Protocol Manual

Normal Scan
Comma-Shaped

Abnormal Scan
Period-Shaped
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Section 1

Introduction
Introduction

1.1 Scope

This document describes the procedure and parameters for visual interpretation of single-photon emission computed tomography (SPECT) images acquired after administration of DaTscan. It is assumed that the person reading the images is a clinician with expertise in the interpretation of nuclear medicine studies and has a detailed knowledge of brain anatomy. In addition, for this document to be applicable, DaTscan must have been prescribed and administered according to the Full Prescribing Information, and the images must have been acquired and processed with the GE Healthcare-recommended protocols specified in sections 2.3 and 2.4.

1.2 What is DaTscan?

DaTscan is a radiopharmaceutical indicated for striatal dopamine transporter (DaT) visualization using SPECT brain imaging to assist in the evaluation of adult patients with suspected parkinsonian syndrome (PS). The density of DaT in the striatum progressively decreases in specific patterns in PS (including idiopathic Parkinson’s disease, multiple system atrophy, and progressive supranuclear palsy). Following intravenous injection of DaTscan, the active substance, [123I]ioflupane, distributes to the striata in the brain, where it binds with high affinity to the presynaptic DaT protein. In adult patients with suspected PS, DaTscan may be used to help differentiate essential tremor (ET) from tremor due to PS. DaTscan is an adjunct to other diagnostic evaluations.

DaTscan is a federally controlled DEA Schedule II (CII) substance. A DEA license is required for handling or administering this controlled substance. Learn more at www.datscan.com.

Important Risk and Safety Information About DaTscan

DaTscan is contraindicated in patients with known hypersensitivity to the active substance, any of its excipients, or iodine.

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
Section 2

Image Acquisition, Interpretation, and Reporting
2.1 Imaging Guidelines for DaTscan¹

Begin SPECT imaging three to six hours following DaTscan administration. Acquire images using a gamma camera fitted with low-energy, high-resolution (LEHR) collimators and set to a photopeak of 159 keV with a ±10% energy window. Angular sampling should not be less than 120 views over 360 degrees. Position the patient 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 can also be used to help avoid movement. Set a circular orbit for the detector heads with the radius as small as possible (11 to a maximum of 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.

2.2 Patient Positioning

The following factors in patient positioning are critical to acquiring interpretable images with DaTscan.

- **Proper head tilt**: A lateral head tilt may make a normal image appear abnormal. Always use an off-the-table headrest to help avoid abnormal images¹

- **Small acquisition radius**: Place the camera detectors as close to the patient’s head as physically possible without touching. The best image resolution occurs with a circular orbit and radius of rotation of 11 to a maximum of 15 cm.¹

- **Minimal patient motion**: Decrease excess motion with head, arm, and leg straps

**Best practices for patient positioning can help avoid imaging problems:**

- Communicate clearly with the patient, emphasizing the need to remain still and reassuring the patient during the test
- Always use an off-the-table headrest, and consider using head, arm, or leg straps to minimize patient motion
- For additional patient support and comfort, you may want to use a pillow or foam block placed under the knees and a blanket tucked around the upper body. Do not use a standard pillow under the head
- If you do not have an off-the-table headrest, do not perform imaging with DaTscan

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
### 2.3 Recommended Image Acquisition Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gamma camera</strong></td>
<td>Double- or triple-headed SPECT gamma camera system</td>
</tr>
<tr>
<td><strong>Collimators</strong></td>
<td>Only low-energy, high-resolution (LEHR) collimators (parallel hole or fanbeam) or ultra–high-resolution (UHR) fanbeam collimators have been tested for use with this guide. Use of UHR parallel hole or any type of medium energy or general-purpose collimator is not recommended with DaTscan.</td>
</tr>
<tr>
<td><strong>Patient positioning</strong></td>
<td>Supine with the head off the imaging table in a suitable off-the-table headrest with restraint to minimize radius of rotation and prevent patient motion. Middle of the ear must be in the field of view.</td>
</tr>
<tr>
<td><strong>Orbit</strong></td>
<td>Circular, 360°</td>
</tr>
<tr>
<td><strong>Radius of rotation of detector heads</strong></td>
<td>As close as possible, with a maximum radius of rotation of 15 cm</td>
</tr>
<tr>
<td><strong>Acquisition type</strong></td>
<td>Step and shoot, 3° per step, 30 seconds per step (dual-headed cameras) or 45 seconds per step (triple-headed cameras)</td>
</tr>
<tr>
<td><strong>Acquisition start time</strong></td>
<td>Three to six hours postinjection</td>
</tr>
<tr>
<td><strong>Matrix</strong></td>
<td>128 x 128</td>
</tr>
<tr>
<td><strong>Zoom</strong></td>
<td>Sufficient for 3.5 mm to 4.5 mm pixel size</td>
</tr>
<tr>
<td><strong>Total counts</strong></td>
<td>At least 1.5 million total counts should be acquired for optimal images</td>
</tr>
<tr>
<td><strong>Energy window</strong></td>
<td>±10% (20% total window width)</td>
</tr>
<tr>
<td><strong>Photopeak</strong></td>
<td>Centered on 159 keV</td>
</tr>
</tbody>
</table>

