SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Striascan 74 MBq/mL solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of solution contains 74 MBq of ioflupane (^{123}I) at reference time (0.07 to 0.13 µg/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.

Iodine-123 has a physical half-life of 13.2 hours. It decays emitting gamma radiation with a predominant energy of 159 keV and X-rays of 27 keV.

3 PHARMACEUTICAL FORM

Solution for injection.
Clear colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.
Striascan is indicated for detecting loss of functional dopaminergic neuron terminals in the striatum:

- In adult patients with clinically uncertain parkinsonian syndromes, for example those with early symptoms, in order to help differentiate essential tremor from parkinsonian syndromes related to idiopathic Parkinson's disease, multiple system atrophy and progressive supranuclear palsy. Striascan is unable to discriminate between Parkinson's disease, multiple system atrophy and progressive supranuclear palsy.
- In adult patients, to help differentiate probable dementia with Lewy bodies from Alzheimer's disease. Striascan is unable to discriminate between dementia with Lewy bodies and Parkinson's disease dementia.

4.2 Posology and method of administration

Striascan should only be used in adult patients referred by physicians experienced in the management of movement disorders and/or dementia.

This medical product is for use in hospitals or in designated nuclear medicine facilities only.

Posology
Clinical efficacy has been demonstrated across the range 110 to 185 MBq. Do not exceed 185 MBq and do not use when the activity is below 110 MBq.

Patients must undergo appropriate thyroid blocking treatment prior to injection to minimise thyroid uptake of radioactive iodine, for example by oral administration of approximately 120 mg potassium iodide 1 to 4 hours prior to injection of Striascan.

Special populations
Renal and hepatic impairment
Formal studies have not been carried out in patients with significant renal or hepatic impairment. No data are available (see section 4.4).
Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

Paediatric population
The safety and efficacy of Striascan in children and adolescents aged 0 to 18 years has not been established. No data are available.

Method of administration
Striascan is for intravenous use.

For patient preparation, see section 4.4.

Precautions to be taken before handling or administering the medicinal product

Striascan should be used without dilution. To minimise 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.

Image acquisition
SPECT imaging should take place between three and 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 preferably be not 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 11-15 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 3.5-4.5 mm for those systems currently in use. A minimum of 500 k counts should be collected for optimal images.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions
If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification
For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required diagnostic information.

Renal impairment / Hepatic impairment
Formal studies have not been carried out in patients with significant renal or hepatic impairment. In the absence of data, Striascan is not recommended in cases of moderate to severe renal or hepatic impairment.
Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Patient preparation
The patient should be well hydrated before and after the examination and urged to void as often as possible during the first 48 hours after the procedure in order to minimise radiation exposure.

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Interpretation of Striascan Images

Striascan images are interpreted visually, based upon the appearance of the striata. 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 (in relation to the background) of the striatal signal.

Normal images are characterised by two symmetrical crescent-shaped areas of equal intensity. Abnormal images are either asymmetric or symmetric with unequal or reduced intensity and/or loss of crescent.

As an adjunct, visual interpretation may be assisted by semi-quantitative assessment using
CE-marked software, where Striascan uptake in the striatum is compared with uptake in a reference region and ratios are compared against an age adjusted healthy subjects' database. The evaluation of ratios, such as the left/right striatum Striascan uptake (symmetry) or caudate/putamen uptake, may further help with the image assessment.

The following precautions should be taken when using semi-quantitative methods:

- Semi-quantification should only be used an adjunct to visual assessment
- Only CE marked software should be used
- Users should be trained in the use of CE marked software by the manufacturer and follow EANM practice guidelines for image acquisition, reconstruction and assessment
- Readers should interpret the scan visually and then perform the semi-quantitative analysis according to manufacturer's instructions including quality checks for the quantitation process
    - ROI /VOI techniques should be used to compare uptake in the striatum with uptake in a reference region
    - Comparison against an age adjusted healthy subjects database is recommended to account for age-expected decrease in striatal binding
    - The reconstruction and filter settings (including attenuation correction) used can affect the semi-quantitative values. The reconstruction and filter settings recommended by the manufacturer of the CE marked software should be followed and should match those used for semi-quantification of the healthy subjects database.
    - The intensity of the striatal signal as measured by SBR (striatal binding ratio) and asymmetry and caudate to putamen ratio provide objective numerical values corresponding to the visual assessment parameters and can be helpful in difficult to read cases
    - If the semi-quantitative values are inconsistent with the visual interpretation, the scan should be evaluated for appropriate placement of the ROIs /VOIs, correct image orientation and appropriate parameters for image acquisition and attenuation correction should be verified. Some software packages can support these processes to reduce operator-dependent variability
    - Final assessment should always consider both visual appearance and semi-quantitative results

Specific warnings
This medicinal product contains up to 197 mg of alcohol (ethanol) in each dose which is equivalent to 39.5 mg/mL (5% by volume). The amount in 5 mL of this medicinal product is equivalent to 5 mL beer or 2 mL wine. The small amount of alcohol in this medicinal product will not have any noticeable effects.

