

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

INDICATIONS AND USAGE

Ioflupane I 123 Injection is a radiopharmaceutical indicated for striatal dopamine transporter visualization using single photon emission computed tomography (SPECT) brain imaging to assist in the evaluation of adult patients with suspected Parkinsonian syndromes (PS). In these patients, Ioflupane I 123 Injection may be used to help differentiate essential tremor from tremor due to PS (idiopathic Parkinson's disease, multiple system atrophy and progressive supranuclear palsy). Ioflupane I 123 Injection is an adjunct to other diagnostic evaluations. (1)

DOSAGE AND ADMINISTRATION

- Ioflupane I 123 Injection emits gamma radiation and must be handled with safety measures. (2.1)
- Measure patient dose by a suitable radioactivity calibration system immediately prior to administration. (2.1)
- Administer a thyroid-blocking agent at least one hour before the dose of Ioflupane I 123 Injection. (2.2)
- The recommended Ioflupane I 123 Injection dose is 111 to 185 MBq (3 to 5 mCi). (2.4)
- Begin SPECT imaging between 3 and 6 hours post-injection. (2.6)

DOSAGE FORMS AND STRENGTHS

2.5 mL of sterile solution for intravenous injection in a single-dose vial [74 MBq (2 mCi)/mL at calibration time]. (3)

CONTRAINDICATIONS

Known hypersensitivity to the active substance or to any of the excipients, or to iodine. (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity reactions have been reported following Ioflupane I 123 Injection administration. Have anaphylactic and hypersensitivity treatment measures available prior to Ioflupane I 123 Injection administration. (5.1)
- Administer a thyroid-blocking agent before Ioflupane I 123 Injection administration. (5.2)

ADVERSE REACTIONS

Hypersensitivity and injection site reactions have been reported following Ioflupane I 123 Injection administration. (6.2) In clinical trials, the most common adverse reactions, headache, nausea, vertigo, dry mouth or dizziness occurred in < 1% of subjects. (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, benzotropine, bupropion, buspirone, cocaine, mazindol, methamphetamine, methylphenidate, norephedrine, phentermine, phenylpropanolamine, selegiline, sertraline, citalopram and paroxetine may interfere with Ioflupane I 123 Injection imaging. (7) The effects of dopamine agonists and antagonists on Ioflupane I 123 Injection imaging have not been established.

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 Ioflupane I 123 Injection administration. (8.2)
- Pediatric: Safety and effectiveness have not been established. (8.4)

See 17 for PATIENT COUNSELING INFORMATION.

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Ioflupane I 123 Injection is a radiopharmaceutical indicated for striatal dopamine transporter visualization using single photon emission computed tomography (SPECT) brain imaging to assist in the evaluation of adult patients with suspected Parkinsonian syndromes (PS). In these patients, Ioflupane I 123 Injection may be used to help differentiate essential tremor from tremor due to PS (idiopathic Parkinson's disease, multiple system atrophy and progressive supranuclear palsy). Ioflupane I 123 Injection is an adjunct to other diagnostic evaluations.

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 clinical personnel and patients. Radiopharmaceuticals should be used by or under the control of physicians 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. Ioflupane I 123 Injection dosing is based upon the radioactivity determined using a suitably calibrated instrument immediately prior to administration.

To minimize radiation dose to the bladder, 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

Before administration of Ioflupane I 123 Injection, administer Potassium Iodide Oral Solution or Lugol's Solution (equivalent to 100 mg iodide) or potassium perchlorate (400 mg) to block uptake of iodine 123 by the patient's thyroid. Administer the blocking agent at least one hour before the dose of Ioflupane I 123 Injection [*see Warnings and Precautions (5.2)*].

2.3 Preparation and Administration

- Assess pregnancy status before administering Ioflupane I 123 Injection to a female of reproductive potential.
- Use aseptic procedures and radiation shielding during preparation and administration. Inspect the Ioflupane I 123 Injection vial prior to administration and do not use it if the vial contains particulate matter or discoloration [*see Description (11)*]. Administer Ioflupane I 123 Injection as a slow intravenous injection (administered over a period of not less than 15 to 20 seconds) via an arm vein.

