

IOFLUPANE I 123- ioflupane i-123 injection, solution

Curium US LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use IOFLUPANE I 123 INJECTION safely and effectively. See full prescribing information for IOFLUPANE I 123 INJECTION.

IOFLUPANE I 123 injection, for intravenous use
Initial U.S. Approval: 2011

RECENT MAJOR CHANGES

Indications and Usage (1) 11/2022
Contraindications (4) 11/2022
Warnings and Precautions, Radiation Risk (5.3) 11/2022

INDICATIONS AND USAGE

loflupane I 123 Injection is a radioactive diagnostic agent indicated as an adjunct to other diagnostic evaluations for striatal dopamine transporter visualization using single photon emission computed tomography (SPECT) brain imaging in adult patients with:

- suspected Parkinsonian syndromes (PS) or
- suspected dementia with Lewy bodies (DLB). (1)

DOSAGE AND ADMINISTRATION

- Administer a thyroid-blocking agent at least one hour before the dose of loflupane I 123 Injection. (2.2)
- The recommended dose of loflupane I 123 Injection in adult patients is 111 MBq to 185 MBq (3 mCi to 5 mCi) administered intravenously over at least 20 seconds. (2.3)
- Measure patient dose using a dose calibrator immediately prior to administration. (2.4)
- Begin SPECT imaging between 3 hours and 6 hours post-injection. (2.6)

DOSAGE FORMS AND STRENGTHS

Injection: 185 MBq (5 mCi) in 2.5 mL at a concentration of 74 MBq/mL (2 mCi/mL) of loflupane I 123 at calibration date and time supplied in single-dose vials. (3)

CONTRAINDICATIONS

Known serious hypersensitivity to ioflupane I 123 (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity Reactions: Hypersensitivity reactions including dyspnea, edema, rash, erythema, and pruritus have been reported. Have treatment measures available prior to loflupane I 123 Injection administration. (5.1)
- Thyroid Accumulation of Iodine-123: Thyroid uptake of iodine-123 may result in an increased long-term risk for thyroid neoplasia. (2.2, 5.2)
- Radiation Risk: Ensure safe handling to minimize radiation exposure to the patient and healthcare providers. Advise patients to hydrate before and after administration and to void frequently after administration. (2.1, 5.3)

ADVERSE REACTIONS

The following adverse reactions were reported at $\leq 1\%$: headache, nausea, vertigo, dry mouth and dizziness. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact CURIUM US LLC at 1-866-789-2211 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Amoxapine, amphetamine, armodafinil, benzotropine, bupropion, buspirone, cocaine, mazindol, methamphetamine, methylphenidate, modafinil norephedrine, phentermine, phenylpropanolamine, selegiline, sertraline, citalopram and paroxetine may interfere with loflupane I 123 Injection imaging. The effects of dopamine agonists and antagonists on loflupane I 123 Injection imaging have not been established. (7)

USE IN SPECIFIC POPULATIONS

- Pregnancy: May cause fetal harm. (8.1)
- Lactation: Advise a lactating woman to interrupt breastfeeding and pump and discard breastmilk for at least 6 days after loflupane I 123 Injection administration. (8.2)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 12/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

- 1 INDICATIONS AND USAGE**
- 2 DOSAGE AND ADMINISTRATION**
 - 2.1 Radiation Safety**
 - 2.2 Thyroid Blockade Before Ioflupane I 123 Injection Administration**
 - 2.3 Recommended Dosage**
 - 2.4 Preparation and Administration**
 - 2.5 Radiation Dosimetry**
 - 2.6 Imaging Instructions**
 - 2.7 Image Interpretation**
- 3 DOSAGE FORMS AND STRENGTHS**
- 4 CONTRAINDICATIONS**
- 5 WARNINGS AND PRECAUTIONS**
 - 5.1 Hypersensitivity Reactions**
 - 5.2 Thyroid Accumulation of Iodine-123**
 - 5.3 Radiation Risk**
- 6 ADVERSE REACTIONS**
 - 6.1 Clinical Trials Experience**
 - 6.2 Postmarketing Experience**
- 7 DRUG INTERACTIONS**
- 8 USE IN SPECIFIC POPULATIONS**
 - 8.1 Pregnancy**
 - 8.2 Lactation**
 - 8.4 Pediatric Use**
 - 8.5 Geriatric Use**
 - 8.6 Renal Impairment**
- 10 OVERDOSAGE**
- 11 DESCRIPTION**
 - 11.1 Chemical Characteristics**
 - 11.2 Physical Characteristics**
 - 11.3 External Radiation**
- 12 CLINICAL PHARMACOLOGY**
 - 12.1 Mechanism of Action**
 - 12.2 Pharmacodynamics**
 - 12.3 Pharmacokinetics**
- 13 NONCLINICAL TOXICOLOGY**
 - 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**
 - 13.2 Animal Toxicology and/or Pharmacology**
- 14 CLINICAL STUDIES**
 - 14.1 Suspected Parkinsonian Syndromes**
 - 14.2 Suspected Dementia with Lewy Bodies**
- 16 HOW SUPPLIED/STORAGE AND HANDLING**
- 17 PATIENT COUNSELING INFORMATION**