Please see **Important Risk and Safety Information** on page 32 and **Full Prescribing Information** at the end of this document prior to administration.
### 2.4 Image Processing Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reconstruction algorithm</strong></td>
<td>Filtered back projection (FBP) or iterative reconstruction (eg, OSEM)</td>
</tr>
<tr>
<td><strong>Filtering (pre-2D or post-3D)</strong></td>
<td>Butterworth (or other low-pass linear filter)</td>
</tr>
<tr>
<td><strong>Filter power factor</strong></td>
<td>8 to 10 (system-dependent)</td>
</tr>
<tr>
<td><strong>Cutoff</strong></td>
<td>Changing the filter cutoff will affect image resolution. 0.5 to 0.6 cycles per cm nominally (or as appropriate to achieve approximately the same level of smoothing as the images shown throughout this guide)</td>
</tr>
<tr>
<td><strong>Attenuation correction</strong></td>
<td>Not necessary. If desired, can use Chang (also known as linear or zero-order)</td>
</tr>
<tr>
<td><strong>Attenuation correction coefficient (if used)</strong></td>
<td>A locally calculated attenuation correction coefficient from a phantom measurement should be used if available. Otherwise, use nominal value of 0.11 cm⁻¹</td>
</tr>
<tr>
<td><strong>Background subtraction</strong></td>
<td>No background subtraction</td>
</tr>
<tr>
<td><strong>Pixel (voxel) size</strong></td>
<td>3.5 mm to 4.5 mm isotropic</td>
</tr>
<tr>
<td><strong>Presentation</strong></td>
<td>Transaxial (transverse) slices parallel to the anterior commissure-posterior commissure (AC-PC) line with single-pixel thickness</td>
</tr>
<tr>
<td><strong>Color scale</strong></td>
<td>The preferred option for displaying images is the &quot;cool&quot; color scale shown below</td>
</tr>
</tbody>
</table>

![B/W, Linear](image1.png)  
![GE Color, Rainbow, Cool](image2.png)

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
2.4.1 Camera-Specific Parameters

**GE Millennium VG/ Elscint Varicam**
- Radius of rotation – <14 cm
- Collimation – LEHR parallel
- Energy window – 159 keV, 20%
- Projection angles – 120 over 360°
- Image matrix – 128 x 128, zoom 1.2 (3.7 mm)
- Time per projection – 30 sec
- Filter depends on system: IGE Butterworth factor 8-10, cutoff 0.32

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GE Discovery 670/630 Dual Head

- Radius of rotation – ~13 cm
- Collimation – LEHR
- Must select “scan on extender” and use the head holder
- Energy window – 159 keV, 20%
- Projection angles – 120 (60 on each head) over 360°
- Image matrix – 128x128, zoom 1.25 (~3.53 mm)
- Time per projection – 30 sec
- FBP, 2-D Butterworth prefilter, power factor 10, cutoff 0.6
- Total counts – ~1.8 million

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**GE Infinia**

- Radius of rotation – 13 cm
- Collimation – LEHR
- Energy window – 159 keV, 20%
- Projection angles – 120 over 360°
- Image matrix – 128 x 128, zoom 1.2 (~3.7 mm)
- Time per projection – 30 sec
- FBP, 2-D Butterworth prefilter, power factor 10, cutoff 0.6

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ADAC Forte
- Radius of rotation – <15 cm
- Collimation – Parallel VXGP/VXHR
- Energy window – 159 keV, 20%
- Projection angles – 120 over 360°
- Image matrix – 128 x 128, no zoom (~4.6 mm)
- Time per projection – 30 sec
- FBP Butterworth cutoff 0.6, order 8

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
**Philips Axis**

- Radius of rotation – 13 cm
- Collimation – Parallel, HR(1) or fanbeam(2)
- Energy window – 159 keV, 20%
- Projection angles – 120 over 360°
- Image matrix – 128 x 128, zoom 1.33 (~3.5 mm)
- Time per projection – 30 sec
- FBP, 3-D low-pass postfilter; 0.5 cycles/pixel, power factor 8