2.4 Recommended Dose

The recommended dose is 111 to 185 MBq (3 to 5 mCi) administered intravenously [*see Clinical Studies (14)*].

2.5 Radiation Dosimetry

The estimated radiation absorbed doses to an average 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 ($\mu\text{Gy}/\text{MBq}$)
	Adrenals	12.9
	Brain	17.8
	Striata	230
	Breasts	7.8
	Esophagus	10
	Gallbladder Wall	26.4
GI Tract	Stomach Wall	11.2
	Small Intestine Wall	21.2
	Colon Wall *	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
	Esophagus	10
	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 ($\mu\text{Sv}/\text{MBq}$)	21.3

* The absorbed dose to the colon wall is the mass- weighted sum of the absorbed doses to the upper and lower large intestine walls, $D_{\text{Colon}} = 0.57 D_{\text{ULI}} + 0.43 D_{\text{LLI}}$ [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 Guidelines

Begin SPECT imaging 3 to 6 hours following Ioflupane I 123 Injection administration. Acquire images using 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 not less than 120 views over 360 degrees. Position the subject supine with the head on an off-the-table headrest, a flexible head restraint such as a strip of tape across the chin or forehead may be used to help avoid movement, and set a circular orbit for the detector heads with the radius 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. Collect a minimum of 1.5 million counts for optimal images.

2.7 Image Interpretation

Ioflupane I 123 Injection images are interpreted visually, based upon the appearance of the striata. Reconstructed pixel size should be between 3.5 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 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

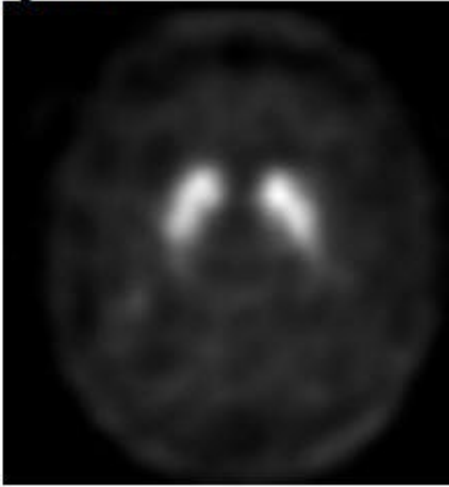


Figure 2

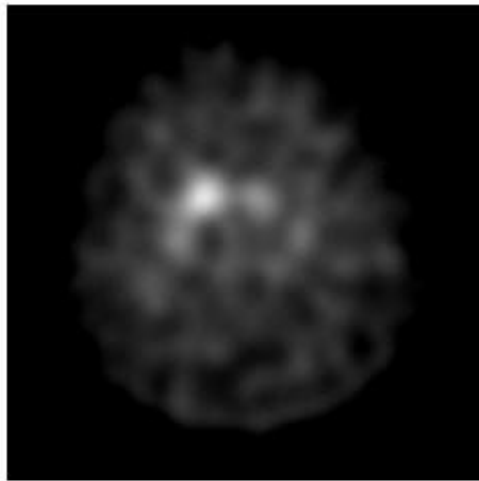
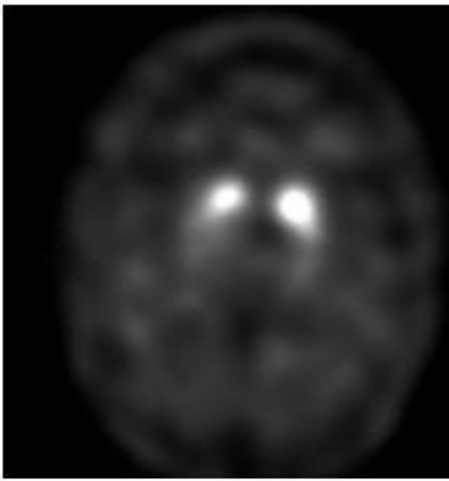
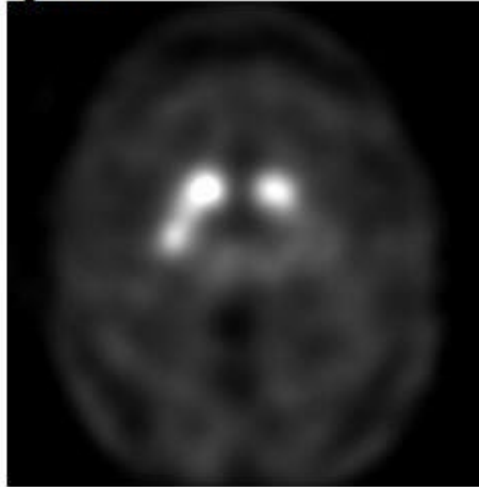


