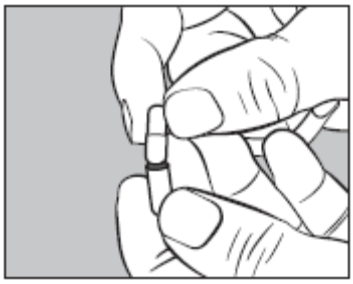
1. HICON® includes one **LARGE** gelatin capsule and one **SMALL** gelatin capsule for each dose prepared. Each **LARGE** capsule is empty and each small capsule contains approximately 300 mg of dibasic sodium phosphate anhydrous USP as the absorbing buffer.

2. Using the calibration date and radionuclide concentration on the label of the product vial, calculate the required volume to produce the necessary dose in MBq or mCi.

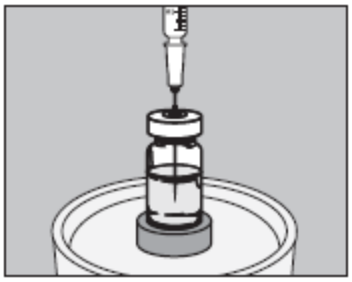
3. Open one **LARGE** capsule supplied with HICON® by pulling apart the capsule into two pieces as illustrated below:



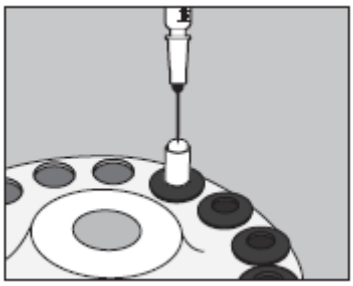
4. Insert an unopened **SMALL** capsule supplied with HICON® into the bottom half of the empty **LARGE** capsule as illustrated below:



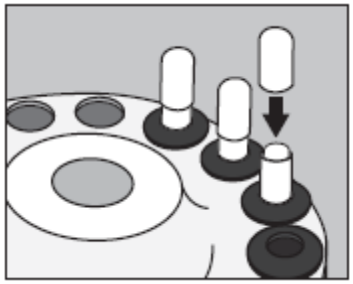
5. With an appropriate syringe, withdraw the required volume of sodium iodide I 131 solution USP (maximum 150 microliters) from the vial as illustrated below:



6. Inject slowly into the center of the **SMALL** capsule through the top as illustrated below and wait for 30 seconds to allow the solution to be absorbed by the absorbing buffer:



7. Slip the upper half of the **LARGE** capsule over the bottom half to completely cover the **SMALL** capsule and push down gently until locked as illustrated below:



8. Measure the patient dose in a suitable radioactivity calibration system immediately prior to administration.

9. Prepared capsules may be stored in a suitable polypropylene container and placed inside a lead pot until use, within seven days.

4.5 Directions for Quality Control

The solution should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. The solution should not be used if cloudy, discolored, or found to contain particulate matter. However, it is well known that glass tends to darken in the presence of high radioactivity.

5 RADIATION DOSIMETRY

- The biokinetic modeling and radiation dose distributions associated with thyroid uptake of iodide I 131 depend on dietary intake of stable iodide and presume normal production of thyroid hormone. Table 1 shows a range of uptake percentages in an average adult (73.7 kg reference model). Table 1 is not intended to be used for treatment planning.
- For a thyroid blocked from iodide uptake in the production of hormones, the effective half-life of iodide I 131 is approximately 1.4 hours; for “low” to “high” uptake, the effective half-life of I 131 ranges from approximately 80 to 90 hours.

Table 1[*]
Absorbed dose per unit activity sodium iodide I 131 administered orally (mGy/MBq) in adult (73.7-kg reference model)

Organ	Thyroid uptake of I 131 (% administered activity A_0) 24 h after oral administration			
	Blocked thyroid (0% A_0)	Low uptake[**] (16% A_0)	Medium uptake[**] (26% A_0)	High uptake[**] (36% A_0)