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Ioflupane I 123 Injection is indicated as an adjunct to other diagnostic evaluations for striatal dopamine transporter visualization using single photon emission computed tomography (SPECT) brain imaging in adult patients with:

- suspected Parkinsonian syndromes (PS) or
- suspected dementia with Lewy bodies (DLB).

2 DOSAGE AND ADMINISTRATION

2.1 Radiation Safety

Ioflupane I 123 Injection emits radiation and must be handled with safety measures to minimize radiation exposure to healthcare providers and patients [see *Warnings and Precautions* (5.3)]. Radiopharmaceuticals should be used by or under the control of healthcare providers who are qualified by specific training and experienced 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.

To minimize radiation exposure, encourage hydration prior to and following Ioflupane I 123 Injection administration in order to permit frequent voiding. Encourage the patient to void frequently for the first 48 hours following Ioflupane I 123 Injection administration [see *Dosage and Administration* (2.5)].

2.2 Thyroid Blockade Before Ioflupane I 123 Injection Administration

Administer Potassium Iodide Oral Solution or Strong Iodine Solution (e.g., Lugol's Solution) equivalent to 100 mg iodide to block uptake of iodine-123 by the patient's thyroid at least one hour before the dose of Ioflupane I 123 Injection [see *Warnings and Precautions* (5.2)].

2.3 Recommended Dosage

The recommended dose of Ioflupane I 123 Injection in adult patients is 111 MBq to 185 MBq (3 mCi to 5 mCi) administered intravenously over at least 20 seconds.

2.4 Preparation and Administration

- Assess pregnancy status before administering Ioflupane I 123 Injection to a female of reproductive potential [see *Use in Specific Populations* (8.1)].
- Use aseptic procedures and radiation shielding during preparation and administration.
- Inspect the Ioflupane I 123 Injection vial for particulate matter and discoloration prior to administration and do not use it if the vial contains particulate matter or discoloration.
- Measure patient dose using a dose calibrator immediately prior to administration.
- Discard unused portion.

2.5 Radiation Dosimetry

The estimated radiation absorbed doses to an adult from intravenous injection of Ioflupane I 123 Injection are shown in Table 1. The values are calculated assuming urinary bladder emptying at 4.8-hour intervals and appropriate thyroid blocking (iodine-123 is a known Auger electron emitter).

Table 1 Estimated Radiation Absorbed Doses from Ioflupane I 123 Injection

	ORGAN / TISSUE	ABSORBED DOSE PER UNIT ADMINISTERED ACTIVITY (μGy / MBq)
	Adrenals	12.9
	Brain	17.8
	Striata	230
	Breasts	7.8
	Gallbladder Wall	26.4
GI Tract	Esophagus	10
	Stomach Wall	11.2
	Small Intestine Wall	21.2

Colon Wall ^a	39.8
Upper Large Intestine Wall	38.1
Lower Large Intestine Wall	42
Heart Wall	12.9
Kidneys	10.9
Liver	27.9
Lungs	41.2
Muscle	9.4
Osteogenic Cells	28.2
Ovaries	16.8
Pancreas	13
Red Marrow	9.2
Skin	6
Spleen	10.4
Testes	8.5
Thymus	10
Thyroid	9
Urinary Bladder Wall	53.1
Uterus	16.1
Total Body	11.3
EFFECTIVE DOSE PER UNIT ADMINISTERED ACTIVITY (μSv/MBq)	21.3

^a The absorbed dose to the colon wall is the mass-weighted sum of the absorbed doses to the upper and lower large intestine walls, $D_{colon} = 0.57D_{ULI} + 0.43D_{LLI}$ [Publication 80 of the ICRP (International Commission on Radiological Protection); Annals of the ICRP 28 (3). Oxford: Pergamon Press; 1998]

The Effective Dose resulting from a Ioflupane I 123 Injection administration with an administered activity of 185 MBq (5 mCi) is 3.94 mSv in an adult.

2.6 Imaging Instructions

Begin SPECT imaging 3 hours to 6 hours following Ioflupane I 123 Injection administration.

