PRODUCT MONOGRAPH

Sodium Iodide (^{131}I) Solution

Oral Solution

Therapeutic Radiopharmaceutical

IsoLogic Innovative Radiopharmaceuticals Ltd.

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Table 1. Summary Information

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

DESCRIPTION

Sodium Iodide (^{131}I) Solution is an oral therapeutic radiopharmaceutical for the treatment of thyroid disorders.

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

Physical Characteristics

Iodine (^{131}I) decays by beta emission and associated gamma emission with a physical half-life of 8.04 days[1]. The principal beta emissions and gamma photons are listed in Table 2.

Table 2: Principal Emission Data for Iodine (^{131}I)

Radiation/Emission	Beta-1	Beta-3	Beta-4	Gamma-7	Gamma-14	Gamma-17
Photons per Disintegration	2.12	7.36	89.3	6.05	81.2	7.26
Mean Energy (keV)	69.4	96.6	191.4	284.3	364.5	637.0

From reference 1

External Radiation

The specific gamma-ray constant for iodine (^{131}I) is 15.8 $\mu C \cdot kg^{-1} \cdot MBq^{-1} \cdot hr^{-1}$ at 1 cm.

The first half-value thickness of lead (Pb) for iodine (^{131}I) is 0.24 cm. A range of values for the relative attenuation of the radiation resulting from the interposition of various thicknesses of lead is shown in Table 3. For example, the use of 2.55 cm of lead will attenuate the radiation emitted by a factor of about 1000.

Table 3: Radiation Attenuation by Lead Shielding

cm Pb	0.24	0.89	1.6	2.55	3.73
Coefficient of Attenuation	0.5	0.1	0.01	.001	0.0001

Physical Decay

To correct for physical decay of this radionuclide, the fractions that remain at selected intervals after calibration are shown in Table 4.

Table 4. Physical Decay

Day	%	Day	%	Day	%	Day	%
*0	100						
1	91.7%	8	50.1	15	27.4	22	14.9
2	84.2%	9	46.0	16	25.1	23	13.7
3	77.2%	10	42.1	17	23.0	24	12.6
4	70.8%	11	38.7	18	21.1	25	11.5
5	65.0%	12	35.5	19	19.4	26	10.6
6	59.6%	13	32.5	20	17.8	27	9.7
7	54.7%	14	29.8	21	16.3	28	8.9

* Calibration date and time

Exact amounts can be calculated as percent remaining = $e^{(-0.086212*t)}$ where *t* is time from calibration in days.

INDICATIONS AND CLINICAL USE

Sodium Iodide (^{131}I) Solution is indicated for the treatment of hyperthyroidism (diffuse toxic goiter and single or multiple toxic nodular goiter). They may also be used for the treatment of recurrent hyperthyroidism after surgery.

Sodium Iodide (^{131}I) Solution may also be used for therapy of some thyroid carcinomas such as functioning metastatic papillary or follicular carcinoma of the thyroid.

CONTRAINDICATIONS

Because iodide (^{131}I) may cause fetal harm, it is contraindicated in women who are or may become pregnant. Therefore, this radiopharmaceutical should only be administered to a woman of childbearing capability if pregnancy (β-HCG) tests are negative.

Sodium iodide (^{131}I) is contraindicated in patients who are vomiting or have diarrhea, in patients with moderate or severe renal dysfunction, and in those with thyrotoxic cardiac disease, particularly the elderly.

Sodium iodide (^{131}I) is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see *Dosage Forms, Composition and Packaging*.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Sodium iodide (^{131}I) should not be administered to pregnant women.

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

General

Sodium iodide (^{131}I) is radioactive and therefore adequate shielding of the radiopharmaceutical must be maintained.

Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

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.

The radiopharmaceutical product may be received, used and administered only by authorized persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of local competent official organizations.

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.