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**Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.**
**Philips Prism 2000**
- Radius of rotation – 14 cm
- Collimation – UHR
- Energy window – 159 keV, 20%
- Projection angles – 120 over 360°
- Image matrix – 128 x 128, zoom 1.33 (~3.5 mm)
- Time per projection – 30 sec
- FBP, 3-D low-pass postfilter; 0.6 cycles/pixel, power factor 8

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
Siemens ECAM Dual Head

- Radius of rotation – 13 cm
- Collimation – LEHR
- Energy window – 159 keV, 15%
- Projection angles – 120 over 360°
- Image matrix – 128 x 128, zoom 1.23 (~3.89 mm)
- Time per projection – 30 sec
- FBP, 2-D Butterworth prefilter, power factor 8, cutoff 0.6

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
Siemens Symbia Dual Head

- Radius of rotation – 13.0 cm (14-cm CT headrest)
- Collimation – LEHR
- Energy window – 159keV, 15%
- Projection angles – 120 over 360°
- Image matrix – 128x128, zoom 1.23 (~3.89 mm)
- Time per projection – 30 sec
- FBP, 2-D Butterworth prefilter, power factor 8, cutoff 0.6

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
2.5 Quality Checks

Prior to interpretation, images should be reviewed for correct acquisition and processing procedures:

- All parameters stated in sections 2.3 and 2.4 should be followed
- Radius of rotation must be 11 to a maximum of 15 cm
- FOV should extend from the top of the head to the level of the middle ear
- Minimum 1.5 M total counts
- Pixel size must be between 3.5 mm and 4.5 mm
- No visible patient motion or camera-head misalignment in the rotating tomograms
- No more than two dropped frames are allowed in the study, and they cannot be consecutive (adjacent)
- The patient’s head should not show a lateral (left or right ear toward shoulder) tilt. A slight caudal tilt (chin up or down) or rotation of the head is acceptable
- Transaxial slices should be oriented with the front of the head pointing up

Images should be reviewed for quality problems immediately after acquisition. If image quality problems are detected (such as patient motion, incorrect pixel size, dropped frames, or low total counts), it is preferable to reimage the patient (while still within the three- to six-hour window postinjection) than to apply a software corrective solution. The start time for the second acquisition should occur no later than six hours postinjection.

2.6 Examples of Deficient Image Quality Causes

2.6.1 Radius of Rotation

As the radius of rotation of the camera heads increases, spatial resolution decreases, and visibility of activity in the putamen is reduced.

Phantom images showing the effect of increasing the radius of rotation

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
2.6.2 Lateral Head Tilt

Lateral head tilt during imaging can cause the striatal uptake in the transaxial slices to appear asymmetric or abnormal, even in a healthy patient. If the striatal uptake of DaTscan appears to be reduced on one side in higher slices and on the other side in lower slices, it often is caused by lateral head tilt. Lateral head tilt also can be noted by viewing the rotating tomogram.

Example of the effect of lateral tilt on a subject with normal uptake of DaTscan.

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
2.7 Normal vs Abnormal Images

DaTscan images are interpreted visually, based on the appearance of the striata. Reconstructed pixel size should be between 3.5 and 4.5 mm with slices one pixel thick. Optimum presentation of the reconstructed images for visual interpretation is transaxial slices parallel to the 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.

A number of neurologic disorders of movement and executive function involve changes in the dopaminergic neurons of the striata. [123I]ioflupane binds tightly to the DaT in the brain and allows visualization of striatal DaT. The brain structures with highest activity of [123I]ioflupane following DaTscan injection (in patients with normal DaT distribution) are the left and right caudate and putamen, known collectively as the left and right striata. 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.

Important Risk and Safety Information About DaTscan

Drugs that bind to the dopamine transporter with high affinity may interfere with the DaTscan image. The impact of dopamine agonists and antagonists on DaTscan imaging results has not been established.

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
2.8 Normal Uptake

In transaxial images, normal uptake is 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. Examples are shown below with measurements of average counts per pixel in both striata (using crescent-shaped regions of interest [ROIs]) normalized to the background region (occipital cortex). ROI values are provided for reference and should not be used in place of visual interpretation of images as normal or abnormal.

Examples of normal DaTscan uptake with ratios of activity in both striata to background.

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Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
2.9 Abnormal Uptake

With disorders involving striatal DaT, [123I]ioflupane activity is almost always reduced first in the posterior putamen, often asymmetrically. The side on which the putamen uptake is reduced most is typically the side contralateral to the side of the body on which the patient’s motor symptoms first began. As degeneration progresses, [123I]ioflupane activity may become symmetric and circular or oval in appearance. The contrast between the foci and the surrounding brain tissue also decreases and, in cases of severe DaT depletion, may be difficult to distinguish from background tissue.