Adrenals	0.044	0.051	0.055	0.059
Bone surfaces	0.030	0.089	0.12	0.16
Brain	0.021	0.093	0.13	0.17
Breast	0.020	0.038	0.048	0.058
Gallbladder wall	0.037	0.043	0.046	0.049
Gastrointestinal tract				
Esophagus	0.024	0.10	0.14	0.19
Stomach wall	0.87	0.77	0.71	0.66
Small intestine wall	0.035	0.033	0.032	0.032
Colon wall	0.14	0.14	0.14	0.14
(Upper large intestine wall)	0.12	0.12	0.12	0.12
(Lower large intestine wall)	0.17	0.17	0.17	0.16
Heart wall	0.062	0.089	0.10	0.12
Kidneys	0.27	0.27	0.27	0.27
Liver	0.050	0.093	0.12	0.14
Lungs	0.053	0.10	0.13	0.15
Muscles	0.026	0.084	0.12	0.15
Ovaries	0.038	0.037	0.036	0.035
Pancreas	0.060	0.064	0.066	0.068
Red marrow	0.031	0.072	0.095	0.12
Salivary glands	0.27	0.22	0.19	0.16
Skin	0.019	0.043	0.057	0.071
Spleen	0.064	0.069	0.072	0.075
Testes	0.025	0.024	0.023	0.22
Thymus	0.024	0.10	0.14	0.19
Thyroid	2.2	280 #	430 #	580 #
Urinary bladder wall	0.54	0.45	0.39	0.34
Uterus	0.045	0.042	0.040	0.038
Remaining organs	0.029	0.084	0.11	0.15
Effective dose per administered activity (mSv/MBq)	0.28	14 #	22 #	29 #

* Table 1 is not intended for treatment planning.

** These columns are not applicable to estimate organ or effective doses in patients following thyroidectomy. In patients with thyroid cancer following thyroidectomy, organ and effective doses can be estimated from the "blocked"-thyroid-uptake values.

\# These values presume unimpeded production of thyroid hormone and may not be applicable to estimate thyroid dose and effective dose in patients who have had previous treatment with I 131 for hyperthyroidism.

6 OVERDOSAGE

In case of exposure to a radioactive dose of sodium iodide I 131 exceeding the intended therapeutic dose, provide general supportive care, promote frequent voiding, monitor for bone marrow and thyroid suppression. Consider administering a thyroid blocking agent (e.g. potassium iodide (KI) or perchlorate) promptly within 4 to 6 hours after the exposure. Assess the benefit of administering a thyroid blocking agent against the risk of failure of sodium iodide I 131 therapy. Appropriate replacement therapy is recommended if hypothyroidism occurs.

7 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 2
Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Oral	Solution 37 GBq/mL	None For a complete listing see Dosage Forms, Composition and Packaging section

HICON® is available in 1 mL size, clear vials containing a colorless, aqueous, concentrated Sodium Iodide I 131 Solution containing approximately 9,250 MBq (250 mCi), 18,500 MBq (500 mCi), and 37,000 MBq (1,0000 mCi) at time of calibration for the preparation of sodium iodide I 131 capsules, therapeutic or sodium iodide I 131 solution, therapeutic. Refer to Table 3 for the radioactivity and volume in each vial.

Table 3
HICON® Concentrated Sodium Iodide I 131 Solution

Total Radioactivity / Vial MBq*	Solution Volume mL/Vial
9,250 (250 mCi)	0.25
18,500 (500 mCi)	0.5
37,000 (1000 mCi)	1

* At time of calibration.

Each of the 9.25 GBq (250 mCi), 18 GBq (500 mCi) or 37 GBq (1,000 mCi)* kit includes:

- a minimum of one blister package of ten (10) **small** hard gelatin capsules each containing approximately 300 mg of Dibasic Sodium Phosphate Anhydrous USP as absorbing buffer;
- a minimum of one blister package of ten (10) empty **large** hard gelatin capsules;
- a 1 mL vial containing 0.25 mL to 1 mL of Sodium Iodide I 131 Solution USP, therapeutic oral solution.