Carcinogenesis, Mutagenesis, and Impairment of Fertility

No long term animal studies have been performed to evaluate the carcinogenic or mutagenic potential of sodium iodide (^{131}I) or whether this drug affects fertility in males or females.

Special Populations

Pregnant Women: Animal reproduction and teratogenicity studies have not been conducted with sodium iodide (^{131}I). It is also not known whether sodium iodide (^{131}I) can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. There have been no studies in pregnant women.

Sodium iodide (^{131}I) should only be administered to a woman of childbearing capability when appropriate contraceptive measures have been taken or when pregnancy tests are negative. See *CONTRAINDICATIONS*.

Nursing Women: Iodine (^{131}I) is excreted in human milk during lactation. Therefore, formula feedings must be substituted for breast feedings.

Pediatrics: Because of the increased absorbed radiation dose from ^{131}I in pediatric patients, the risks and benefits from therapy with sodium iodide (^{131}I) must be assessed before consideration is given to the use of this radiopharmaceutical in pediatric patients.

Geriatrics: There are no known limitations on the use of sodium iodide (^{131}I) in geriatric patients.

ADVERSE REACTIONS

With the use of large doses of sodium iodide (^{131}I), potential side effects include acute radiation sickness, sialoadenitis, pain, hemorrhage and swelling in tumors, hyperthyroidism, bone marrow suppression (leukopenia, thrombocytopenia, anemia), and radiation thyroiditis.

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.

DRUG INTERACTIONS

Concomitant use of bone marrow depressants may enhance the depression of the hematopoietic system caused by the use of large doses of sodium iodide (^{131}I).

Goitrogenic foods, many drugs (antitussives, expectorants, glucocorticoids, monovalent anions, sodium nitroprusside, synthetic and natural thyroid preparations, and anti-thyroid medications, iodinated radiographic media, phenylbutazone, salicylates, vitamins, etc.) and certain diseases (nephrosis, impaired renal function, etc.) interfere with the accumulation of radioiodide by the thyroid. Therefore, a careful review of the patient's history, current medication and recent diagnostic tests is required prior to the administration of Sodium Iodide (^{131}I).

DOSAGE AND ADMINISTRATION

Dosing considerations

Sodium Iodide (^{131}I) Solution is not intended for direct administration to patients. Sodium Iodide (^{131}I) Solution should diluted for administration of an oral solution, or injected into hard gelatin capsules. See *Instructions for Preparation and Use*.

Dosage

The recommended activities of sodium iodide (^{131}I) for therapy in a 70 kg adult are:

Hyperthyroidism: 148 - 370 MBq. 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 GBq for ablation of normal thyroid tissue.

3.7 - 7.4 GBq for subsequent treatments.

Administration

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

Instructions for Preparation and Use

Drug Handling

Sodium iodide (^{131}I) should not be used after the expiration date stated on the label.

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.

Care should be taken to minimize radiation exposure to the patient consistent with proper patient management and to insure minimum radiation exposure to occupational workers. Waterproof gloves should be used during the entire handling and administration procedure. Adequate shielding should be maintained during the life of the product.

Preparation of Dilute Sodium Iodide (^{131}I) Solution USP

1. Using the calibration date and radioconcentration on the vial label, calculate the required volume to produce the activity to be administered.
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. The recommended diluent is Purified Water USP containing 0.2% Sodium Thiosulfate USP as a reducing agent. The use of acidic diluents may cause the pH to drop below 7.5 and stimulate the volatilization of hydriodic (^{131}I) acid.

Immediately prior to administration, the patient dose should be measured in a suitable radioactivity calibration system. The finished preparation should not be used after the expiration date stated on the container label.