The following are commonly seen abnormal patterns of DaTscan uptake:

- 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.

Examples of abnormal DaTscan uptake with ratios of activity in both striata to background.

3.3 : 1  3.0 : 1  2.8 : 1

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Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
2.9 Abnormal Uptake (cont’d)

- 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.

- 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.

Examples of abnormal DaTscan uptake with ratios of activity in both striata to background.

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Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
2.10 Unexpected Results

There can be images acquired after administration of DaTscan that do not conform to the standard normal or abnormal patterns as shown in the previous examples. These may be indicative of a different problem with the patient or an artifact from incorrect acquisition or processing.

An image that is severely asymmetrical (left to right) or which does not show preferential loss in the putamen could be due to problems such as abnormal perfusion, striatal infarction, or interference from medications. **See Section 3.1 for medications that may affect a DaTscan image.**

![Image 1](image1.png)

The MRI subsequently showed a lesion affecting the striatal area for this patient.

Patient motion or improper center of rotation (COR) correction in the camera can cause the left and right striata to appear fused together or not to appear at all.

![Image 2](image2.png)

Examples of artifacts caused by patient motion during imaging.

Please see **Important Risk and Safety Information** on page 32 and **Full Prescribing Information** at the end of this document prior to administration.
2.11 Reporting Reminders

Be sure to consider the following points when reporting the results of DaTscan imaging to the referring physician:

- Results of visual examination
- Results of quantification (if performed). Please note that quantification is not necessary for the interpretation of DaTscan SPECT images
- Accuracy of acquisition
- How much DaTscan was injected
- Time point of acquisition

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Section 3

Step-by-Step Guide to DaTscan
Patient Preparation

3.1 Patient Protocols

Patient preparation for the SPECT process with DaTscan™ (Ioflupane I 123 Injection):

1. Drug Interactions
   Prior to administering DaTscan, review current medications to determine possible drug interactions.1,4
   - Amoxapine
   - Amphetamine
   - Benztropine
   - Bupropion
   - Buspirone
   - Citalopram
   - Cocaine
   - Mazindol
   - Methamphetamine
   - Methylphenidate
   - Norephedrine
   - Paroxetine
   - Phentermine
   - Phenylpropanolamine
   - Selegiline

   It is unknown if discontinuation of these drugs prior to administration of DaTscan may minimize the interference with imaging with DaTscan.

2. Hydrate
   Advise patient to hydrate prior to and following administration of DaTscan to permit frequent voiding.

3. Comfortable Clothing
   Advise patient to wear comfortable clothing (patient will not need to remove clothes).

4. Thyroid-Blocking Agent
   Administer thyroid-blocking agent at least one hour before administration of DaTscan.

5. DaTscan Administration
   Administer DaTscan via slow intravenous injection and wait three to six hours before SPECT imaging.

6. SPECT Procedure
   Advise patient to lie still for an approximately 30-minute SPECT procedure.

7. Continue Hydration
   Instruct patient to continue hydration and to void frequently for 48 hours.

Important Risk and Safety Information About DaTscan
In clinical trials, reported adverse events consisted of headache, nausea, vertigo, dry mouth, or dizziness. These reactions were of mild to moderate severity. In the postmarketing experience, hypersensitivity reactions have been reported, generally consisting of skin erythema and pruritus. Injection-site pain also has been reported. To decrease thyroid accumulation of iodine 123, block the thyroid gland at least one hour before DaTscan administration. Failure to do so may result in an increased long-term risk for thyroid neoplasia.

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
3.2 Patient Counseling

Instruct patients to inform you if they:

- Have reduced renal or hepatic function
- Are sensitive to DaTscan or iodine
- Are sensitive to potassium iodide oral solution or Lugol's Solution
- May be pregnant, are trying to become pregnant, or are breastfeeding

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

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
Dosing

3.3 Thyroid Blocking
To minimize thyroid uptake of radioactive iodine, administer a thyroid-blocking agent at least one hour prior to DaTscan injection.¹

**Thyroid Blocking — Commonly Used Protocols¹**
- Potassium iodide/iodate
- Potassium perchlorate
- Lugol’s Solution

3.4 Dose Administration and Calibration
- The recommended adult dose for DaTscan is 3-5 mCi, administered intravenously¹
- This dose must be measured using a suitable radioactivity calibration system immediately prior to administration¹

Please direct questions regarding dose calibration for DaTscan to GE Healthcare Medical Affairs at 800 654 0118 (option 2, then option 3).

