SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

DaTSCAN 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) (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.

Excipient(s) with known effect

This medicinal product contains 39.5 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.

DaTSCAN 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. DaTSCAN 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.
  DaTSCAN is unable to discriminate between dementia with Lewy bodies and Parkinson's disease dementia.

4.2 Posology and method of administration

Prior to administration appropriate resuscitation equipment should be available.

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

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).

Paediatric population

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

Method of Administration

For intravenous use.

DaTSCAN 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 11-15cm). 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 500k 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

If hypersensitivity reactions occur, the administration of the medicinal product must be discontinued immediately and, if necessary, intravenous treatment initiated. Resuscitative medicinal products and equipment (e.g. endotracheal tube and ventilator) have to be readily available.

This radiopharmaceutical may be received, used and administered only by authorised persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and the appropriate licences of the local competent official organisations.

For each patient, exposure to ionising radiation must be justifiable on the basis of likely benefit. The activity administered must be such that the resulting dose is as low as reasonably achievable bearing in mind the need to obtain the intended diagnostic result.

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.

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

This medicinal product contains 39.5 g/l (5% volume) ethanol (alcohol), up to 197 mg per dose, equivalent to 5 ml beer or 2 ml wine. Harmful for those suffering from alcoholism. To be taken into account in high-risk groups such as patients with liver disease or epilepsy.

Interpretation of DaTSCAN Images

DaTSCAN 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 DaTSCAN 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 DaTSCAN 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

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 DaTSCAN diagnosis. These include amfetamine, bupropion, cocaine, codeine, dexamfetamine, methylphenidate, modafinil, and phentermine. Selective serotonin reuptake inhibitors, such as sertraline, may increase or decrease ioflupane binding to the dopamine transporter.

Medicines shown during clinical trials not to interfere with DaTSCAN 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 DaTSCAN imaging and can therefore be continued if desired. Medicinal products shown in animal studies not to interfere with DaTSCAN 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 3.0 mGy. DaTSCAN is contraindicated in pregnancy (see section 4.3).

Breastfeeding

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 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

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

4.8 Undesirable effects

The following undesirable effects are recognised for DaTSCAN:

Tabulated summary of adverse reactions

The frequencies of adverse reactions are defined as follows:

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) and not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Immune system disorders

Not known: Hypersensitivity

Metabolism and nutrition disorders

Uncommon: Appetite increased

Nervous system disorders

Common: Headache

Uncommon: Dizziness, formication (paraesthesia), dysgeusia

Ear and labyrinth disorders

Uncommon: Vertigo

Skin and subcutaneous tissue disorders

Not known: Erythema, pruritus, rash, urticaria, hyperhidrosis

Respiratory, thoracic and mediastinal disorders

Not known: Dyspnea

Gastrointestinal disorders

Uncommon: Nausea, dry mouth

Not known: Vomiting

Vascular disorders

Not known: Blood pressure decreased

General disorders and administration site conditions

Uncommon: Injection site pain (intense pain or burning sensation following administration into small veins)

Not known: Feeling hot

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 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 Yellow Card Scheme at https://yellowcard.mhra.gov.uk/.

4.9 Overdose

In cases of overdose of radioactivity, 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.

Due to the low quantities of ioflupane injected, pharmacological effects are not expected following intravenous administration of DaTSCAN 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 DaTSCAN 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 DaTSCAN 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 DaTSCAN 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetic acid

Sodium acetate

Ethanol

Water for injections

6.2 Incompatibilities

Not applicable

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

Do not store above 25^{o}C. Do not freeze.

6.5 Nature and contents of container

2.5 or 5 ml solution in a single colourless 10 ml glass vial sealed with a rubber closure and metal overseal.

Pack size of 1.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

General warning

Normal safety precautions for handling radioactive materials should be observed.

Disposal

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.

7 MARKETING AUTHORISATION HOLDER

GE Healthcare Limited

Pollards Wood

Nightingales Lane

Chalfont St Giles

Buckinghamshire, HP8 4SP

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 00221/0387

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/01/2021

10 DATE OF REVISION OF THE TEXT

13/08/2024

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 estimated absorbed radiation doses to an average adult patient (70 kg) from intravenous injection of ioflupane (^{123}I) are listed in the Table 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.

Target Organ	**Absorbed radiation dose** **µGy/MBq**
Adrenals	17.0

Bone surface	15.0
Brain	16.0
Breast	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
Muscles	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 (µSv/MBq)	**25.0**

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 DaTSCAN 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.

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. See also section 6.6.