Product Monograph

Including Patient Medication Information

DATSCAN

Ioflupane (^{123}I)

Solution in single-use vial administered by intravenous injection

74 MBq/mL per vial at calibration

Diagnostic Radiopharmaceutical

GE Healthcare Canada Inc.
1919 Minnesota Court,
Mississauga, Ontario
L5N 0C9

Date of Authorization:
2026-05-05

Control Number: 304653

Recent Major Label Changes

None at time of the most recent authorization	2026-05

Table of Contents

Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Part 1: Healthcare Professional Information

1. Indications

DaTscan (Ioflupane (^{123}I)) is indicated for visualization of functional striatal dopamine transporter using single photon emission computed tomography (SPECT) brain imaging. In adult patients with suspected Parkinsonian Syndromes (PS), DaTscan SPECT imaging may be used as an adjunct to other established evaluations to help differentiate essential tremor from tremor due to PS related to idiopathic Parkinson's Disease (PD), multiple system atrophy (MSA) and progressive supranuclear palsy (PSP).

DaTscan is unable to discriminate between PD, MSA and PSP.

1.1. Pediatrics

Pediatrics (≤18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2. Geriatrics

Geriatrics (>65 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness.

2. Contraindications

- DaTscan is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 Dosage Forms, Strengths, Composition, and Packaging.

3. Serious Warnings and Precautions Box

- Radiopharmaceuticals should be used only by those healthcare professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans.
- Hypersensitivity reactions have been reported following DaTscan administration. Prior to administration appropriate resuscitation equipment should be available.

4. Dosage and Administration

4.1. Dosing Considerations

Patient Preparation

Prior to administration, question the patient for:

- a history of prior reactions to iodine, an iodine-containing contrast agent or other products containing iodine,
- prior or current medications,
- history of head trauma, stroke, psychiatric illness, epilepsy, or tumor, and
- the patient's ability to lie still for approximately 30 to 45 minutes.

Patients should have discontinued all medications that could interfere with uptake of DaTscan (see 7 Warnings and Precautions, Risks with Concomitant Medications Withdrawal, and 9 Drug Interactions).

4.2. Recommended Dose and Dosage Adjustment

Thyroid Blockade

To reduce exposure of the thyroid to free ^{123}I, administer a single 400-mg dose of potassium perchlorate or a single dose of potassium iodide oral solution or Lugol's solution (equivalent to 100 mg iodide) at least 1 hour before the tracer injection.

Dosage

Recommended dose is 111 to 185 MBq administered intravenously. Do not exceed 185 MBq and do not use when the activity is below 110 MBq. In the event of overdose, refer to section 5 Overdose.

Health Canada has not authorized an indication for pediatric use (see 1.1 Pediatrics).

4.4. Administration

- Prior to administration, appropriate resuscitation equipment should be available.
- DaTscan is a solution for intravenous injection. It should be used without dilution.
- Aseptic technique using sterile syringes and needles should be used.
- The patient dose should be measured by a suitable radioactivity calibration system prior to administration.
- To minimize the potential for pain at the injection site during administration, a slow intravenous injection (not less than 15 to 20 seconds) via an arm vein is recommended.
- Prior to imaging, patients should be encouraged to drink large volumes of fluids and to void frequently prior to imaging, to facilitate excretion of DaTscan.

4.6. Image Acquisition and Interpretation

Image Acquisition

Images may be acquired using either multi-headed gamma cameras or multi-detector single slice systems. Each gamma camera system must be capable of single-photon emission computed tomography (SPECT) acquisition and reconstruction to produce transverse slices including a clear visualization of the striatum (head of caudate nucleus and putamen). The single slice detector systems must also be capable of imaging these structures (5-cm minimum detector width to capture the entire striatum in a single acquisition).

SPECT imaging should take place three to six hours post-injection. Images should be acquired using a gamma camera fitted with a high-resolution collimator and calibrated using the 159 keV photopeak and a ± 10% energy window. Angular sampling should not be less than 120 views over 360 degrees. For high-resolution collimators, the radius of rotation should be consistent and set as small as possible (typically 11 to 15 cm). Experimental studies with a striatal phantom suggest that optimal images are obtained with matrix size and zoom factors selected to give a pixel size of 3.5 to 4.5 mm

for those systems currently in use. A minimum of 1500k counts should be collected for optimal images.

Image Interpretation

DaTscan images are interpreted visually or in combination with semiquantification, based upon the appearance of the striata.

Reconstructed pixel size should be between 3.5 mm and 4.5 mm with slices 1 pixel thick. Optimum presentation of the reconstructed images for visual interpretation is transaxial slices parallel to the anterior commissure-posterior commissure (AC-PC) line. Determination of whether an image is normal or abnormal is made by assessing the extent (as indicated by shape) and intensity of the striatal signal. Image interpretation does not involve integration of the striatal image appearance with clinical signs and/or symptoms.

Normal:

In transaxial images, normal images of the striatal binding are characterized by two symmetric comma- or crescent-shaped focal regions of activity mirrored about the median plane. Striatal activity is distinct, relative to surrounding brain tissue (Figure 1).