Figure 3

Figure 4

3 DOSAGE FORMS AND STRENGTHS

Single-dose vials containing 185 MBq (5 mCi) in 2.5 mL sterile solution for intravenous injection [74 MBq (2 mCi) per mL at calibration time].

4 CONTRAINDICATIONS

Ioflupane I 123 Injection is contraindicated in patients with known hypersensitivity to the active substance or to any of the excipients, or to iodine.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions have been reported following Ioflupane I 123 Injection administration [see *Adverse Reactions* (6.2)]. The reactions have generally consisted of skin erythema and pruritis and have either resolved spontaneously or following the administration of corticosteroids and anti-histamines. Prior to administration, question the patient for a history of prior reactions to Ioflupane I 123 Injection. If the

patient is known or strongly suspected of having had a hypersensitivity reaction to Ioflupane I 123 Injection, the decision to administer Ioflupane I 123 Injection should be based upon an assessment of the expected benefits compared to the potential hypersensitivity risks. Have anaphylactic and hypersensitivity treatment measures available prior to Ioflupane I 123 Injection administration and, following administration, observe patients for symptoms or signs of a hypersensitivity reaction.

5.2 Thyroid Accumulation

The Ioflupane I 123 Injection may contain up to 6% of free iodide (iodine 123). To decrease thyroid accumulation of iodine 123, block the thyroid gland before administration of Ioflupane I 123 Injection [*see Dosage and Administration (2.2)*]. Avoid the use of Potassium Iodide Oral Solution or Lugol's Solution in patients who are sensitive to such products. Failure to block thyroid uptake of iodine 123 may result in an increased long term risk for thyroid neoplasia.

6 ADVERSE REACTIONS

6.1 Clinical Study Experience

The data from clinical studies reflect exposure to Ioflupane I 123 Injection in 942 subjects with a mean age of 66 years (range 25 to 90 years). Among these subjects, 42% were women and 99% Caucasian. 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. In clinical trials, no serious adverse reactions were reported. Other adverse reactions occurred at a rate of 1% or less and the reported events consisted of headache, nausea, vertigo, dry mouth or dizziness. These reactions were of mild to moderate severity.

6.2 Postmarketing Experience

Because postmarketing 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. In the postmarketing experience, hypersensitivity reactions have been reported. The reactions generally related to rash and pruritis within minutes of Ioflupane I 123 Injection administration. The reactions either resolved spontaneously or following the administration of corticosteroids and antihistamines. Injection site pain has also been reported.

7 DRUG INTERACTIONS

The ioflupane within Ioflupane I 123 Injection binds to the dopamine transporter. 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, benztropine, bupropion, buspirone, cocaine, mazindol, methamphetamine, methylphenidate, 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 I 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 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

Iodide 123 (I 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

Ioflupane I 123 Injection is not indicated for use in children. 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, 45% of the subjects were aged 65 and over. There were no differences in response compared to younger subjects that would require a dose adjustment. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

8.6 Renal and Hepatic Impairment

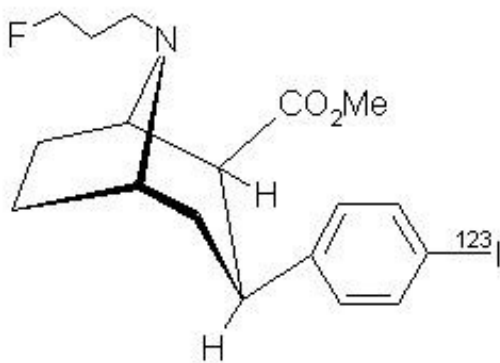
The effect of renal or hepatic impairment upon Ioflupane I 123 Injection imaging has not been established. Ioflupane I 123 Injection is excreted by the kidney and patients with severe renal impairment may have increased radiation exposure and altered Ioflupane I 123 Injection images.