Use a gamma camera fitted with high-resolution collimators and set to a photopeak of 159 keV with a $\pm 10\%$ energy window. Angular sampling should be at least 120 views over 360 degrees.

Position the patient supine with the head on an off-the-table headrest, use a flexible head restraint such as a strip of tape across the chin or forehead if necessary to help avoid movement, and set a circular orbit for the detector heads with the radius as small as possible (typically 11 cm to 15 cm).

Obtain images with matrix size and zoom factors selected to give a pixel size of 3.5 mm to 4.5 mm. Collect a minimum of 1.5 million counts for optimal images.

2.7 Image Interpretation

Interpret Ioflupane I 123 Injection images visually, 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.

Determine whether an image is normal or abnormal 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 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 Ioflupane I 123 Injection 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 symmetric 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

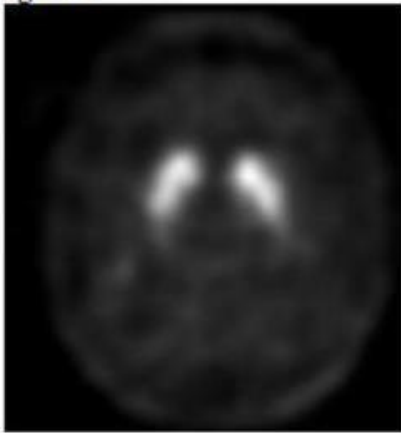


Figure 2

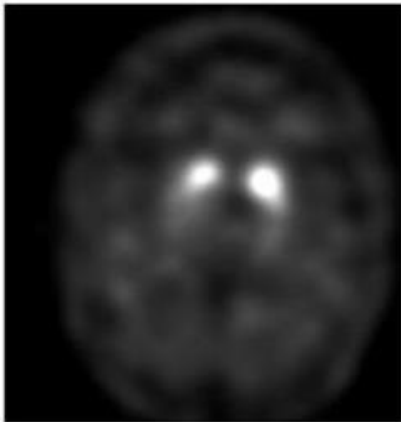
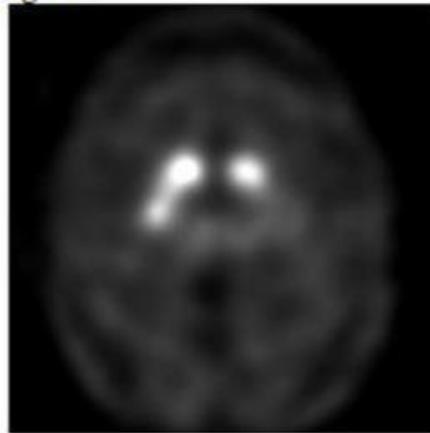


Figure 3

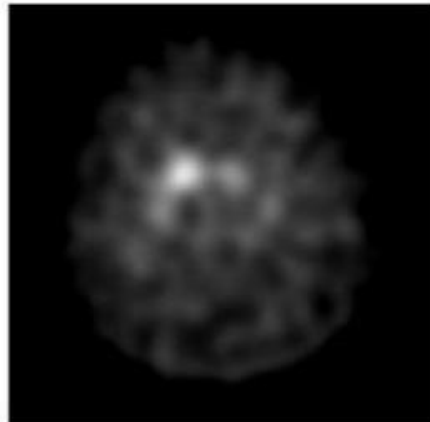


Figure 4

3 DOSAGE FORMS AND STRENGTHS

Injection: clear, colorless solution containing 185 MBq (5 mCi) in 2.5 mL at a concentration of 74 MBq/mL (2 mCi/mL) of ioflupane I-123 at calibration date and time supplied in single-dose vials.

4 CONTRAINDICATIONS

Ioflupane I 123 Injection is contraindicated in patients with known serious hypersensitivity to ioflupane I-123 [see *Warnings and Precautions* (5.1)].

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions, including dyspnea, edema, rash, erythema, and pruritus, have been reported following Ioflupane I 123 Injection administration [see *Adverse Reactions* (6.2)]. The reactions have generally occurred within minutes of Ioflupane I 123 Injection administration and have either resolved spontaneously or following the administration of corticosteroids and antihistamines.

Ioflupane I 123 Injection is contraindicated in patients with known serious hypersensitivity to Ioflupane I-123 [see *Contraindications* (4)]. Have treatment measures available and monitor patients for symptoms or signs of a hypersensitivity reaction.