Abnormal:

Abnormal DaTscan images fall into at least one of the following three categories (all are considered abnormal).

- Activity is asymmetric, e.g. activity in the region of the putamen of one hemisphere is absent or greatly reduced with respect to the other. Activity is still visible in the caudate nuclei of both hemispheres resulting in a comma or crescent shape in one and a circular or oval focus in the other. There may be reduced activity between at least one striatum and surrounding tissues (Figure 2).
- Activity is absent in the putamen of both hemispheres and confined to the caudate nuclei. Activity is relatively symmetrical and forms two, roughly circular or oval, foci. Activity of one or both is generally reduced (Figure 3).
- Activity is absent in the putamen of both hemispheres and greatly reduced in one or both caudate nuclei. Activity of the striata with respect to the background is reduced (Figure 4).

Figure 1

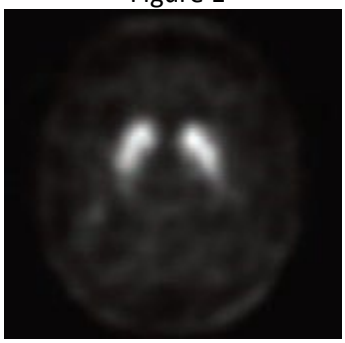


Figure 2

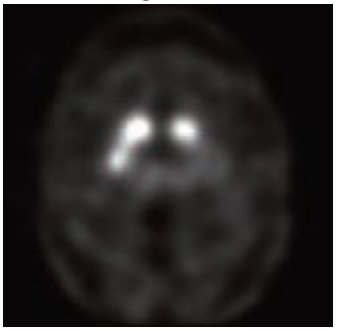


Figure 3

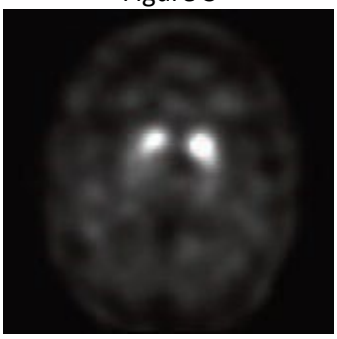
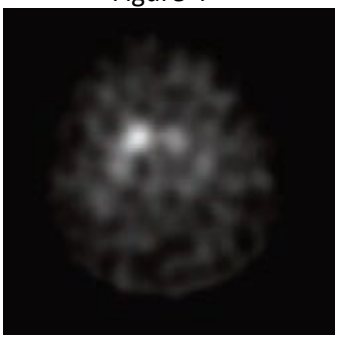


Figure 4



Semiquantification

Semiquantification is defined as the ratio of activity in a structure of interest to activity in a reference region. For semiquantification of ^{123}I-ioflupane DaT SPECT, binding ratios are calculated by comparing activity in the striatum with activity in an area of low DaT concentration (usually the occipital area). Good results for diagnosis based solely on semiquantification have been reported. Semiquantification may yield more objective results and may be of benefit to the inexperienced reader. Semiquantitative data must be compared with an established set of reference values, preferably age-matched.

4.7. Instructions for Preparation and Use of Radiopharmaceuticals

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.

Use aseptic technique and wear waterproof gloves throughout the entire preparation procedure.

DaTscan is a sterile solution for intravenous administration. Reconstitution is not required.

4.8. Radiation Dosimetry

The estimated absorbed radiation doses are listed below (Table 1). The biokinetic model for ioflupane (^{123}I) adopted here assumes initial uptake of 31% of the administered activity in the liver, 11% in the lungs, and 4% in the brain. The rest is assumed to be distributed uniformly in the remaining organs and tissues. For all organs and tissues, 80% is assumed to be excreted with a biological half-life of 58 hours, and 20% with a half-life of 1.6 hours. It is further assumed that 60% of the injected activity is excreted to the urine, and 40% is excreted to the gastrointestinal tract for all organs and tissues. Activity in the liver is excreted according to the Publication 53 gallbladder model (ICRP, 1987), where 30% is eliminated via the gallbladder and the remainder passes directly into the small intestine.

Table 1 – The Estimated Absorbed Radiation Doses for ioflupane (^{123}I)

ORGAN	Absorbed radiation dose (µGy/MBq)	Absorbed radiation dose rad/mCi
Adrenals	17.0	0.063
Bone surfaces	15.0	0.056

ORGAN	Absorbed radiation dose (μGy/MBq)	Absorbed radiation dose rad/mCi
Brain	16.0	0.059
Breasts	7.3	0.027
Gallbladder Wall	44.0	0.163
Gastrointestinal tract		
Stomach wall	12.0	0.044
Small intestine wall	26.0	0.096
Colon Wall	59.0	0.218
(Upper large intestine wall)	57.0	0.211
(Lower large intestine wall)	62.0	0.229
Heart Wall	32.0	0.118
Kidneys	13.0	0.048
Liver	85.0	0.315
Lungs	42.0	0.155
Muscle	8.9	0.033
Esophagus	9.4	0.035
Ovaries	18.0	0.067
Pancreas	17.0	0.063
Red Marrow	9.3	0.034
Salivary glands	41.0	0.152
Skin	5.2	0.019
Spleen	26.0	0.096
Testes	6.3	0.023
Thymus	9.4	0.035
Thyroid	6.7	0.025
Urinary bladder wall	35.0	0.130
Uterus	14.0	0.052
Remaining organs	10.0	0.037
Effective dose	25.0 μSv/MBq	925 μSv/mCi

ICRP Publication 128 (International Commission of Radiological Protection, Radiation Dose to Patients from Radiopharmaceuticals: A Compendium of Current Information Related to Frequently Used Substances, Ann ICRP 2015.