This medicinal product contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

Precautions with respect to environmental hazard see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed in humans.
Ioflupane binds to the dopamine transporter. Active substances that bind to the dopamine transporter with high affinity may therefore interfere with Striascan diagnosis. These include:

- amfetamine,
- bupropion,
- cocaine,
- codeine,
- dexamfetamine,
- methylphenidate,
- modainil,
- phentermine.

Selective serotonin reuptake inhibitors (SSRIs), such as sertraline, may increase or decrease ioflupane binding to the dopamine transporter. Serotonin-norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine, may decrease ioflupane binding to the dopamine transporter especially in patients on higher doses.

Active substances shown during clinical trials not to interfere with Striascan imaging include:

- amantadine,
- trihexyphenidyl,
- budipine,
- levodopa,
- metoprolol,
- primidone,
- propranolol and
- selegiline.

Dopamine agonists and antagonists acting on the postsynaptic dopamine receptors are not expected to interfere with Striascan imaging and can therefore be continued if desired. Medicinal products shown in animal studies not to interfere with Striascan imaging include pergolide.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy
Animal reproductive toxicity studies have not been performed with this product. Radionuclide procedures carried out on pregnant women also involve radiation dose to the foetus. Administration of 185 MBq of ioflupane (^{123}I) results in an absorbed dose to the uterus of 2.6 mGy. Striascan is contraindicated in pregnancy (see section 4.3).

Breastfeeding
It is not known whether ioflupane (^{123}I) is excreted in human milk. Before administering radiopharmaceuticals to a mother who is breast-feeding, consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding, and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk.
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.

Fertility
No fertility studies have been performed. No data are available.

4.7 Effects on ability to drive and use machines

Striascan has no known influence on the ability to drive and use machines.

4.8 Undesirable effects

The following undesirable effects are recognised for ioflupane (^{123}I).

Very common	(≥1/10)
Common	(≥1/100 to <1/10)
Uncommon	(≥1/1,000 to <1/100)
Rare	(≥1/10,000 to <1/1,000)
Very rare	(<1/10,000)
Not known	(cannot be estimated from the available data)

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

MedDRA Body system SOCs	Adverse reaction Preferred term	Frequency
Immune system disorders	Hypersensitivity	Not known
Metabolism and nutrition disorders	Appetite increased	Uncommon
Nervous system disorders	Headache	Common
	Dizziness, formication (paraesthesia), dysgeusia	Uncommon
Ear and labyrinth disorders	Vertigo	Uncommon
Vascular disorders	Blood pressure decreased	Not known
Respiratory, thoracic and mediastinal disorders	Dyspnea	Not known
Gastrointestinal disorders	Nausea, dry mouth	Uncommon
	Vomiting	Not known
Skin and subcutaneous tissue disorders	Erythema, pruritus, rash, urticaria, hyperhidrosis	Not known
General disorders and administration site conditions	Injection site pain (intense pain or burning sensation following administration into small veins)	Uncommon
	Feeling hot	Not known

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 4.6 mSv when the maximal recommended activity of 185 MBq is administered these adverse events are expected to occur with a low probability.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In the event of administration of a radiation overdose, frequent micturition and defaecation should be encouraged in order to minimise radiation dose to the patient.

Care should be taken to avoid contamination from the radioactivity eliminated by the patient using such methods.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceutical central nervous system,
ATC code: V09AB03.

At the chemical concentrations used for diagnostic examinations, Striascan does not appear to have any pharmacodynamic activity.

Mechanism of action
Ioflupane is a cocaine analogue. Studies in animals have shown that ioflupane binds with high affinity to the presynaptic dopamine transporter and so radiolabelled ioflupane (^{123}I) can be used as a surrogate marker to examine the integrity of the dopaminergic nigrostriatal neurons. Ioflupane also binds to the serotonin transporter on 5-HT neurons but with lower (approximately 10-fold) binding affinity.

There is no experience in types of tremor other than essential tremor.

Clinical efficacy
Clinical studies in patients with dementia with Lewy bodies.
In a clinical trial including evaluation of 288 subjects with dementia with Lewy bodies (DLB) (144 subjects), Alzheimer's disease (124 subjects), vascular dementia (9 subjects) or other (11 subjects), the results of an independent, blinded visual assessment of the ioflupane (^{123}I) images were compared to the clinical diagnosis as determined by physicians experienced in the management and diagnosis of dementias. Clinical categorisation into the respective dementia group was based on a standardised and comprehensive clinical and neuropsychiatric evaluation. The values for the sensitivity of ioflupane (^{123}I) in determining probable DLB from non-DLB ranged from 75.0% to 80.2% and specificity from 88.6% to 91.4%. The positive predictive value ranged from 78.9% to 84.4% and the negative predictive value from 86.1% to 88.7%. Analyses in which both possible and probable DLB patients were compared with non-DLB dementia patients demonstrated values for the sensitivity of ioflupane (^{123}I) ranging from 75.0% to 80.2% and specificity from 81.3% to 83.9% when the possible DLB patients were included as non-DLB patients. The sensitivity ranged from 60.6% to 63.4% and specificity from 88.6% to 91.4% when the possible DLB patients were included as DLB patients.