5.2 Thyroid Accumulation of Iodine-123

Ioflupane I 123 Injection may contain up to 6% of free iodide (iodine-123). Thyroid uptake of iodine-123 may result in an increased long-term risk for thyroid neoplasia. To decrease thyroid accumulation of iodine-123, block the thyroid gland before administration of Ioflupane I 123 Injection [see *Dosage and Administration* (2.2)].

5.3 Radiation Risk

Ioflupane I 123 Injection contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer. Ensure safe handling to minimize radiation exposure to patients and healthcare providers. Advise patients to hydrate before and after administration and to void frequently after administration [see *Dosage and Administration* (2.1)].

6 ADVERSE REACTIONS

The following clinically significant adverse reaction is described elsewhere in the labeling:

- Hypersensitivity Reactions [see *Warnings and Precautions* (5.1)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of Ioflupane I 123 Injection cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data from clinical trials reflect exposure to Ioflupane I 123 Injection in 942 subjects with a mean age of 66 years (range 25 years to 90 years). Among these subjects, 42% were female and 99% White. Subjects received 88 MBq to 287 MBq (2 mCi to 8 mCi) [median 173 MBq (4.7 mCi)] intravenously as a single dose. The recommended dose of Ioflupane I 123 Injection is 111 MBq to 185 MBq (3 mCi to 5 mCi) [see *Dosage and Administration* (2.3)].

The following adverse reactions were reported at a rate of 1% or less: headache, nausea, vertigo, dry mouth, and dizziness.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of Ioflupane I 123 Injection. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune system disorders: Hypersensitivity, including dyspnea, edema, rash, erythema, and pruritus

General disorders and administration site conditions: Injection site pain

7 DRUG INTERACTIONS

Ioflupane I 123 binds to the dopamine transporter [see *Clinical Pharmacology* (12.1)].

Drugs that bind to the dopamine transporter with high affinity may interfere with the image obtained following Ioflupane I 123 Injection administration. These potentially interfering drugs consist of: amoxapine, amphetamine, armodafinil, benztropine, bupropion, buspirone, cocaine, mazindol, methamphetamine, methylphenidate, modafinil, norephedrine, phentermine, phenylpropanolamine, selegiline, and sertraline. Selective serotonin reuptake inhibitors (paroxetine and citalopram) may increase or decrease ioflupane binding to the dopamine transporter. Whether discontinuation of these drugs prior to Ioflupane I 123 Injection administration may minimize the interference with a Ioflupane I 123 Injection image is unknown.

The impact of dopamine agonists and antagonists upon Ioflupane I 123 Injection imaging results has not been established.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Radioactive iodine products cross the placenta and can permanently impair fetal thyroid function. Administration of an appropriate thyroid blocking agent is recommended before use of Ioflupane I 123 Injection in a pregnant woman to protect the woman and fetus from accumulation of iodine-123 [see *Dosage and Administration (2.2)*].

There are no available data on Ioflupane I 123 Injection use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with Ioflupane I-123. All radiopharmaceuticals have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of the radiation dose. Administration of Ioflupane I 123 Injection at a dose of 185 MBq (5 mCi) results in an absorbed radiation dose to the uterus of 0.3 rad (3.0 mGy). Radiation doses greater than 15 rad (150 mGy) have been associated with congenital anomalies but doses under 5 rad (50 mGy) generally have not. Advise pregnant women of the potential risks of fetal exposure to radiation doses with administration of Ioflupane I 123 Injection.

The estimated background risk of major birth defects and miscarriage for the indicated population(s) is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

8.2 Lactation

Risk Summary

Iodine-123, the radionuclide in Ioflupane I 123 Injection, is present in human milk. There is no information on the effects on the breastfed infant or on milk production. Advise a lactating woman to interrupt breastfeeding and pump and discard breastmilk for at least 6 days (>10 physical half-lives) after Ioflupane I 123 Injection administration in order to minimize radiation exposure to a breastfed infant.

8.4 Pediatric Use

The safety and efficacy of Ioflupane I 123 Injection have not been established in pediatric patients.

8.5 Geriatric Use

In the two principal clinical studies of Ioflupane I 123 Injection for suspected Parkinsonian syndromes, 45% of the subjects were aged 65 and over, while 10% were 75 and over [see *Clinical Studies (14.1)*]. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

8.6 Renal Impairment

Ioflupane I 123 Injection is excreted by the kidney and patients with severe renal impairment may have increased radiation exposure and altered Ioflupane I 123 Injection images.