The effective dose (*E*) resulting from administration of 185 MBq of DaTscan injection is estimated at 4.63 mSv. The above data are valid in normal pharmacokinetic behavior.

When renal or hepatic function is impaired, the effective dose and the radiation dose delivered to organs might be increased.

5. Overdose

In cases of overdose of radioactivity, frequent micturition and defecation should be encouraged to minimize radiation dosage to the patient. Care should be taken to avoid contamination from the radioactivity eliminated by the patient using such methods.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6. Dosage Forms, Strengths, Composition, and Packaging

Table 2 – Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form/ Strength/Composition	Non-Medicinal Ingredients
Intravenous	Solution for injection/ 74 MBq/mL (2mCi/mL) at calibration	acetic acid sodium acetate 5% v/v ethanol water for injection

DaTscan is a sterile solution for intravenous administration containing ioflupane (^{123}I) 74 MBq/mL (2 mCi/ mL) at reference time (0.07 to 0.13 mcg/ mL of ioflupane).

- Each 2.5 mL single-dose vial contains 185 MBq ioflupane (^{123}I) (specific activity range 2.5 to 4.5 x 10^{14} Bq/mmol) at reference time.
- Each 5 mL single-dose vial contains 370 MBq ioflupane (^{123}I) (specific activity range 2.5 to 4.5 x 10^{14} Bq/mmol) at reference time.

The product is supplied as 2.5 mL or 5 mL solution in a single colourless 10 mL glass vial sealed with a rubber closure and metal overseal.

6.1. Physical Characteristics

The radioactive label in DaTscan is Iodine-123, a cyclotron-produced radionuclide with a half-life of 13.2 hours through proton bombardment of enriched Xenon-124.

Table 3 - Principal Radiation Emission Data ^{123}I

Radiation	Energy level (keV)	Abundance (%)
Gamma	159	83

6.2. External Radiation

The specific gamma ray constant for iodine 123 is 1.6 R/mCi-hr at 1 cm. The first half-value thickness of lead (Pb) for ^{123}I is 0.04 cm. The relative transmission of radiation emitted by the radionuclide that results from interposition of various thicknesses of Pb is shown in Table 4 (e.g., the use of 2.16 cm Pb will decrease the external radiation exposure by a factor of about 1,000).

Table 4 - Reduction in In-air Collision Kerma Caused by Lead Shielding*

Shield Thickness cm of Lead (Pb)	Reduction in In-Air Collision Kerma
0.04	0.5
0.13	0.1
0.77	0.01
2.16	0.001
3.67	0.0001

*Calculation based on attenuation and energy-transfer coefficients obtained from National Institute of Standards & Technology Report NISTIR 5632

7. Warnings and Precautions

See 3 Serious Warnings and Precautions Box.

The product should be administered under the supervision of a healthcare 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.

General

DaTscan contains alcohol (ethanol) 5 % by volume. Each dose contains up to 197 mg alcohol which is the amount contained in approximately 5 mL of beer or 2 mL of wine. The alcohol content should be taken into consideration when DaTscan is to be administered to patients who have alcoholism, liver disease, or epilepsy, and also in patients who are pregnant or breastfeeding.

Contamination

The following measures should be taken for up to 12 hours after receiving the radiopharmaceutical product: Toilet should be used instead of urinal. Toilet should be flushed several times after use. If blood or urine gets onto clothing such clothing should be washed separately or stored for 1 to 2 weeks to allow for radioactive decay.

Special precautions such as bladder catheterization should be taken following administration to incontinent patients to minimize the risk of radioactive contamination of clothing, bed linen and the patient's environment.

Hypersensitivity Reactions

Hypersensitivity reactions have been reported following DaTscan administration. Prior to administration, the patient should be questioned for a history of reactions to iodine, an iodine-containing contrast agent or other products containing iodine. If the patient is known or strongly suspected to have hypersensitivity to any of the above, the decision to administer DaTscan should be based upon an assessment of the expected benefits compared to the potential hypersensitivity risks. Anaphylactic and hypersensitivity treatment measures and resuscitative equipment (e.g., endotracheal tube and ventilator) should be available prior to DaTscan administration. If hypersensitivity reactions occur, DaTscan administration must be discontinued immediately.