Clinical studies demonstrating adjunctive use of semi-quantitative information for image interpretation

The reliability of using semi-quantitative information as an adjunct to visual inspection was analysed in four clinical studies where sensitivity, specificity or overall accuracy between the two methods of image interpretation were compared. In the four studies (total n=578), CE-marked DaTSCAN semi-quantitation software was used. The differences (i.e., improvements when adding semi-quantitative information to visual inspection) in sensitivity ranged between 0.1% and 5.5%, in specificity between 0.0% and 2.0%, and in overall accuracy between 0.0% and 12.0%.

The biggest of these four studies retrospectively assessed a total of 304 DaTSCAN exams from previously conducted Phase 3 or 4 studies, which included subjects with a clinical diagnosis of PS, non-PS (mainly ET), probable DLB, and non-DLB (mainly AD). Five nuclear medicine physicians who had limited prior experience with DaTSCAN interpretation assessed the images in 2 readings (alone and combined with semi-quantitative data provided by DaTQUANT 4.0 software) at least 1 month apart. These results were compared with the subject's 1-to 3-year follow-up diagnosis to determine diagnostic accuracy. The improvements in sensitivity and specificity [with 95% confidence intervals] were 0.1% [-6.2%,6.4%] and 2.0% [-3.0%,7.0%]. Also, the results of the combined reading were associated with an increase in reader confidence.

5.2 Pharmacokinetic properties

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 activity at 10 minutes post-injection and decreasing to 3% after 5 hours. About 30% of the whole brain activity is attributed to striatal uptake.

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

5.3 Preclinical safety data

Non-clinical data for ioflupane reveal no special hazard for humans based on conventional studies of safety pharmacology, single and repeated dose toxicity and genotoxicity.
Studies on reproductive toxicity and to assess the carcinogenic potential of ioflupane have not been performed.

Environmental Risk Assessment (ERA)

After use, all materials associated with the preparation and administration of radiopharmaceuticals, including any unused product and its container, should be

decontaminated or treated as radioactive waste and disposed of in accordance with the conditions specified by the local competent authority. Contaminated material must be disposed of as radioactive waste via an authorised route.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetic acid, glacial (E 260)
Sodium acetate, trihydrate (E 262)
Ethanol, anhydrous (E 1510)
Phosphoric acid, concentrated (E 338)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2.5 mL vial
35 hours from the end of synthesis (7 hours from the activity reference time stated on the label)

5 mL vial
48 hours from the end of synthesis (20 hours from the activity reference time stated on the label)

6.4 Special precautions for storage

Do not store above 25°C. Do not freeze.
Store in the original lead shielding.

Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

6.5 Nature and contents of container

15 mL amber glass vial sealed with a rubber closure and metal overseal.
The vial is placed into a lead container for protective shielding and packed in a metal box.

Pack size: 1 vial containing 2.5 mL or 5 mL of solution.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

General warning
Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.
Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.
If at any time in the preparation of this product the integrity of this vial is compromised it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

CIS bio international
RN 306 – Saclay
B.P. 32
F-91192 Gif-sur-Yvette Cedex

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 11876/0027

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01/01/2021
Date of latest renewal: 11/03/2024

10 DATE OF REVISION OF THE TEXT

28/05/2026

11. DOSIMETRY

The biokinetic model for ioflupane (^{123}I) adopted by ICRP 128 ((International Commission on Radiological Protection ,2015) 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-time of 58 h, and 20% with a half-time of 1.6 h. 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.
The estimated absorbed radiation doses to an average adult patient (70 kg) from intravenous injection of ioflupane (^{123}I) are listed below according to ICRP 128.
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)

Organ	**Absorbed radiation dose µGy/MBq**
Adrenals	17
Bone surfaces	15

Brain	16
Breasts	7.3
Gallbladder wall	44
Gastrointestinal tract	
Stomach wall	12
Small intestine wall	26
Colon wall	59
(Upper large intestine wall)	57
(Lower large intestine wall)	62
Heart wall	32
Kidneys	13
Liver	85
Lungs	42
Muscle	8.9
Oesophagus	9.4
Ovaries	18.0
Pancreas	17.0
Red marrow	9.3
Salivary glands	41.0
Skin	5.2
Spleen	26.0
Testes	6.3
Thymus	9.4
Thyroid	6.7
Urinary bladder wall	35.0
Uterus	14.0
Remaining organs	10.0
Effective Dose	**25.0 µSv/MBq**

The effective dose (E) resulting from administration of 185 MBq of Striascan injection is 4.6 mSv (per 70 kg individual). The above data are valid in normal pharmacokinetic behaviour. When renal or hepatic function is impaired, the effective dose and the radiation dose delivered to organs might be increased.
For an administered activity of 185 MBq the typical radiation dose to the target organ (brain) is 3 mGy and the typical radiation doses to the critical organs: liver and colon wall are 16 mGy and 11 mGy, respectively.

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)

Not relevant.

Deleted: Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.¶