Preparation of Sodium Iodide (^{131}I) Capsules USP

1. Open a number 2 hard gelatin capsule by pulling apart the capsule into two pieces.
2. In the smaller of the two pieces of the n° 2 capsule, place approximately 300 mg of dibasic sodium phosphate anhydrous USP (the absorbing buffer). Close the capsule.
3. Open a number 1 hard gelatin capsule by pulling apart the capsule into two pieces.
4. In the smaller of the two pieces, place the number 2 hard gelatin capsule containing the buffer.
5. Using the calibration date and radioconcentration on the vial label, calculate the required volume to produce the activity to be administered.
6. Using a shielded syringe, remove the required volume.
7. Using the shielded syringe, inject the desired volume into the center of the closed n° 2 capsule, containing the adsorbing buffer.
8. Slip the upper half of the n° 1 capsule over the bottom half to completely cover the small capsule and push down gently until locked.

Immediately prior to administration, the patient dose should be measured in a suitable radioactivity calibration system. The finished preparation should not be used after the expiration date stated on the container label.

RADIATION DOSIMETRY

Table 5. Radiation Dose Estimates (mGy/MBq)

Organ	Thyroid uptake	
	0%	35%
Adrenals	3.7E-02	4.2E-02
Bladder wall	6.1E-01	4.0E-01
Bone surfaces	3.2E-02	7.6E-02
Breast	3.3E-02	6.7E-02
GI-tract		
Stomach wall	3.4E-02	4.6E-01
Small intestine	3.8E-02	2.8E-01
ULI wall	3.7E-02	5.8E-02
LLI wall	4.3E-02	4.0E-02
Kidneys	6.5E-02	5.6E-02
Liver	3.3E-02	3.7E-02
Lungs	3.1E-02	9.0E-02
Ovaries	4.2E-02	4.2E-02
Pancreas	3.5E-02	5.4E-02
Red marrow	3.5E-02	8.6E-02
Spleen	3.4E-02	4.6E-02
Testes	3.7E-02	2.6E-02
Thyroid	2.9E-02	5.0E+02
Uterus	5.4E-02	5.0E-02
Other tissue	3.2E-02	1.1E-01
Effective dose (mSv/MBq)	**6.1E-02**	**2.4E+01**

From ICRP Publications 53[2] and 62[3]

ACTION AND CLINICAL PHARMACOLOGY

Sodium iodide is rapidly absorbed from the gastrointestinal tract. About 10% - 25% of the administered dose is selectively concentrated from the blood by the normal thyroid gland. The thyroid uses iodine to form thyroid hormones [thyroxine (T4), triiodothyronine (T3)] by iodination of tyrosine residues in thyroglobulin. Iodine is also accumulated but not organified by the stomach mucosa, choroid plexus, lactating breast and salivary glands; the remainder is distributed within the extracellular fluid. In euthyroid patients, approximately 60% to 90% of the administered dose is excreted in the urine within 24 hours.

STORAGE AND STABILITY

Sodium Iodide (^{131}I) Solution should be stored between 15° and 30°C.

Expiry is 30 days from End-of-Synthesis.

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.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Sodium Iodide (^{131}I) Solution is supplied in 1, 2, 3, or 5 mL glass V-vials.

Each mL of the aqueous solution contains:

- 37 GBq of sodium iodide (^{131}I)
- < 40 mg dibasic sodium phosphate USP
- < 4.7 mg sodium thiosulphate pentahydrate USP< 1.9 mg sodium hydroxide USP

PART II: SCIENTIFIC INFORMATION

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

Sodium Iodide (^{131}I) Solution is sodium iodide (^{131}I) solution, at a radioconcentration of 37 GBq/mL

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 (^{131}I) in 0.05N NaOH and 0.02N sodium thiosulfate pentahydrate, with up to 40 mg of dibasic sodium phosphate. The pH of the oral solution is 7.5 to 10.0.

Sodium iodide is designated chemically as Na^{131}I (MW 153.99, CAS 7790-26-3).

DETAILED PHARMACOLOGY

Absorption

Following oral administration, sodium iodide (^{131}I) is readily absorbed from the gastrointestinal tract.