Renal and Hepatic Impairment

Formal studies have not been carried out in patients with significant renal or hepatic impairment. In the absence of data, DaTscan is not recommended in cases of moderate to severe renal or hepatic impairment.

Risks with Concomitant Medication Withdrawal

Many medications have the potential to interfere with DaTscan imaging, and may result in unreliable imaging results. Review of the patient's medications in advance of the scheduled DaTscan imaging procedure is required to determine whether any medications should be withdrawn prior to DaTscan dosing, and whether the withdrawal can be accomplished safely. DaTscan imaging should not be performed if discontinuation of these medications would involve risks which outweigh the value of DaTscan imaging (see 9.4 Drug-Drug Interactions).

Thyroid Accumulation of I-123

The DaTscan injection may contain up to 6% of free iodide (iodine 123). Accumulation of radioiodine in the thyroid gland may result in long term risk for thyroid neoplasia. To decrease thyroid accumulation of iodine 123, administer a thyroid blocking agent before administration of DaTscan (see 4 Dosage and Administration). Avoid the use of Potassium Iodide Oral Solution or Lugol's Solution in patients who are sensitive to such products.

7.1. Special Populations

7.1.1. Pregnancy

In women of childbearing potential, examinations using radiopharmaceuticals should ideally be performed during the first ten days following the onset of menses, or after ensuring the woman is not pregnant. The benefit of using a diagnostic radiopharmaceutical should be weighed against the possible risk to an embryo or a fetus.

Where 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. Where uncertainty exists, it is important that radiation exposure should be the minimum consistent with achieving satisfactory imaging. Alternative techniques which do not involve ionizing radiation should be considered.

Since adequate reproduction studies have not been performed in animals to determine whether this drug affects fertility in males or females, has teratogenic potential, or has other adverse reactions on

the fetus, this radiopharmaceutical preparation should not be administered to pregnant women unless it is considered that the benefits to be gained outweigh the potential hazards to the fetus.

7.1.2. Breastfeeding

Before administering a radioactive medicinal product to a mother who is breastfeeding, consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breastfeeding and as to whether the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion of activity in breast milk. It is not known whether ioflupane (^{123}I) is secreted in human milk, therefore, if administration is considered necessary, breast-feeding should be interrupted for 3 days and substituted by formula feeding. During this time, breast milk should be expressed at regular intervals and the expressed feeds should be discarded.

7.1.3. Pediatrics

Pediatrics (≤18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4. Geriatrics

Geriatrics (>65 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness.

8. Adverse Reactions

8.1. Adverse Reaction Overview

No serious adverse effects related to DaTscan administration have been reported in eight clinical trials (942 patients) that were used to assess the clinical safety of DaTscan.

8.2. Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies reported in clinical trials of another drug.

The data from clinical studies reflect exposure to DaTscan in 942 subjects with a mean age of 66 years (range 25 to 90 years). Among these subjects, 42% were women and 99% Caucasian. In clinical trials, no serious adverse reactions were reported.

Adverse events (AEs) that were commonly reported (≥2%) in these clinical trials were headache, nausea and dizziness. Not all cases were considered related to DaTscan administration. AEs considered by the investigator to be at least possibly related to DaTscan, were less commonly reported. These included vertigo, increased appetite, dry mouth, formication, and dysgeusia. Most of these AEs were mild and none were assessed to be adverse drug reactions. Injection site pain was uncommonly reported.

8.5. Post-Market Adverse Reactions

Reports of serious and nonserious hypersensitivity or associated manifestations (e.g., erythema, generalized pruritus, dyspnea, oedema, skin lesion, and skin discoloration), as well as reports of injection site pain, headache, dizziness, formication (paresthesia), dysgeusia, nausea and dry mouth have been received from post-marketing surveillance.

Exposure to ionizing radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 4.35 mSv when the maximal recommended activity of 185 MBq is administered, these adverse events are expected to occur with a low probability.

For each patient, exposure to ionizing radiation must be justifiable on the basis of likely benefit and the injected activity should be kept to a minimum but sufficient to obtain the intended diagnostic signal.

9. Drug Interactions

9.2. Drug Interactions Overview

No GE Healthcare sponsored drug interaction studies have been carried out in humans.

Ioflupane binds to the dopamine transporter. Drugs that bind to the dopamine transporter with high affinity can interfere with DaTscan binding and may affect the images obtained following DaTscan administration (see Table 5).

9.4. Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 5 – Established or Potential Drug-Drug Interactions

Non-proprietary names of the drug products	Source of evidence	Effect	Clinical comment
Amphetamine	T	Potential reduction of ioflupane striatal binding	Consider temporary discontinuation of use
Benzatropine	T	Potential reduction of ioflupane striatal binding	Consider temporary discontinuation of use
Bupropion	T	Potential reduction of ioflupane striatal binding	Consider temporary discontinuation of use
Cocaine	T	Potential reduction of ioflupane striatal binding	Consider temporary discontinuation of use
Mazindol	T	Potential reduction of ioflupane striatal binding	Consider temporary discontinuation of use
Methylphenidate	T, CT	Reduction of ioflupane striatal binding ratios	Consider temporary discontinuation of use
Phentermine	T	Not specified	Consider temporary discontinuation of use

Sertraline	T	Not specified	Consider temporary discontinuation of use

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

Serotonin-norepinephrine reuptake inhibitors (SNRIs) such as venlafaxine may decrease ioflupane binding to the dopamine transporter, especially in patients receiving higher doses.

