Package leaflet: Information for the patient

Ioflupane (^{123}I) Rotop 74 MBq/ml Solution for injection

Ioflupane (^{123}I)

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Ioflupane (^{123}I) Rotop is and what it is used for

This medicine is a radiopharmaceutical product for diagnostic use only.

Ioflupane (^{123}I) Rotop contains the active substance ioflupane (^{123}I) which is used to help identify (diagnose) conditions in the brain. It belongs to a group of medicines called "radiopharmaceuticals", which contain a small amount of radioactivity.
- When a radiopharmaceutical is injected, it collects in a specific organ or area of the body for a short time.
- Because it contains a small amount of radioactivity it can be detected from outside the body using special cameras.
- A picture, known as a scan, can be taken. This scan will show exactly where the radioactivity is inside the organ and the body. This can give the doctor valuable information about how that organ is working.

When Ioflupane (^{123}I) Rotop is injected into an adult, it is carried around the body in the blood. It collects in a small area of your brain. Changes in this area of the brain occur in:
- Parkinsonism (including Parkinson's disease) and
- dementia with Lewy bodies.

A scan will give your doctor information about any changes in this area of your brain. Your doctor may feel that the scan would help in finding out more about your condition and deciding on possible treatment.

When Ioflupane (^{123}I) Rotop is used, you are exposed to small amounts of radioactivity. This exposure is less than in some types of X-ray investigation. Your doctor and the nuclear medicine doctor have considered that the clinical benefit of this procedure with the radiopharmaceutical outweighs the risk of being exposed to these small amounts of radiation.

2. What you need to know before Ioflupane (^{123}I) Rotop is used

Do not use Ioflupane (^{123}I) Rotop
- if you are allergic to ioflupane (^{123}I) or any of the other ingredients of this medicine (listed in section 6).
- if you are pregnant.

Warnings and precautions

Talk to your nuclear medicine doctor before using Ioflupane (^{123}I) Rotop if you have moderate or severe problems with your kidneys or liver.

Before administration of Ioflupane (^{123}I) Rotop you should drink plenty of water before the start of the examination in order to urinate as often as possible during the first hours after the study.

Children and adolescents

Ioflupane (^{123}I) Rotop is not recommended for children aged 0 to 18 years.

Other medicines and Ioflupane (^{123}I) Rotop

Tell your nuclear medicine doctor if you are taking or have recently taken any other medicines. Some medicines or substances can affect the way this medicine works. These include:
- bupropion (used to treat depression (sadness))
- benzatropine (used to treat Parkinson's disease)
- mazindol (reduces appetite, as a means to treat obesity)
- sertraline (used to treat depression (sadness))
- methylphenidate (used to treat hyperactivity in children and narcolepsy (excessive sleepiness))
- phentermine (reduces appetite, as a means to treat obesity)
- amphetamine (used to treat hyperactivity in children and narcolepsy (excessive sleepiness); also, a drug of abuse)
- cocaine (sometimes used as an anaesthetic for nose surgery; also, a drug of abuse)

Some medicines may reduce the quality of the picture obtained. The doctor may ask you to stop taking them for a short time before you receive Ioflupane (^{123}I) Rotop.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your nuclear medicine doctor for advice before you are given this medicine.

You must inform the nuclear medicine doctor before the administration of Ioflupane (^{123}I) Rotop if there is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding.

When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

If you are pregnant, do not use Ioflupane (^{123}I) Rotop. This is because the child may receive some of the radioactivity. Alternative techniques which do not involve radioactivity should be considered.

If you are breast-feeding, your nuclear medicine doctor may delay the use of Ioflupane (^{123}I) Rotop or ask you to stop breast-feeding. It is not known whether ioflupane (^{123}I) is passed into breast milk.
- You should not breast-feed your child for 3 days after Ioflupane (^{123}I) Rotop 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.

Driving and using machines

Ioflupane (^{123}I) Rotop has no known influence on the ability to drive and use machines.

Ioflupane (^{123}I) Rotop contains alcohol (ethanol) 4 % by volume. Each dose contains up to 158 mg of alcohol. This is equivalent to less than 4 ml beer or 1.6 ml wine.

The small amount of alcohol in this medicine will not have any noticeable effects.

Ioflupane (^{123}I) Rotop contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

3. How to use Ioflupane (^{123}I) Rotop

There are strict laws on the use, handling and disposal of radioactivity. Ioflupane (^{123}I) Rotop will always be used in a hospital or a similar place. It will only be handled and given to you by people who are trained and qualified to use it safely. They should tell you anything you need to do for the safe use of this medicine.