10 OVERDOSAGE

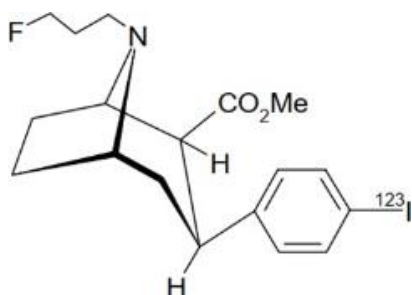
The risks of overdose relate predominantly to increased radiation exposure, with the long-term risks for neoplasia. In case of overdosage of radioactivity, frequent urination and defecation should be encouraged to minimize radiation exposure to the patient.

11 DESCRIPTION

11.1 Chemical Characteristics

Ioflupane I 123 Injection is a sterile, pyrogen-free radioactive diagnostic agent for intravenous use. Ioflupane I 123 Injection is a clear and colorless solution is supplied in single-dose vials. Each milliliter contains 0.07 to 0.13 mcg ioflupane, 74 MBq (2 mCi) of iodine-123 (as ioflupane I-123) at calibration time, 5.7 mg acetic acid, 7.8 mg sodium acetate and 0.05 mL (5%) ethanol. The pH of the solution is between 4.2 and 5.2.

The chemical name for ioflupane I-123 is N- ω -fluoropropyl-2 β -carbomethoxy-3 β -(4-[¹²³I]iodophenyl)nortropane and it has the following structural formula:



11.2 Physical Characteristics

Iodine-123 is a cyclotron-produced radionuclide that decays to tellurium-123 by electron capture and has a physical half-life of 13.2 hours. The photon that is useful for detection and imaging studies is listed in Table 2.

Table 2 Principal Radiation Emission Data - Iodine-123

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

11.3 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 iodine-123 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 3 (e.g., the use of 2.16 cm Pb will decrease the external radiation exposure by a factor of about 1,000).

Table 3 Reduction in In-air Collision Kerma Caused by Lead Shielding ^a

Shield Thickness cm of lead (Pb)	Reduction in In-air Collision Kerma
0.04	0.5

0.13	10^{-1}
0.77	10^{-2}
2.16	10^{-3}
3.67	10^{-4}

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

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The active drug substance in Ioflupane I 123 Injection is N- ω -fluoropropyl-2 β -carbomethoxy-3 β -(4-[¹²³I]iodophenyl)nortropane or ioflupane I-123.

In vitro, ioflupane binds reversibly to the human dopamine transporter (DaT) ($K_i = 0.62$ nM; $IC_{50} = 0.71$ nM). Autoradiography of post-mortem human brain slices exposed to radiolabeled ioflupane shows concentration of the radiolabel in striatum (caudate nucleus and putamen). The specificity of the binding of ioflupane I-125 to dopamine transporter was demonstrated by competition studies with the DaT inhibitor GBR 12909 (a dopamine reuptake inhibitor), the serotonin reuptake inhibitor citalopram, and the norepinephrine reuptake inhibitor desipramine in post-mortem human brain slices exposed to radiolabeled ioflupane. Citalopram reduced binding in the neocortex and thalamus with only minor effects in the striatum. This indicated that the binding in the cortex and thalamus is mainly to the serotonin reuptake sites. Desipramine showed no effect on the level of striatal binding of ioflupane I-125, but reduced extrastriatal binding by 60 to 85%. The binding of ioflupane I-125 to the striatum was abolished in the presence of high concentrations of GBR 12909, indicating selectivity of ioflupane binding for the pre-synaptic DaT.

Following administration of Ioflupane I 123 Injection to humans, radioactive decay of the iodine-123 emits gamma radiation which can be detected externally using gamma detectors, allowing visualization of the brain striata through SPECT imaging [see *Clinical Pharmacology* (12.3)].

12.2 Pharmacodynamics

As Ioflupane I 123 Injection contains a very small quantity of ioflupane, no ioflupane pharmacologic effects are expected [see *Description* (11)].

12.3 Pharmacokinetics

The pharmacokinetics of ioflupane I-123 were studied by monitoring radioactivity following intravenous injection; only 5% of the administered radioactivity remained in whole blood at 5 minutes post-injection. Uptake in the brain reached approximately 7% of injected radioactivity at 10 minutes post-injection and decreased to 3% after 5 hours; striata to background ratios were relatively constant between 3 hours and 6 hours post-injection. About 30% of the whole brain radioactivity was attributed to striatal uptake. By 48 hours post-injection, approximately 60% of the injected radioactivity has been excreted in the urine, with fecal excretion estimated to be approximately 14%.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies on reproductive toxicity have not been conducted. Ioflupane showed no evidence of mutagenic potential in *in vitro* or *in vivo* mutagenicity studies. Studies to assess the carcinogenic potential of ioflupane have not been performed.