Medicines shown during clinical trials not to interfere with DaTscan imaging include amantadine, trihexyphenidyl, budipine, levodopa, metoprolol, primidone, propranolol and selegiline. The impact of dopamine agonists and antagonists have not been established.

9.5. Drug-Food Interactions

Interactions with food have not been established.

9.6. Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7. Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10. Clinical Pharmacology

DaTscan is a radiolabeled tropane compound with high affinity for the dopamine transporter (DaT). DaTs are present exclusively on dopamine-synthesizing neurons and DaTs can therefore be considered a specific marker of these neurons in the central nervous system. Because DaT distribution in the CNS coincides with dopaminergic innervation, tropane analogues with high DaT binding affinity have been developed for use in neuroimaging as *in vivo* markers of functional dopaminergic systems. Biological studies *in vitro* and *in vivo* have demonstrated that when radiolabelled with the gamma-emitting isotope iodine-123, ioflupane has the appropriate characteristics to enable SPECT visualization of regions of the brain with high expression of DaTs.

10.1. Mechanism of Action

DaTscan is a diagnostic radiopharmaceutical containing ioflupane (^{123}I), used for detecting loss of functional nigrostriatal dopaminergic neurons by SPECT imaging. It is intended to detect or exclude a substantial (>60%) loss of nigrostriatal dopaminergic neurons in patients with signs and symptoms of movement disorders. The mechanism is that the active component in DaTscan, ioflupane (^{123}I), distributes to the brain and preferentially binds to DaTs located predominantly on the nigrostriatal dopaminergic neurons. In healthy humans, this results in visualization of the striata as two “comma”- or “half-moon”-shaped areas of brightness on SPECT imaging. However, loss of the nigrostriatal dopaminergic neurons (e.g., in PD or DLB) results in loss of DaTs associated with those neurons and an absence of signal where it would normally be expected.

10.2. Pharmacodynamics

In the absence of receptor agonist activity and because of the tracer amounts required for such diagnostic procedures (approximately 0.3 mcg), there is no possibility of pharmacodynamic effects. Taking into account the percent of ioflupane (^{123}I) distributed to the brain (9%) and the total number

of DaTs in the human striatum (approximately 16 nmol), the maximum dose of ioflupane is estimated to occupy approximately 0.01% of the total DaT available. In comparison, the DaT occupancy required by cocaine to induce any psychotropic effects in humans is approximately 45% of the total DaT in the striatum.

10.3. Pharmacokinetics

The pharmacokinetics of ioflupane (^{123}I) has been studied in 12 healthy adults. The biodistribution of ioflupane (^{123}I) may not be the same in older subjects with Parkinsonian syndromes.

Absorption

Because administration is intravenous, absorption is complete and ioflupane (^{123}I) is completely bioavailable.

Distribution

Ioflupane (^{123}I) is cleared rapidly from the blood after intravenous injection; only 5% of the administered activity remains in whole blood at 5 minutes post-injection.

Organ Uptake

Uptake in the brain is rapid, reaching about 7% of injected radioactivity at 10 minutes post-injection and decreasing to 3% after 5 hours. Striatal activity is relatively constant between 3 and 6 hours post-injection. About 30% of the whole brain radioactivity is attributed to striatal uptake. The highest levels of radioactivity were measured in the lungs, liver, and brain. The lung showed the widest (inter-subject) variation in initial uptake and in residence times.

Metabolism

Analysis of metabolites in human plasma has been reported. Since none of the metabolites are expected to cross the blood brain barrier, they are considered unlikely to alter the diagnostic efficacy of DaTscan.

Elimination

At 48 hours post-injection, approximately 60% of the injected radioactivity is excreted in the urine, with fecal excretion calculated at approximately 14%.

11. Storage, Stability, and Disposal

The test product should be stored at room temperature (20° to 25°C) in a lead shielded container. Do not freeze.

Shelf-life of the product: 7 hours from the reference time for the 2.5 mL vial and 20 hours from the reference time for the 5.0 mL vial.

12. 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 2: Scientific Information

13. Pharmaceutical Information

Drug Substance

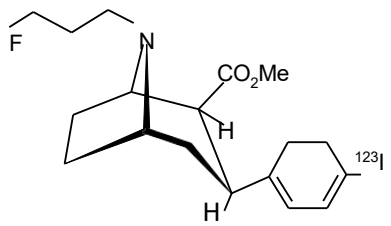
Non-proprietary name of the drug substance(s): Ioflupane (^{123}I)

Chemical name: Methyl (1*R*-2*S*-3*S*-5*S*)-8-(3-fluoropropyl)-3-(4-iodophenyl)-8- azabicyclo[3.2.1] octane-2-carboxylate

Trivial Chemical Name: N-ω-fluoropropyl-2β-carbomethoxy-3 β -(4- [^{123}I]iodophenyl)nortropane

Molecular formula and molecular mass: $C_{18}H_{23}F^{123}INO_2$ and 427.29 (for the iodine-123 compound)

Structural formula:



Physicochemical properties: The molecule is optically active. The route of manufacture ensures that only the 2β,3β- isomer is present in the active substance

Product Characteristics:

Ioflupane (^{123}I) injection is a clear, colourless aqueous solution with a pH of 4.0 to 6.0.