The nuclear medicine doctor supervising the procedure will decide on the quantity of Ioflupane (^{123}I) Rotop to be used in your case. It will be the smallest quantity necessary to get the desired information.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ioflupane (^{123}I) Rotop 74 MBq/ml Solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains ioflupane (^{123}I) 74 MBq 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) (molar 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) (molar activity range 2.5 to 4.5 x 10^{14} Bq/mmol) at reference time.

Excipient(s) with known effect:

This medicinal product contains 31.6 g/l ethanol. For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Ioflupane (^{123}I) Rotop 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. Ioflupane (^{123}I) Rotop 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. Ioflupane (^{123}I) Rotop is unable to discriminate between dementia with Lewy bodies and Parkinson's disease dementia.

4.2 Posology and method of administration

Ioflupane (^{123}I) Rotop should only be used in adult patients referred by physicians experienced in the management of movement disorders and/or dementia. Ioflupane (^{123}I) Rotop should only be used by qualified personnel with the appropriate government authorisation for the use and manipulation of radionuclides within a designated clinical setting.

Posology

Clinical efficacy has been demonstrated across the range 111 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 Ioflupane (^{123}I) Rotop.

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 benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Paediatric population

The safety and efficacy of Ioflupane (^{123}I) Rotop in children aged 0 to 18 years has not been established. No data are available.

Method of administration

For intravenous use.

For patient preparation, see section 4.4.

Ioflupane (^{123}I) Rotop 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, ioflupane (^{123}I) 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 the start of the examination and urged to void as often as possible during the first hours after the examination in order to reduce radiation.

Interpretation of Ioflupane (^{123}I) ROTOP Images

Ioflupane (^{123}I) ROTOP 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 Ioflupane (^{123}I) ROTOP 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 Ioflupane (^{123}I) ROTOP 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 31.6 g/l (4 % volume) ethanol (alcohol), up to 158 mg per dose, equivalent to 4 ml beer or 1.6 ml wine. The small amount of alcohol in this medicine 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. Medicines that bind to the dopamine transporter with high affinity may therefore interfere with ioflupane (^{123}I) diagnosis. These include amphetamine, benzatropine, bupropion, cocaine, mazindol, methylphenidate, phentermine and sertraline.

Medicines shown during clinical trials not to interfere with ioflupane (^{123}I) 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 ioflupane (^{123}I) imaging and can therefore be continued if desired. Medicinal products shown in animal studies not to interfere with ioflupane (^{123}I) imaging include pergolide.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

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 ionising radiation should be considered.

Pregnancy

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

Breast-feeding

It is not known whether ioflupane (^{123}I) is excreted in human milk. Before administering a radioactive medicinal product to a breast-feeding mother, consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breast-feeding and as to whether the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion of radioactivity in breast milk. If the administration is considered necessary, breastfeeding 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

Ioflupane (^{123}I) Rotop 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 4.63 mSv when the maximal recommended activity of 185 MBq is administered these adverse reactions 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 Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

4.9 Overdose

In the event of administration of a radiation overdose the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by frequent micturition and defecation. Care should be taken to avoid contamination from the radioactivity eliminated by the patient using such methods.

Before you receive Ioflupane (^{123}I) Rotop, your nuclear medicine doctor will ask you to take some tablets or liquid that contain iodine. These stop the radioactivity building-up in your thyroid gland. It is important that you take the tablets or liquid as the doctor tells you.

Administration of Ioflupane (^{123}I) Rotop and conduct of the procedure

Ioflupane (^{123}I) Rotop is given to you as an injection, usually into a vein in your arm. The quantity to be administered usually recommended for an adult ranges from 111 to 185 MBq (megabecquerel, the unit used to express radioactivity). A single injection is enough.

Duration of the procedure

The camera pictures are usually taken 3 to 6 hours after the injection of Ioflupane (^{123}I) Rotop.

Your nuclear medicine doctor will inform you about the usual duration of the procedure.

After administration of Ioflupane (^{123}I) Rotop, you should urinate frequently in order to eliminate the product from your body quickly.

The Nuclear medicine doctor will inform you if you need to take any special precautions after receiving this medicine. Contact your nuclear medicine doctor if you have any questions.

If you have been given more Ioflupane (^{123}I) Rotop than you should

Since Ioflupane (^{123}I) Rotop is given by a doctor under controlled conditions, it is unlikely that you will get an overdose. Your nuclear medicine doctor will suggest that you drink plenty of fluids to help the body get rid of the medicine. You will need to be careful with the water (urine) that you pass - your doctor will tell you what to do. This is normal practice with medicines like Ioflupane (^{123}I) Rotop.

Any ioflupane (^{123}I) which remains in your body will naturally lose its radioactivity.