Each mL of the aqueous product contains:

37 gigabecquerels of Sodium Iodide I-131
< 2.0 mg of Disodium Edetate Dihydrate USP
< 22 mg of Sodium Thiosulphate Pentahydrate USP
< 40 mg of Dibasic Sodium Phosphate Anhydrous USP

*Note that not all filled volumes/radioactivity within the range may be commercially available

8 DESCRIPTION

HICON®, a radioactive therapeutic agent, provides a concentrated solution of sodium iodide I 131 with a radioconcentration of 37,000 MBq/mL (1,000 mCi/mL). Each mL of the concentrated solution contains 37,000 MBq of no-carrier-added sodium iodide I 131, disodium edetate dihydrate USP as a stabilizer, sodium thiosulfate pentahydrate USP as a reducing agent, and dibasic sodium phosphate anhydrous USP. The pH of the concentrated solution is between 7.5 and 10.

The concentrated solution provided with HICON® is used for the preparation of sodium iodide I 131 capsules or sodium iodide I 131 solution of varying strengths for oral administration for therapy.

Sodium iodide I 131 solution is designated chemically as Na ^{131}I and has a molecular weight of 153.99 g/mol. Hard gelatin capsules, provided for the preparation of the sodium iodide I 131 capsules final dosage form, contain approximately 300 mg of dibasic sodium phosphate anhydrous USP as the absorbing buffer.

Physical Characteristics
Iodine 131 decays by beta emission and associated gamma emission with a physical half-life of 8.04 days. The principal emissions are listed in Table 4.

Table 4
Principal Radiation Emission Data from Decay of Sodium Iodide I 131

Radiation	Mean % per Disintegration	Mean Energy (keV)
Beta-1	2.1	69.4
Beta-3	7.2	96.6
Beta-4	89.4	191.4
Gamma-7	6.1	284.3
Gamma-14	81.2	364.5
Gamma-18	7.1	637.0

External Radiation
The specific gamma-ray constant for iodide I 131 is 4.26×10^{-13} C•m^2•kg^{-1}•MBq^{-1}•s^{-1} (2.2 R•cm^2/mCi•hr). The first half-value thickness of lead (Pb) for iodide I 131 is 0.27 cm. A range of values for the relative attenuation of the radiation emitted by iodide I 131 that results from the interposition of various thicknesses of Pb is shown in Table 5. For example, the use of 2.59 cm of Pb will decrease the external radiation exposure by a factor of about 1,000.

Table 5
Radiation Attenuation of Iodide I 131 by Lead Shielding

Shield Thickness (Pb) cm	Coefficient of Attenuation
0.27	0.5
0.56	0.25
0.99	10^{-1}
2.59	10^{-2}
4.53	10^{-3}

To correct for physical decay of iodine I 131, the fractions that remain at selected intervals after the time of calibration are shown in Table 6.

Table 6
Physical Decay Chart - Iodine 131: Half-life 8.04 days

Days	Fraction Remaining	Days	Fraction Remaining	Days	Fraction Remaining
0*	1.000	11	.388	22	.151
1	.918	12	.356	23	.138
2	.842	13	.327	24	.127
3	.773	14	.300	25	.116
4	.709	15	.275	26	.107
5	.651	16	.253	27	.098
6	.597	17	.232	28	.090
7	.548	18	.213	29	.083
8	.503	19	.195	30	.076
9	.461	20	.179		
10	.423	21	.164		

*Calibration Time

9 WARNINGS AND PRECAUTIONS

Please see the Serious Warnings and Precautions Box at the beginning of Part I: Health Professional Information.

General
The product should be administered under the supervision of a health professional who is experienced in the use of radiopharmaceuticals. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

Contamination (risk of unintentional radiation exposure)
As in the use of any other radioactive material, care should be taken to minimize radiation exposure to patients consistent with proper patient management, and to minimize radiation exposure to occupational workers.

HICON® contributes to a patient's overall long-term cumulative radiation exposure, which is associated with an increased risk of cancer. Follow safe handling and administration to minimize radiation exposure to the patient and healthcare providers.

Instruct patients to follow radiation safety precautions after receiving HICON® to minimize the radiation contamination of other persons or the environment. Patients should avoid close contact with others, especially pregnant women and children, and take care to avoid contamination of other persons or the environment with body fluids.

Hypersensitivity Reactions
Hypersensitivity reactions including anaphylaxis may occur in patients who receive sodium iodide I 131. Although iodide is not considered an allergen, hypersensitivity reactions may occur in relation with excipients or chemical component of the capsule, such as sodium thiosulfate. Obtain and document an allergy history, particularly a sulfite allergy. Emergency resuscitation equipment and personnel should be immediately available (Section 10 Adverse Reactions).