Each vial contains 185 MBq ioflupane (^{123}I) at reference time in 2.5 mL of solution. The 5.0 mL presentation contains 370 MBq at reference.

Radiochemical purity: Not less than 96% ioflupane (^{123}I) at release, not less than 94 % at expiry.

Not more than 4% [^{123}I]iodide at release, not more than 6% at expiry.

Not more than 2% [^{123}I]FP-CIT acid at release and expiry.

DaTscan is carrier-added.

14. Clinical Trials

14.1. Clinical Trials by Indication

Table 6 – Summary of Patient Demographics for Pivotal Clinical Trials in Parkinson's Syndrome

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Age (range)	Sex	Race (%) H&Y Staging
DP008-003 [DP008-003 CREP US]	Phase 3, multicenter, comparator-group, open-label, non-controlled, non-randomized	111 to 185 MBq (3 to 5 mCi), intravenous injection, 1 day	Subjects diagnosed with PD, MSA, PSP or ET aged 40-80 years; healthy volunteers aged 50-80 years (n = 224)	63 years (40 – 80)	M/F: 137/87	Race: Caucasian: 98% H&Y: Stage 1: 15% Stage 2: 21% Stage 3: 13% Stage 4: 11%
PDT03004 (aka PDT304) [PDT304 CREP US]	Phase 3, multicenter, open-label, non-comparative, non-randomized, repeat administration, non-controlled	111 to 185 MBq (3 to 5 mCi), intravenous injection, 36 months	Subjects 30-90 years old with early PD or with other causes of tremor (mainly ET); healthy volunteers (n = 179)	63 years (34 – 86)	M/F: 102/77	Race: Caucasian: 100% H&Y: mean 1.5 (range: 1-3)

ET = essential tremor; iv = intravenous; MSA = multiple system atrophy; PD = Parkinson's disease; PS = Parkinsonian syndrome; PSP = progressive supranuclear palsy

Study Results

Study DP008-003

Study DP008-003 was a pivotal, multicenter, Phase 3 study that evaluated the diagnostic performance of DaTscan images in patients diagnosed with movement disorders and in healthy volunteers. Patients aged 40 to 80 years old with a clinically established diagnosis of Parkinson's Disease (PD), Multiple System Atrophy (MSA), Progressive Supranuclear Palsy (PSP) or Essential Tremor (ET) and healthy volunteers aged 50 to 80 years old were enrolled into the study.

The primary efficacy endpoint was the diagnostic efficacy of DaTscan SPECT image assessment by institutional reader. Secondary endpoints were the diagnostic efficacy of DaTscan SPECT image visual assessment by blinded consensus read and semiquantitative Region of Interest (ROI) analysis of SPECT images.

Each subject received a single intravenous (IV) injection of 111 to 185 MBq (3 to 5 mCi) DaTscan followed 3 to 6 hours later by SPECT imaging. In addition, a Blinded Image Evaluation (BIE) was performed on images that had been processed to a uniform colour scale and format, blinded, and randomized. In both image evaluations, images were classified as normal or abnormal based on the appearance of the striata. The BIE was performed by a panel consisting of 5 of the 13 study investigators and each of these 5 readers independently viewed and classified all blinded images. "Consensus" (majority) blinded image interpretations were derived from the individual blinded readers' interpretations for each subject (e.g., if 3 of 5 readers called the image abnormal, then the "consensus" (majority) assessment was abnormal). As an additional analysis in the original study protocol, a semi-quantitative assessment was performed by the core imaging laboratory based on ROI analysis.

Each image interpretation was compared to the standard of truth (SOT; categorization of patient status at study entry as Striatal Dopaminergic Denervation (SDD) present or absent), and classified as TN, TP, FN, or FP and the classification counts were used to determine sensitivity and specificity as described above. The per-reader sensitivity of the blinded visual assessment for the intent-to-diagnose (ITD) population in identifying a SDD ranged from 92.4% to 96.8%, and specificity ranged from 80.6% to 96.8%. Inter-reader agreement (Cohen's kappa) ranged from 0.81 to 0.95. The results of the semi- quantitative ROI analysis were consistent with the visual image assessments and with the known pathology of these disorders.