13.2 Animal Toxicology and/or Pharmacology

Single- and repeated-dose intravenous toxicity studies have been performed using

loflupane in rats, rabbits, and dogs. Additionally, single-dose acute toxicity studies have been performed in cynomolgus monkeys. No mortality or other toxicity was observed at doses up to 5,500 times the maximum clinical dose of loflupane I 123 Injection; at doses greater than 1,500 times the maximum clinical dose, pharmacological responses such as mydriasis and hyperactivity were seen in some species.

14 CLINICAL STUDIES

14.1 Suspected Parkinsonian Syndromes

The safety and efficacy of loflupane I 123 Injection were evaluated in two multicenter, single-arm, open-label studies (Study 1 and Study 2) that enrolled 284 adult patients with suspected PS.

In these studies, loflupane I 123 Injection image interpretation was compared to a reference clinical diagnostic standard of "PS" or "non-PS". PS consisted of Parkinson's disease (PD), multiple system atrophy (MSA), and progressive supranuclear palsy (PSP). These conditions have been associated with dopaminergic neurodegeneration and loflupane I 123 Injection imaging was not designed to distinguish among the conditions. Among the non-PS population, subjects with a history of the following conditions were included: vascular parkinsonism, psychogenic parkinsonism, essential tremor (ET), various forms of tremor, and other non-PS diagnoses; loflupane I 123 Injection imaging was not designed to distinguish among these conditions.

Patients underwent SPECT imaging with a variety of multi-headed cameras or multi-detector single-slice systems 3 to 6 hours after loflupane I 123 Injection administration. The loflupane I 123 Injection activity in these two clinical studies ranged from 111 MBq to 201 MBq (3 mCi to 5.4 mCi) [median 167.8 MBq (4.5 mCi)]. Readers blinded to clinical information interpreted loflupane I 123 Injection imaging as normal or abnormal [see *Dosage and Administration* (2.7)]. A normal image is inconsistent with clinical conditions associated with PS and an abnormal image is consistent with clinical conditions associated with PS.

Study 1 consisted of 99 patients with early features of Parkinsonism; patients with features suggestive of MSA or PSP were excluded. The baseline clinical diagnoses consisted of: probable PD (44%), possible PD (31%), "benign" PD (6%), possible ET (11%), and other diagnoses (7%). The patients were 44% female, 42% of age 65 years or over, and all were White. Study 1 readers had no other role in patient assessment. The reference clinical diagnostic standard consisted of the clinical diagnoses established by a consensus panel of movement disorder specialists that evaluated data inclusive through 36 months of follow-up.

Study 2 consisted of 185 patients with clinically established diagnosis of PS (PD, MSA, PSP) or ET. The baseline clinical diagnoses consisted of: PD (70%), MSA (10%), PSP (5%), and ET (15%). The patients were 35% female, 48% of age 65 years or over, and 99% were White. Study 2 readers included site investigators. The reference clinical diagnostic standard consisted of the investigator-determined baseline clinical diagnosis.

Table 4 shows the positive percent agreement and negative percent agreement of the loflupane I 123 Injection image results with the reference clinical diagnostic standard. Positive percent agreement represents the percent of patients with abnormal loflupane I 123 Injection images among all the patients with a clinical diagnostic reference standard of PS. Negative percent agreement represents the percent of patients with normal loflupane I 123 Injection images among the patients with a non-PS clinical diagnostic reference standard.

Table 4: Positive and Negative Percent Agreements for Studies 1 and 2

	Positive percent agreement (95 % CI)	Negative percent agreement (95 % CI)
Study 1 (patients with early signs and/or symptoms of PS)		
Reader A, n =	77 (66 87)	96 (87 100)

99	77 (66, 87)	96 (82, 100)
Reader B, n = 96	78 (66, 87)	96 (82, 100)
Reader C, n = 98	79 (67, 87)	96 (82, 100)
Study 2 (patients with established diagnoses of PS or ET)		
Reader A, n = 185	93 (88, 97)	96 (81, 100)
Reader B, n = 185	97 (93, 99)	74 (54, 89)
Reader C, n = 185	96 (92, 99)	85 (66, 96)
Reader D, n = 185	92 (87, 96)	93 (76, 99)
Reader E, n = 185	94 (90, 97)	93 (76, 99)

14.2 Suspected Dementia with Lewy Bodies

The evidence for the efficacy of Ioflupane I 123 Injection in visualizing striatal dopamine transporters in adult patients with DLB is derived from the scientific literature. In 55 patients clinically diagnosed with DLB or with Alzheimer's disease, the results of consensus blinded visual assessment of the Ioflupane I 123 Injection images were compared to neuropathological diagnosis made using standard international criteria at autopsy. The patients were 38% female and of ages 63 to 95 years (mean 77 years) at the time of Ioflupane I 123 Injection imaging. The median administered Ioflupane I 123 Injection activity was 150 MBq to 185 MBq (4.1 mCi to 4.9 mCi). Ioflupane I 123 Injection images were rated as normal or abnormal [see *Dosage and Administration* (2.7)]. Based on autopsy diagnosis, the sensitivity and specificity of Ioflupane I 123 Injection for DLB was 80% (95% CI 61% to 92%) and 92% (95% CI 74% to 99%), respectively.