Monitoring and Laboratory Tests
HICON® is contraindicated in pregnancy because of the risk of fetal hypothyroidism. Obtain a pregnancy test in females of reproductive potential and verify the absence of pregnancy before initiating treatment (Section 9.1.1 *Warnings and Precautions*).

Obtain a complete blood count within one month of therapy. If patients show leukopenia or thrombocytopenia, dosimetry should be used to determine a safe sodium iodide I 131 activity, while delivering less than 2 Gy to the bone marrow (Section 10 *Adverse Reactions*).

Radiation-induced Thyroiditis
Sodium iodide I 131 may cause thyroiditis with release of thyroid hormone, which may aggravate hyperthyroidism and thyrotoxic cardiac disease. When treating hyperthyroidism, consider pre-treatment anti-thyroid medication to help deplete the thyroid hormone. Discontinue the anti-thyroid therapy three days before administration of sodium iodide I 131. Consider a beta-blocker pre or post-treatment to minimize the risk of hyperthyroidism and thyroid storm.

The thyroiditis may cause gland enlargement resulting in tenderness and swelling of the neck, pain on swallowing, sore throat, and cough; which may occur approximately the third day after sodium iodide I 131 administration. Consider management with pain-reliever or anti-inflammatory medications (Section 10 *Adverse Reactions*).

Radiation-induced Toxicities
Sodium Iodide I 131 may cause radiation induced toxicities (Section 10 Adverse Reactions):

- Dose-dependent fatalities (bone marrow suppression, malignancy).
- Dose-dependent hematopoietic suppression which manifests as a transient thrombocytopenia or neutropenia 3-5 weeks following sodium iodide I 131 administrations, may lead to increased susceptibility to infections or bleeding.
- Salivary gland toxicity: sialadenitis, xerostomia.
- Lacrimal gland toxicity: conjunctivitis, xerophthalmia, and epiphora.

Advise good hydration for one week following sodium iodide I 131 administration and stimulate salivary flow via a sialagogue (e.g. sugar-free candy or gum, pilocarpine, and ascorbic acid) to

reduce radiation exposure to the salivary glands.

Advise patients to void frequently after administration of radioiodide to enhance excretion.

Renal Impairment
HICON® is primarily excreted by the kidneys. Renal function impairment decreases excretion of sodium iodide I 131 and increases the radiation exposure and risk of radiation toxicity. For patients with a history of renal impairment, evaluate renal function for therapeutic planning and consider dosimetry. Sodium Iodide I 131 is dialyzable. Hemodialysis can be used to reduce total body radiation exposure (Section 12 *Action and Clinical Pharmacology*).

Risk of Decreased Effectiveness in Therapy
Certain food or drugs may alter the thyroid uptake of sodium iodide I 131 and diminish its effectiveness. Recent intake of stable iodide in any form, or the use of thyroid or anti-thyroid drugs may diminish thyroid uptake of sodium iodide I 131 (Section 11 *Drug Interactions*).

Sexual Health
Reproduction
HICON® is contraindicated in pregnancy because of the risk of fetal hypothyroidism. Advise females and males of reproductive potential to use effective contraception during treatment with HICON® and for at least six months after the last dose of HICON® (Section 9.1.1 *Warnings and Precautions*).

Fertility
Females
Fertility may be impaired with HICON® treatment. Transient amenorrhea and ovarian insufficiency have been observed after sodium iodide I 131 therapy in females. The literature describes reports of transient menstrual cycle irregularities, including amenorrhea, and ovarian failure in females treated with cumulative doses of 1000 – 59,000 MBq (27 – 1594 mCi) sodium iodide I 131.

Males
Fertility may be impaired with HICON® treatment. Discuss sperm banking for males who are expected to receive a high cumulative dose of sodium iodide I 131. Transient dose-related impairment of testicular function after sodium iodide I 131 therapy has been reported in the published literature. The literature describes reports of males treated with sodium iodide I 131 at doses of 370 MBq – 22,000 MBq (10 – 595 mCi) resulting in transiently impaired testicular function (including spermatogenesis). Permanent impairment is described with high cumulative doses ranging from 19,000 – 29,000 MBq (520 – 800 mCi).