If you have any further question on the use of this medicine, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The frequency of side effects is:

Common: may affect up to 1 in 10 people

- Headache

Uncommon: may affect up to 1 in 100 people

- Increased appetite
- Dizziness
- Taste disturbance
- Nausea
- Dry mouth
- Vertigo
- A brief irritating feeling similar to ants crawling over your skin (formication)
- Intense pain (or burning sensation) at the site of injection. This has been reported among patients receiving Ioflupane (^{123}I) Rotop into a small vein.

Not known: frequency cannot be estimated from the available data

- Hypersensitivity (allergic)
- Shortness of breath
- Redness of the skin
- Itching
- Rash
- Hives (urticaria)
- Excessive sweating
- Vomiting
- Low blood pressure
- Feeling hot

This radiopharmaceutical will deliver low amounts of ionising radiation associated with the least risk of cancer and hereditary abnormalities.

Reporting of side effects

If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard

or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Ioflupane (^{123}I) Rotop

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

The following information is intended for the specialist only.

Do not use this medicine after the expiry date which is stated on the label.

Hospital staff will ensure that the product is stored and thrown away correctly and not used after the expiry date stated on the label.

6. Contents of the pack and other information

What Ioflupane (^{123}I) Rotop contains

- The active substance is ioflupane (^{123}I). Each ml of solution contains ioflupane (^{123}I) 74 MBq at reference time (0.07 to 0.13 µg/ml of ioflupane).
- The other ingredients are acetic acid, sodium acetate, ethanol and water for injections.

What Ioflupane (^{123}I) Rotop looks like and contents of the pack

Ioflupane (^{123}I) Rotop is a colourless solution for injection. 2.5 ml or 5 ml of this solution are supplied in a single colourless 10 ml glass vial sealed with a butyl rubber stopper and metal overseal.

Marketing Authorisation Holder and Manufacturer

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This leaflet was last revised in December 2022.

The following information is intended for healthcare professionals only:

The complete Summary of Product Characteristics (SmPC) of Ioflupane (^{123}I) Rotop 74 MBq/ml Solution for injection is provided as a tear-off section at the end of the printed leaflet in the product package, with the objective to provide healthcare professionals with other additional scientific and practical information about the administration and use of this radiopharmaceutical. Please refer to the SmPC.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceutical central nervous system,

ATC code: V09AB03.

Due to the low quantities of ioflupane injected, pharmacological effects are not expected following intravenous administration of Ioflupane (^{123}I) Rotop at the recommended dosage.

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 pivotal 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 %.

Renal/Hepatic impairment

The pharmacokinetics in patients with renal or hepatic impairment has not been characterised.

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetic acid (for pH adjustment)
Sodium acetate (for pH adjustment)
Ethanol, anhydrous
Water for injections

6.2 Incompatibilities

Studies have shown that the product is compatible with water for injection and saline.

6.3 Shelf life

2.5 ml vial: 7 hours from the activity reference time stated on the label.

5 ml vial: 20 hours from the activity reference time stated on the label.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

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

6.5 Nature and contents of container

2.5 ml or 5 ml solution in a colourless glass vial (Type I, Ph. Eur.) of 10 ml nominal capacity, closed with a butyl rubber stopper and metal overseal.

Pack size of 1 vial.

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 product 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.

Disposal

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

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

PL 53373/0001

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

06/01/2021

10. DATE OF REVISION OF THE TEXT

21/12/2022

11. DOSIMETRY

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.

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. 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).

Frequent bladder emptying should be encouraged after dosing to minimise radiation exposure.

Organ	Absorbed radiation dose µGy/MBq
Adrenals	17.0
Bone surfaces	15.0
Brain	16.0
Breasts	7.3
Gallbladder wall	44.0
Gastrointestinal tract	
Stomach wall	12.0
Small intestine wall	26.0
Colon wall	59.0
(Upper large intestine wall)	57.0
(Lower large intestine wall)	62.0
Heart wall	32.0
Kidneys	13.0
Liver	85.0
Lungs	42.0
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**

Ref.: Publication 128 of the Annals of ICRP (Radiation dose to Patients from Radiopharmaceuticals: A Compendium of Current Information Related to Frequently Used Substances, 2015

The effective dose (E) resulting from administration of 185 MBq of Ioflupane (^{123}I) ROTOP injection is 4.63 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

Please see section 6.6.

UK/PL+SmPC

Ioflupane (^{123}I) Rotop 74 MBq/ml Solution for injection

Information for the patient (Package leaflet) &
Information for healthcare professionals (SUMMARY OF PRODUCT CHARACTERISTICS)

GB-16-01-ENG-16

PL+SmPC-Ioflupan-UK-eng-01