Table 7– Summary of Sensitivity and Specificity by Standard of Truth (SOT) Diagnosis

	Sensitivity (95 % CI) (% subjects with an abnormal DaTSCAN image among patients with PS)	**Specificity (95 % CI) (% subjects with a normal DaTSCAN image among patients with non-PS)**
Reader A, n = 220	93% (88, 97)	94% (84, 98)
Reader B, n = 220	97% (93, 99)	81% (69, 90)
Reader C, n = 220	96% (92, 99)	92% (82, 97)
Reader D, n = 220	92% (87, 96)	97% (89, 100)
Reader E, n = 220	94% (90, 97)	92% (82, 97)

Study PDT03004 (also known as PDT304)

Study PDT03004 was a pivotal, multicenter, Phase 3 study that evaluated the diagnostic performance of DaTscan images in differentiating between subjects with early symptoms and signs of movement disorders, specifically Parkinsonism (Striatal Dopaminergic Denervation (SDD) present), other causes of tremor (mainly ET, no SDD), and healthy volunteers (no SDD). Key inclusion criteria were age 30 to 90 years, UPDRS part III score of 16 or less and subjects either with cardinal features of Parkinsonism and fulfilling UK Brain Bank criteria or with any single feature of Parkinsonism but the diagnosis was not clear. The study excluded patients with history and evidence of stroke, depression, Multiple System Atrophy (MSA), Progressive Supranuclear Palsy (PSP) and dementia.

There were 202 subjects enrolled in the study, including 3 healthy volunteers. A total of 99 subjects underwent DaTscan SPECT imaging at 0, 18, and 36 months and were evaluated against the Standard of Truth (SOT). At each time point, SPECT imaging was conducted 3 to 6 hours following a single

intravenous (IV) injection of 111 to 185 MBq (3 to 5 mCi) of DaTscan. Scans were read independently by 3 blinded readers for the main efficacy analysis and on-site for secondary analyses.

Patients were videotaped undergoing neurological examination at 18 and 36 months. The 36 month videos were used as the SOT and were reviewed by 2 movement disorder specialists (MDS), who each decided on the SOT diagnosis. If the two diagnoses did not agree, both MDS discussed the video and reached consensus on the SOT diagnosis.

Each DaTscan image interpretation was compared to the corresponding SOT diagnosis and classified as TP, TN, FP, or FN, and the classification counts were used to determine sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV).

The primary endpoint was diagnostic efficacy of DaTscan SPECT images taken at month 0 compared with clinical diagnosis at month 36. The secondary endpoint was diagnostic efficacy of DaTscan SPECT images taken at month 0 compared with expert diagnosis at other time points.

The sensitivity and specificity of the blinded visual interpretations of DaTscan SPECT images acquired at baseline (month 0), month 18 and month 36 for the ITD population are presented in Table 8. The results remained stable over the course of the study. Pairwise inter-reader agreement (Cohen's kappa) among the blinded readers ranged from 0.98 to 1.00.

Table 8 – Summary of Sensitivity and Specificity by Standard of Truth (SOT) Diagnosis

	Sensitivity (95 % CI) (% subjects with an abnormal DaTSCAN image among patients with PS)	**Specificity (95 % CI) (95 % CI) (% subjects with a normal DaTSCAN image among patients with non-PS**
DaTscan imaging at Baseline (Month 0)		
Reader A, n = 102	78% (66, 87)	97% (83, 100)
Reader B, n = 99	78% (66, 87)	97% (83, 100)
Reader C, n = 101	79% (67, 88)	97% (83, 100)
DaTscan imaging at Month 18		
Reader A, n = 102	78% (66, 87)	97% (83, 100)
Reader B, n = 99	78% (66, 87)	94% (79, 99)
Reader C, n = 101	82% (71, 90)	97% (83, 100)
DaTscan Imaging at Month 36		
Reader A, n = 102	75% (63, 85)	97% (83, 100)
Reader B, n = 99	77% (65, 87)	97% (83, 100)
Reader C, n = 101	78% (66, 87)	97% (83, 100)

16. Non-Clinical Toxicology

Acute Toxicity

Acute toxicity studies of ioflupane (the active ingredient of DaTscan) showed that the highest doses that caused neither death nor signs of toxicity were 1 mg/kg in rats, 0.06 mg/kg in rabbits, 0.3 mg/kg in dogs and 0.1 mg/kg in cynomolgus monkeys. When adjusted for surface area, these doses are approximately 27000, 3200, 30000 and 5500 times the maximum human equivalent dose of ioflupane that could be administered by the 2.5 mL formulation of DaTscan, respectively. For the 5 mL formulation, divide the value by two.

Repeat-Dose Studies

In 14-day repeat-dose studies, no evidence of toxicity was observed in rats or rabbits following daily doses of ioflupane of up to 0.6 mg/kg or in dogs up to doses of 1 mcg/kg (between 100 and 32000 times the maximum human single dose based on the 2.5 mL formulation). Behavioural effects due to pharmacological activity were observed in these studies.

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential, or whether DaTscan affects fertility in males or females.

As with other radiopharmaceuticals which distribute intracellularly, there may be increased risk of chromosome damage from Auger electrons if nuclear uptake occurs.