9.1 Special Populations

9.1.1 Pregnant Women

HICON® is contraindicated in pregnancy because fetal exposure can lead to neonatal hypothyroidism, which in some cases is severe and irreversible.

Data from the published literature describe thyroid abnormalities after fetal exposure; including agenesis of the thyroid and neonatal hypothyroidism. Delay in diagnosis of neonatal hypothyroidism after exposure to sodium iodide I 131 in utero can result in severe sequelae

such as decreased mental capacity and delayed bone age. Monitor thyroid function in any infant born after in utero exposure to sodium iodide I 131.

Sodium iodide I 131 crosses the placenta and the fetal thyroid begins to concentrate iodide during the 10-12th week of gestation. In literature reports of maternal exposures to sodium iodide I 131 at doses of 333 – 8325 MBq (9 – 225 mCi) during 4-26 weeks gestational age, the most common adverse outcomes were hypothyroid infants and children.

9.1.2 Breast-feeding

HICON® is contraindicated during lactation because I 131 concentrates in the breast during lactation via the increased expression of the sodium iodide symporter in breast tissue. If sodium iodide I 131 is administered in the postpartum period, the lactating mother should not breastfeed.

Limited published literature describes sodium iodide I 131 transfer into breast milk and thyroidal uptake by the breastfed infant. The amount of sodium Iodide I 131 detected in the breast milk at 36-48 hours after administration is 1-27% of the injected dose (with injected doses between 1.1 – 5143 MBq). Infants exposed to sodium iodide I 131 through breast milk are at risk for development of hypothyroidism because sodium iodide I 131 is distributed into breast milk and may reach concentrations equal to or greater than concentrations in maternal plasma.

The literature describes moderate to marked radioiodine uptake in the breast tissue for 5-32 weeks post cessation of breast feeding. Advise lactating women to discontinue breast feeding at least 6 weeks prior to administration of sodium iodide I 131 to allow sufficient time for involution to occur and to avoid excess concentration of sodium iodide I 131 in breast tissue. Consider administration of drugs to suppress lactation. Consider diagnostic scintigraphy before administration of sodium iodide I 131 to assess the persistence of uptake by breast tissue. Women may breast feed with the birth of another child.

9.1.3 Pediatrics

Safety and efficacy in pediatric patients have not been established. Because of the increased absorbed radiation dose from I 131 in pediatric patients, the risks and benefits from therapy with Sodium Iodide I 131 must be assessed before consideration is given to the use of this radiopharmaceutical in pediatric patients. Pediatric patients are at an increased lifetime risk for malignancy from radiation exposure.

9.1.4 Geriatrics

Clinical experience has not identified differences in safety or effectiveness in geriatric patients compared to younger patients. However, elderly patients are more likely to have decreased renal function and radiation exposure is greater in patients with impaired renal function.

10 ADVERSE REACTIONS

10.1 Adverse Reaction Overview

The following serious adverse reactions are described below and in Section 9 *Warnings and Precautions*:

- Hypersensitivity Reactions
- Radiation-induced Thyroiditis
- Radiation-induced Toxicities
- Fertility

With the use of large doses of sodium iodide I 131, potential side effects include acute radiation sickness, salivary and lacrimal gland dysfunction, hemorrhage and swelling in tumors, hyperthyroidism, bone marrow suppression (leukopenia, thrombocytopenia, anemia, blood dyscrasia), acute leukemia, and chromosomal abnormalities.

Sodium iodide I 131 may cause thyroiditis with release of thyroid hormone, which may aggravate hyperthyroidism and thyrotoxic cardiac disease. Thyroiditis may cause gland enlargement resulting in tenderness and swelling of the neck, pain on swallowing, sore throat, and cough.

About 25% of patients become hypothyroid during the first year post-therapy, while the remainder become hypothyroid at a rate of 2% - 3% per year.

Although rare, hypersensitivity reactions such as itching, rash, hives and anaphylaxis may occur in patients who receive sodium iodide I 131. Nausea, vomiting, chest pain and tachycardia have also been reported.