The effectiveness of Ioflupane I 123 Injection as a screening or confirmatory test and for monitoring disease progression or response to therapy has not been established.

16 HOW SUPPLIED/STORAGE AND HANDLING

Ioflupane I 123 Injection is a sterile, clear, colorless solution supplied in a 10 mL single-dose vial containing a total volume of 2.5 mL with a total radioactivity of 185 MBq (5 mCi) of Ioflupane I 123 at calibration time and date. Each mL contains 74 MBq (2 mCi) of Ioflupane I 123 at calibration time and date. Each vial is enclosed in a lead container of appropriate thickness for radiation protection.

Catalog No.166

185 megabecquerels (5 mCi)

NDC 69945-166-05

Storage

Store Ioflupane I 123 Injection upright at 20° to 25°C (68° to 77°F). This product does not contain a preservative. Store Ioflupane I 123 Injection within the original lead container or equivalent radiation shielding.

Do not use Ioflupane I 123 Injection preparations after the expiration date and time stated on the label. Discard unused portion.

Handling

This preparation is approved for use by persons licensed by the Nuclear Regulatory Commission or an Agreement State.

17 PATIENT COUNSELING INFORMATION

Hypersensitivity Reactions

Inform the patient that hypersensitivity reactions, including dyspnea, edema, rash, erythema and pruritus, have been reported following Ioflupane I 123 Injection administration [see *Warnings and Precautions (5.1)*].

Adequate Hydration

Instruct patients to drink a sufficient amount of water prior to and after receiving Ioflupane I 123 Injection and to void frequently for the first 48 hours following Ioflupane I 123 Injection administration [see *Dosage and Administration (2.1)*].

Lactation

Advise a lactating woman to interrupt breastfeeding and pump and discard breastmilk for at least 6 days (>10 physical half-lives) after Ioflupane I 123 Injection administration in order to minimize radiation exposure to a breastfed infant [see *Use in Specific Populations (8.2)*].

Pregnancy

Advise a pregnant woman of the potential risks of fetal exposure to radiation doses with Ioflupane I 123 Injection [see *Use in Specific Populations (8.1)*].

Manufactured and Distributed by Curium US LLC, 2703 Wagner Pl, Maryland Heights, MO 63043 U.S.A.

Curium™ and the Curium logo are trademarks of a Curium Company.

© 2022 Curium US LLC - All rights reserved.

PRINCIPAL DISPLAY PANEL

NDC 69945-166-05

Ioflupane I 123 Injection

185 MBq (5 mCi) per 2.5 mL at calibration

74 MBq (2 mCi) per 1 mL

Radiopharmaceutical For Intravenous Use Only

Single-Dose Vial – Discard Unused Portion.

Recommended dosage: See Prescribing Information.

Each mL contains: 74 MBq (2 mCi) of Ioflupane I 123 at calibration date and time, 0.07 - 0.13 mcg Ioflupane, 5.7 mg acetic acid, 7.8 mg sodium acetate, 0.05 ml of dehydrated alcohol (ethanol).

Store upright at controlled room temperature 20°C to 25°C (68°F to 77°F) in a shielded container.

Rx only

Total Activity: 185 MBq (5 mCi) at calibration

Radioactivity Concentration: 74 MBq/mL (2 mCi/mL)

Total Volume: 2.5 mL

Cal. time: 1200 ET (1100 CT)

Expires 7 hours after calibration time.