Genotoxicity

Ioflupane showed no evidence of mutagenic potential in *in vitro* or *in vivo* mutagenicity studies.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

DATSCAN

Ioflupane (^{123}I)

This Patient Medication Information is written for the person who will be taking **DATSCAN**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **DATSCAN**, talk to a healthcare professional.

Serious warnings and precautions box

- Serious allergic reactions have occurred in some patients who received DaTscan. Tell your doctor if you have had allergic reactions to other diagnostic agents or iodine-containing products.

What DATSCAN is used for:

- DaTscan is a radioactive diagnostic agent which is used with a special camera to take pictures of the brain.
- In adult patients who have symptoms of Parkinsonian Syndromes (such as Parkinson's disease), DaTscan is used along with other diagnostic tests to give the doctor more information about their condition.

How DATSCAN works:

When DaTscan is injected into a vein, it is carried throughout the body in the blood. It collects in a small area of your brain. The small amount of radioactivity can be detected from outside the body using a special camera that will take a picture, or scan, of your brain.

The scan will show if there are any changes in this area of your brain and will give your doctor more information about your condition.

When DaTscan is used, you are exposed to small amounts of radioactivity. This exposure is less than some other types of X-ray investigation. Your doctor will always consider the possible risks and benefits of DaTscan.

The ingredients in DATSCAN are:

Medicinal ingredient(s): ioflupane (^{123}I)

Non-medicinal ingredients: acetic acid, sodium acetate, ethanol and water for injection

DATSCAN comes in the following dosage form(s):

DaTscan is available as a 2.5mL solution containing 185 MBq ioflupane (^{123}I) or a 5mL solution containing 370 MBq ioflupane (^{123}I).

Do not use DATSCAN if:

- You are allergic to ioflupane or any of the other ingredients of DaTscan.

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

- Are breast-feeding. Your doctor may delay the use of DaTscan or ask you to stop breastfeeding. It is not known whether ioflupane(^{123}I) is passed into breast milk. As a precaution, you should not breast-feed your child for 3 days after DaTscan is given. Instead use formula feed for your child. Express your breast milk regularly and throw away any breast milk you have expressed. You will need to continue to do this for 3 days, until the radioactivity is no longer in your body.
- Have moderate or severe problems with your kidneys or liver.

Other warnings you should know about:

- DaTscan contains alcohol (ethanol) 5 % by volume. Each dose contains up to 197 mg alcohol which is the amount contained in approximately 5 mL of beer or 2 mL of wine. The alcohol content of DaTscan may be harmful to patients who have alcoholism, liver disease, or epilepsy, and also in patients who are pregnant or breastfeeding. If you have concerns in this regard, discuss with your healthcare professional.

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

Some drugs may reduce the quality of the picture obtained with DaTscan. If you are taking any of the drugs listed below or any other drugs that may interfere with DaTscan, you may be asked to stop taking them for a short time before you receive DaTscan. Ask your doctor whether you can safely stop taking your medications.

The following may interact with DATSCAN:

- bupropion
- benzatropine
- mazindol
- sertraline
- methylphenidate
- phentermine
- amphetamine
- cocaine
- venlafaxine

How to take DATSCAN:

- DaTscan will be given to you by a healthcare professional who is experienced in the use of radiopharmaceuticals. They should tell you anything you need to do for the safe use of this medicine. Your doctor will decide the dose that is best for you.
- Before you receive DaTscan, your doctor will ask you to take some tablets or liquid that contain iodine, to help prevent radioactivity from building up in your thyroid gland. It is important that you take the tablets or liquid as the doctor tells you.
- DaTscan is given to you as an injection, usually into a vein in your arm. Pictures of your brain will be taken 3 to 6 hours after the injection of DaTscan.
- You should drink large glasses of water before and after you get your injection of DaTscan and urinate frequently in the hours after your injection to reduce the amount of radioactivity in your bladder.

Usual dose:
Your healthcare professional will decide the dose that is best for you.

Overdose:

In cases of overdose of radioactivity, frequent urination and bowel movements should be encouraged to minimize radiation dosage to the patient. Care should be taken to avoid contamination from the radioactivity eliminated by the patient using such methods.

If you think you, or a person you are caring for, have taken too much DATSCAN, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Possible side effects from using DATSCAN:

These are not all the possible side effects you may have when taking DaTscan. If you experience any side effects not listed here, tell your healthcare professional.

- headache
- dizziness
- nausea
- increased appetite
- taste disturbance
- dry mouth
- vertigo
- a sensation like insects crawling over your skin (formication)
- intense pain on injection (this has been reported among patients receiving DaTscan into a small vein)
- allergic reaction (hypersensitivity)

Serious side effects and what to do about them

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Unknown			
Hypersensitivity (allergic reaction): for example, rash, redness of the skin, hives, itching all over the body, shortness of breath, swelling		✓	Yes

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell 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 (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

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

Storage:

Store at room temperature (20° to 25°C) in a lead shielded container. Do not freeze.

If you want more information about DATSCAN:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website (Drug Product Database: Access the database); or by calling 1-800-387-7146

This leaflet was prepared by GE Healthcare Canada Inc.

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