Following I 131 therapy for thyroid carcinoma with metastases to the brain, cerebral edema has been reported as a possible complication.

10.2 Post-Market Adverse Reactions

The following adverse reactions have been identified during post-market use of sodium iodide I 131. Because these reactions are voluntarily reported by from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

System Organ Class	Symptom
Gastrointestinal disorders	sialadenitis, salivary gland dysfunction, nausea, vomiting, gastritis
Cardiac disorders	chest pain, tachycardia
Skin and subcutaneous tissue disorders	itching, rash, hives
Endocrine disorders	hypothyroidism, hyperthyroidism, thyrotoxic crisis, hypoparathyroidism
General disorders and administration site conditions	local swelling of thyroid or sites of iodide avid tumor
Hematologic and lymphatic disorders including fatalities	bone marrow depression, anemia, leukopenia, thrombocytopenia, and blood dyscrasia

Neoplasms benign, malignant and unspecified (including cysts and polyps)	acute leukemia solid cancer
Eye disorders	lacrimal gland dysfunction
Congenital, familial and genetic disorders	congenital hypothyroidism, chromosomal abnormalities
Immune system disorders	bronchospasm
Nervous system disorders	headache, *cerebral edema.
Respiratory, thoracic and mediastinal disorders	**radiation pneumonitis, **pulmonary fibrosis

* In patients with iodide-avid brain metastases
** In patients with iodide-avid lung metastases

11 DRUG INTERACTIONS

11.1 Serious Drug Interactions Box

Concomitant use of bone marrow depressants may enhance the depression of the hematopoietic system caused by the use of large doses of Sodium Iodide I 131.

11.2 Overview

Concomitant use of bone marrow depressants may enhance the depression of the hematopoietic system caused by the use of large doses of Sodium Iodide I 131.

Many drugs and iodide-containing foods interfere with the accumulation of radioiodide by the thyroid. Review the patient's history, current medications, and recent diagnostic tests prior to the administration of sodium iodide I 131.

11.3 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions. Patients who are using prescription drugs are required to discontinue interfering agents before they undergo the procedure.

Pharmaceuticals/OTCs/Agents Blocking Radioiodine Uptake

Type of Medication	Recommended time of withdrawal
Thionamide medications (e.g., propylthiouracil, methimazole, carbimazole)	3 days
Multivitamins containing iodide	10 days
<u>Natural or synthetic thyroid hormones</u> triiodothyronine thyroxine	 2 weeks 4 weeks

Kelp, agar, carrageenan, Lugol solution	3 weeks
Saturated solution of potassium iodide	3 weeks
Topical iodide (e.g., surgical skin preparation)	3 weeks
Intravenous radiographic contrast agents Water soluble Lipophilic	 2 months 6 months
Amiodarone	6 months

11.4 Drug-Food Interactions

Goitrogenic foods interfere with the accumulation of radioiodide by the thyroid. Advise patients to maintain a low-iodide diet two weeks prior to radioiodide administration [Iodide-containing foods such as iodized salt, dairy products, egg yolks, seafood, turkey and liver] and continue for several days during the uptake or imaging process.

11.5 Drug-Herb Interactions

Interactions with herbal products have not been established.

11.6 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

12 ACTION AND CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Iodide is actively transported by the sodium-iodide symporter (NIS) protein, in thyroid follicular cells. Iodide is concentrated in follicular cells to levels up to 50 times higher than in the plasma. Iodide is metabolically oxidized by thyroid peroxidase to iodinium (I+) which in turn iodinates tyrosine residues of thyroglobulin (tri or tetra-iodinated tyrosine). The beta emission of I 131 is responsible for the therapeutic effect.

12.2 Pharmacodynamics

The relationship between the extent of iodide I 131 exposure and pharmacologic effects has not been explored in clinical trials.

12.3 Pharmacokinetics

Absorption: Following oral administration, of HICON®, 90% of the administered radioactivity of Iodide I 131 is systemically absorbed in the first 60 minutes.