10 OVERDOSAGE

The clinical consequence of overdose with Ioflupane I 123 Injection has not been reported. It is unknown whether or not ioflupane is dialyzable. Due to the small quantity of ioflupane in each vial, overdosage with ioflupane is not expected to result in pharmacologic effects. The major risks of overdose relates 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; care should be taken to avoid contamination from the radioactivity eliminated by the patient.

11 DESCRIPTION

Ioflupane I 123 Injection is a sterile, pyrogen-free radiopharmaceutical for intravenous injection. The clear and colorless solution is supplied in single-dose vials in which 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. Ioflupane I 123 has the following structural formula:



11.1 Physical Characteristics

Iodine 123 is a cyclotron-produced radionuclide that decays to ^{123}Te 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

11.2 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 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*

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

* 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 recombinant dopamine transporter (DaT) (K_i = 0.62 nM; IC₅₀ = 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 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 ioflupane 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 Ioflupane 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

The safety and efficacy of Ioflupane I 123 Injection were evaluated in two multicenter, single-arm studies (Study 1 and Study 2) that evaluated 284 adult patients with tremor. In the studies, Ioflupane I 123 Injection image outcomes were compared to a reference clinical diagnostic standard of "PS" or "non-PS". The reference clinical diagnostic standard for "PS" consisted of the following diagnoses: Parkinson's disease (PD), multiple system atrophy (MSA), and progressive supranuclear palsy (PSP). These three conditions have been associated with dopaminergic neurodegeneration and Ioflupane I 123 Injection imaging was not designed to distinguish among the conditions. The reference clinical diagnostic standard for "non-PS" consisted of an essential tremor (ET) diagnosis or other non-PS diagnosis. Three to 6 hours after Ioflupane I 123 Injection administration, subjects underwent SPECT imaging with a variety of multi-headed cameras or a multi-detector single- slice systems. The median administered activity evaluated in clinical studies was 173 MBq (4.7 mCi) [range, 88 to 287 MBq (2.4 to 7.8 mCi)].

Ioflupane I 123 Injection images were evaluated by readers blinded to clinical information. Study 1 readers had no other role in patient assessment; Study 2 readers included site investigators. The reference clinical diagnostic standards were the clinical diagnoses established by a consensus panel of movement disorder specialists that evaluated data inclusive through 36 months of follow-up (Study 1) or the investigator-determined baseline clinical diagnosis (Study 2). Study 1 consisted of patients with early features of Parkinsonism; patients with features suggestive of MSA or PSP were excluded. Study 2 consisted of patients with clinically established diagnosis of PS (PD, MSA, PSP) or ET.

Among the 99 patients in Study 1, 44% were female, 42% were aged 65 or over and all were Caucasian; among the 185 patients in Study 2, 35% were female, 48% were aged 65 or over and 99% were Caucasian. Among the patients in Study 1, the baseline clinical diagnoses consisted of: probable PD (44%), possible PD (31%), "benign" PD (6%), possible ET (11%), and other diagnoses (7%).

Among the patients in Study 2, the baseline clinical diagnoses consisted of: PD (70%), ET (15%), MSA (10%), and PSP (5%).

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

normal Ioflupane 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) (% patients with an abnormal Ioflupane I 123 Injection image among patients with PS)	Negative percent agreement (95 % CI) (% patients with a normal Ioflupane I 123 Injection image among patients with non-PS)
Study 1 (patients with early signs and/or symptoms of PS)		
Reader A, n = 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)

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

Instruct patients to inform their physician or healthcare provider if they:

1. are pregnant. 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)*].
2. are breast feeding. 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)*].
3. are sensitive to Ioflupane I 123 Injection.
4. are sensitive to Potassium Iodide Oral Solution or Lugol's Solution.
5. have reduced renal or hepatic function.

Instruct patients to increase their level of hydration prior to and after receiving Ioflupane I 123 Injection and to void frequently for the first 48 hours following Ioflupane I 123 Injection administration.

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