Distribution

Following absorption, iodide is primarily distributed within the extra-cellular fluid of the body. It is trapped by the thyroid. The thyroid uptake of iodide is usually increased in hyperthyroidism and in goiter with impaired hormone synthesis, decreased in hypothyroidism, and normal to decreased in hypothyroidism receiving iodine. 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 is also concentrated by the stomach, choroid plexus, and salivary glands, but is not protein-bound.

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).

Excretion

Iodide (^{131}I) is excreted by the kidneys. The normal range of urinary excretion is 37-75% of the administered dose, varying with the thyroid and renal function of the patient.

TOXICOLOGY

Table 6. Toxicology

Species	Route of administration	LD50
Mice	Intra-peritoneal	1690 ± 85 mg/kg
Mice	Intravenous	> 1500 mg/kg
Mice	Oral	1650 ± 90 mg/kg

From Webster 1957[4]

REFERENCES

1 Kocher D, Radioactive Decay Data Tables, DOE/TIC-11026;1981:133

2 International Commission on Radiological Protection. Radiation Dose to Patients from Radiopharmaceuticals. ICRP Publication 53. Ann ICRP. 1987;18(1-4):1-377

3 International Commission on Radiological Protection. Radiological Protection in Biomedical Research. ICRP Publication 62. Ann ICRP. 1993;22 (3):1-28

4 Webster SH, Rice ME, Highman B, Von Ottingen MF. The toxicology of potassium and sodium iodates: acute toxicity in mice. J Pharmacol Exp Ther 1957;120(2):171-8

PART III: CONSUMER INFORMATION

Sodium Iodide (^{131}I) Solution

This leaflet is part III of a three-part "Product Monograph" published when Sodium Iodide (^{131}I) Solution was approved for sale in Canada and is designed specifically for consumers. This leaflet is a summary and will not tell you everything about Sodium Iodide (^{131}I) Solution. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
Sodium Iodide (^{131}I) Solution is used to treat an overactive thyroid. It is also used to treat certain cancers of the thyroid.

What it does:
Sodium Iodide (^{131}I) Solution 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 is captured by the thyroid and the radioactivity then destroys some of the thyroid tissue.

When it should not be used:
Sodium Iodide (^{131}I) Solution is a radioactive product and should not be used if you are pregnant, if you are vomiting or have diarrhea, or if you have moderate or severe kidney disease.

What the medicinal ingredient is:
Sodium iodide (^{131}I).

What the important non-medicinal ingredients are:
There are no important non-medicinal ingredients.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Iodide (^{131}I) should not be administered to pregnant women.
- If you are breastfeeding, you must stop breastfeeding after receiving Iodide (^{131}I).

BEFORE you receive Sodium Iodide (^{131}I) Solution talk to your doctor or pharmacist if:

- If you are not certain that you are not pregnant
- If you are breastfeeding
- If you are felling nauseous, have been vomiting, or have diarrhoea
- If you have kidney disease

INTERACTIONS WITH THIS MEDICATION

A number of prescription and non-prescription drugs may interact with Sodium Iodide (^{131}I) Solution. Make sure your doctor knows all of the drugs you are taking.

PROPER USE OF THIS MEDICATION

This product will be administered under the supervision of a health professional who is experienced in the use of radiopharmaceuticals.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The very small quantity of drug that will be administered is unlikely to cause any side can effects. The radiation that this small quantity carries may cause a little nausea. It may also cause slight swelling or pain in your salivary glands. Any other side effects will only be seen when your doctor does blood tests.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Most known serious side effects will only be detected by blood tests. If you think you are having any serious side effects after receiving Sodium Iodide (^{131}I) Solution contact your doctor or pharmacist.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701D
    Ottawa, Ontario K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor, IsoLogic Innovative Radiopharmaceuticals Ltd., 1855 32nd Avenue, Lachine, Quebec H8T 3J1.
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