Distribution: Following absorption, iodide I 131 is distributed within the extra-cellular space. It is actively transported by the sodium-iodide symporter (NIS) protein, and binds to thyroglobulin resulting in accumulation in the thyroid. The thyroid uptake of iodide is usually increased in hyperthyroidism and in goiter, and is decreased in hypothyroidism. It should be noted that the

uptake of radioactive iodide is a function of stable iodide concentration in the serum and the functional state of the thyroid. The iodine concentrating mechanism of the thyroid, termed the iodide trap or pump, accounts for an iodide concentration of some 25 times plasma levels, but may increase as much as 500 times under certain conditions. It also accumulated in the stomach, choroid plexus, salivary glands, breast, liver, gall bladder, and kidneys.

Metabolism: Trapped iodide is oxidized to iodine and organically incorporated so rapidly that the iodide trap of the thyroid contains less than 0.2% free iodide in comparison to the organically bound iodine. This process results in further concentration of iodine in the thyroid gland to about 500 times that in the blood.

The iodinated organic compounds chiefly consist of thyroxine (T4) and triiodothyronine (T3), which are bound by thyroglobulin in the follicular colloid. T4 and T3 are released by enzymatic proteolysis of thyroglobulin into the blood where they are specifically bound and transported by plasma thyroid binding proteins. These reactions are primarily under the control of anterior pituitary gland release of thyroid stimulating hormone (TSH) and hypothalamic thyroid release factor (TRF).

In thyroidal follicular cells iodide is oxidized through the action of thyroid peroxidase to iodinium (I+) which in turn iodinates tyrosine residues of thyroglobulin.

Elimination: Sodium Iodide I-131 is excreted in urine and feces. The normal range of urinary excretion is 37 to 75% of the administered dose, varying with the thyroid and renal function of the patient. Fecal excretion is about 10%.

13 STORAGE, STABILITY AND DISPOSAL

Store and dispose of HICON® in compliance with the appropriate regulations of the government agency authorized to license the use of this radionuclide. Do not use the kit beyond the expiration date stamped on the label accompanying the product vial. The capsule prepared with HICON® should be used within 7 days from compounding.

The Sodium Iodide I 131 Solution USP provided with HICON® should be stored between 15°C to 30°C.

Discard unused capsules after all HICON® solution has been dispensed or expired. New blister packages of hard gelatin capsules are provided with each new shipment of HICON®.

14 SPECIAL HANDLING INSTRUCTIONS

As in the use of any other radioactive material, care should be taken to minimize radiation exposure to patients consistent with proper patient management, and to minimize radiation exposure to occupational workers.

PART II: SCIENTIFIC INFORMATION

15 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:	Sodium iodide (^{131}I)
Chemical name:	Sodium iodide (^{131}I)
Molecular formula and molecular mass:	NaI; 154 g/mol
Physicochemical properties:	White granular or colorless crystals Odorless Solubility: 184 g/l00 ml water @ 25°C

Product Characteristics

HICON® (Sodium Iodide; I 131) is a kit which provides a solution of Sodium Iodide I 131 with a radioconcentration of 37 GBq/mL, a set of empty hard gelatin capsules and a set of hard gelatin capsules containing approximately 300 mg of Dibasic Sodium Phosphate Anhydrous as the absorbing buffer.

The concentrated solution is intended for use in the preparation of capsules and solutions of varying strengths for oral administration for therapy.

Each mL of the concentrated solution contains 37 GBq of no-carrier-added Sodium Iodide I 131, < 2 mg of Disodium Edetate Dihydrate as a stabilizer, < 22 mg of Sodium Thiosulfate Pentahydrate as a reducing agent, and < 40 mg of Dibasic Sodium Phosphate Anhydrous. The pH of the solution is between 7.5 and 10.0.

Sodium Iodide Solution is designated chemically as Na131I (MW 153.99, CAS 7790-26-3).

16 NON-CLINICAL TOXICOLOGY

Species	Route of administration	LD_{50}
Mice	Intraperitoneal	1690 ± 85 mg/kg
Mice	Intravenous	> 1500 mg/kg
Mice	Oral	1650 ± 90 mg/kg

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

HICON®
Sodium Iodide (I 131)

Read this carefully before you start treatment with **HICON®**. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **HICON®**.

Serious Warnings and Precautions

Radiopharmaceuticals should be used only by those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans.

What is HICON® used for?