Cal. date:

Lot #:

CAUTION

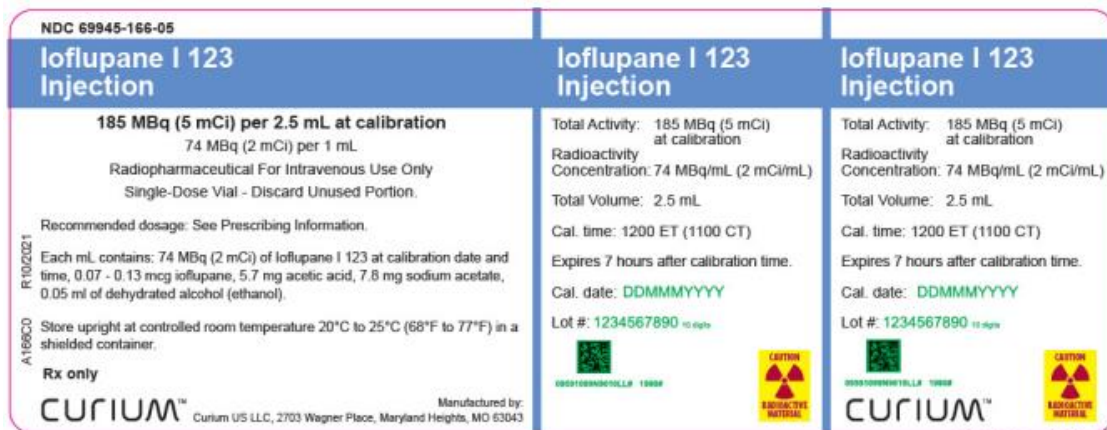
RADIOACTIVE MATERIAL

CURIUM™ Logo

Manufactured by:

Curium US LLC, 2703 Wagner Place, Maryland Heights, MO 63043

R10/2021 A166C0



R102021 Can label

PRINCIPAL DISPLAY PANEL

NDC 69945-166-05

Ioflupane I 123 Injection

185 MBq (5 mCi) per 2.5 mL at calibration

[74 MBq (2 mCi) per 1 mL]

Radiopharmaceutical - For Intravenous Use Only

Single-Dose Vial - Discard Unused Portion.

Cal. time:

1200 ET (1100 CT)

Cal. date:

Lot #:

Volume: 2.5 mL

Radioactive Concentration:

74 MBq/mL (2 mCi/mL)

Total Activity:

185 MBq (5 mCi)

Recommended Dosage:

See Prescribing Information

Rx only

Store upright at controlled

room temperature 20°C to

25°C (68°F to 77°F) in a

shielded container. **Expires**

7 hours after calibration time.

Each mL contains 74 MBq

(2 mCi) of Ioflupane I 123 at

calibration, 0.07 - 0.13 mcg

Ioflupane, 5.7 mg acetic acid,

7.8 mg sodium acetate,

0.05 mL ethanol.

CAUTION

RADIOACTIVE MATERIAL

Manufactured by:


Curium US LLC

2703 Wagner Place

Maryland Heights, MO

63043

A166V0 R12/2021

NDC 69945-166-05	
Ioflupane I 123 Injection	
185 MBq (5 mCi) per 2.5 mL at calibration [74 MBq (2 mCi) per 1 mL]	
Radiopharmaceutical - For Intravenous Use Only Single-Dose Vial - Discard Unused Portion.	
Cal. time: 1200 ET (1100 CT)	Volume: 2.5 mL
Cal. date: DDMMYYYY	Radioactive Concentration: 74 MBq/mL (2 mCi/mL)
Lot #: 1234567890 <small>10 digits</small>	Total Activity: 185 MBq (5 mCi)
Recommended Dosage: See Prescribing Information Rx only Store upright at controlled room temperature 20°C to 25°C (68°F to 77°F) in a shielded container. Expires 7 hours after calibration time. Each mL contains 74 MBq (2 mCi) of Ioflupane I 123 at calibration, 0.07 - 0.13 mcg Ioflupane, 5.7 mg acetic acid, 7.8 mg sodium acetate, 0.05 mL ethanol.	
Manufactured by: Curium US LLC 2703 Wagner Place Maryland Heights, MO 63043	
	
A166V0 R12/2021	

R122021 Vial label

IOFLUPANE I 123

ioflupane i-123 injection, solution

Product Information				
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:69945-166	
Route of Administration	INTRAVENOUS			
Active Ingredient/Active Moiety				
	Ingredient Name	Basis of Strength	Strength	
	IOFLUPANE I-123 (UNII: 3MM99T8R5Q) (IOFLUPANE I-123 - UNII:3MM99T8R5Q)	IOFLUPANE I-123	2 mCi in 1 mL	
Inactive Ingredients				
	Ingredient Name	Strength		
	ACETIC ACID (UNII: Q40Q9N063P)	5.7 mg in 1 mL		
	SODIUM ACETATE (UNII: 4550K0SC9B)	7.8 mg in 1 mL		
	ALCOHOL (UNII: 3K9958V90M)	0.05 mL in 1 mL		
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:69945-166-05	2.5 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product	03/31/2022	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA213792	03/31/2022	

Labeler - Curium US LLC (079875617)

Revised: 12/2022

Curium US LLC