- HICON® is used to treat an overactive thyroid.
- HICON® is also used to treat certain cancers of the thyroid.

How does HICON® work?

HICON® is a radioactive from of iodide. Iodide is an essential element that is part of our normal diet and is used by the thyroid to make thyroid hormone. The radioactive iodide in HICON® is captured by the thyroid and the radioactivity then destroys some of the thyroid tissue.

What are the ingredients in HICON®?

Medicinal ingredients: Sodium iodide (^{131}I)
Non-medicinal ingredients: There are no important non-medicinal ingredients.

HICON® comes in the following dosage forms:

Solution, 37 GBq/mL.

Do not use HICON® if:

HICON® should not be used if:

- You are pregnant
- You are breastfeeding
- You are vomiting, have diarrhea
- You are taking anti-thyroid medication

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take HICON®. Talk about any health conditions or problems you may have, including if you:

- are not certain that you are not pregnant
- are breastfeeding
- are felling nauseous, have been vomiting, or have diarrhea
- have kidney problems
- are allergic to sulfites. HICON® capsules may contain sodium thiosulfate.
- recently received medication containing iodide including contrast dye for x-ray or CT scans

Other warnings you should know about:
Drink fluids and use the toilet as often as possible after receiving HICON® to help reduce to amount of radiation to your organs.

Follow your doctor's instructions after receiving this medication to avoid radiation exposure to other people.

- Radioactive iodine will pass out through your urine, feces, saliva and sweat. Be cautious of your personal hygiene; wash your hands frequently and do not share dishes or personal items such as toothbrushes or towels. Wash items promptly after using.
- Men should sit on the toilet when urinating to avoid any splashing of urine.
- Use a tissue to wipe the toilet bowl, flush the toilet twice and rinse the sink and tub after use
- Avoid close contact with family members and maintain a distance of a least 3 feet from women who are pregnant and children under 18 years old.
- Avoid activities where you may be close to others people for more than 5 minutes, for example, movie theaters, sporting events and public transportation.
- Sleep in a separate room

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with HICON®:
A number of prescription and non-prescription drugs may interact with HICON®. Make sure your doctor knows all of the drugs you are taking.

- Thionamide medications (e.g., propylthiouracil, methimazole, carbimazole)
- Multivitamins containing iodide
- Natural or synthetic; thyroid hormones, triiodothyronine, thyroxine
- Kelp, agar, carrageenan, Lugol solution
- Saturated solution of potassium iodide
- Topical iodide(e.g., surgical skin preparation)
- Intravenous radiographic contrast agents: Water soluble, Lipophilic
- Amiodarone

How to take HICON®:
HICON® will be given to you by a healthcare professional who is experienced in the use of radiopharmaceuticals.

Usual dose:
The recommended dose for orally administered sodium iodide I 131 capsules or solution will be determined by the physician prior to treatment, based on the thyroid gland uptake as well as the size of the gland.

If you think you have been administered too much HICON®, contact your healthcare professional who is experienced in the use of radiopharmaceuticals, or hospital emergency department for appropriate management of possible complications.

What are possible side effects from using HICON®?
These are not all the possible side effects you may feel when taking HICON®. If you experience any side effects not listed here, contact your healthcare professional.

The radiation may cause local swelling, sore throat, cough, dry mouth and pain on swallowing. It may also cause nausea, headache and vomiting.
Most known serious side effects will only be detected by blood tests. If you think you are having any serious side effects of receiving HICON® contact your doctor or pharmacist.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON			
Pain or swelling of neck	**X**		Not applicable for single dose
Pain or swelling of salivary gland	**X**		Not applicable for single dose
Lacrimal gland dysfunction: no tears, dry eyes, increased tearing	**X**		Not applicable for single dose
RARE			
chest pain, rapid heartbeat, sweating		**X**	Not applicable for single dose
shortness of breath, stridor		**X**	Not applicable for single dose
itching , skin rash, hives	**X**		Not applicable for single dose

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Store between 15°C to 30°C.

If you want more information about HICON®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website; the manufacturer's website http://www.draximage.com/catalogue-can.html , or by calling 1-800-633-5343.

This leaflet was prepared by Jubilant DraxImage Inc.

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