Important Risk and Safety Information About DaTscan

**Radiation Safety:** To minimize radiation dose to the bladder, encourage hydration prior to and following DaTscan administration in order to permit frequent voiding. Encourage the patient to void frequently for the first 48 hours following DaTscan administration.

Please see **Important Risk and Safety Information** on page 32 and **Full Prescribing Information** at the end of this document prior to administration.
3.5 Administration of DaTscan

DaTscan should be administered via a slow intravenous (IV) injection in an arm vein (no less than 15-20 seconds)\(^1\)

- SPECT imaging should be performed within three to six hours postinjection\(^1\)
- It is recommended to keep imaging times postinjection as consistent as possible for all patient studies

3.6 Storage of DaTscan

- DaTscan is a DEA Schedule II (CII) controlled substance
- Store DaTscan in its original lead container (or an equivalent radiation shielding) in a securely locked, substantially constructed cabinet at 68°-77°F (20°-25°C)\(^1,3\)

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
3.7 Schedule II Radiopharmaceutical Requirements

The following checklist summarizes the licensing requirements and GE Healthcare's shipping requirements for a Schedule II product:

Current and Valid Drug Enforcement Administration (DEA) and Radioactive Materials (RAM) Licenses

- In order for GE Healthcare to deliver DaTscan, the address on both licenses must be the same and must be the address to which the product will be shipped.

Ordering DaTscan

After you obtain DEA and RAM licenses, DaTscan can be ordered online through the Controlled Substance Ordering System (CSOS) or with a paper DEA Form 222. It is important to note that the paper form will soon be phased out and DaTscan will be available only through online orders.

Ordering Online Via CSOS

- You can order DaTscan online at http://www.orderdatscan.com

Ordering Using DEA Form 222

- Use DEA Form 222 (sample form on right)
- DaTscan can be ordered by a hospital's central pharmacy or a nuclear medicine department
- DaTscan must be ordered at least four business days in advance of planned administration to allow for Form 222 processing

Delivery and Storage

- Secure Storage
  - Upon receipt, DaTscan must be stored in a securely locked, substantially constructed cabinet compliant with DEA requirements for Schedule II substances.

This checklist contains suggestions for preparing your department for ordering Schedule II radiopharmaceuticals and is not an exhaustive list of requirements. It is not a substitute for legal or regulatory advice. Please consult the relevant DEA regulations for further guidance.

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.
Section 4

Important Risk and Safety Information
Section 4

Important Risk and Safety Information About DaTscan™ (Ioflupane I 123 Injection)

**INDICATIONS AND USE:** DaTscan 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 (PSs). DaTscan may be used to help differentiate essential tremor from tremor due to PS (idiopathic Parkinson’s disease [PD], multiple system atrophy [MSA], and progressive supranuclear palsy [PSP]). DaTscan is an adjunct to other diagnostic evaluations. DaTscan was not designed to distinguish among PD, MSA, and PSP. The effectiveness of DaTscan as a screening or confirmatory test and for monitoring disease progression or response to therapy has not been established. **CONTRAINDICATIONS:** DaTscan is contraindicated in patients with known hypersensitivity to the active substance, any of the excipients, or iodine. **WARNINGS AND PRECAUTIONS — Hypersensitivity Reactions:** Hypersensitivity reactions, generally consisting of skin erythema and pruritus, have been reported following DaTscan administration. **Thyroid Accumulation:** The DaTscan injection may contain up to 6% of free iodide (iodine 123 or I-123). To decrease thyroid accumulation of I-123, block the thyroid gland at least one hour before administration of DaTscan; failure to do so may increase the long-term risk for thyroid neoplasia. **ADVERSE REACTIONS:** In clinical trials, headache, nausea, vertigo, dry mouth, or dizziness of mild to moderate severity were reported. In postmarketing experience, hypersensitivity reactions and injection-site pain have been reported. **DRUG INTERACTIONS:** Drugs that bind to the dopamine transporter with high affinity may interfere with the DaTscan image. The impact of dopamine agonists and antagonists on DaTscan imaging results has not been established. **SPECIFIC POPULATIONS — Pregnancy:** It is unknown whether DaTscan can cause fetal harm or increase the risk of pregnancy loss in pregnant women. DaTscan should be given to pregnant women only if clearly needed. Like all radiopharmaceuticals, DaTscan may cause fetal harm, depending on the stage of fetal development and the magnitude of the radionuclide dose. **Nursing Mothers:** It is not known whether DaTscan is excreted into human milk; however, I-123 is excreted into human milk. Because many drugs are excreted into human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to interrupt nursing after administration of DaTscan or not to administer DaTscan at all. Nursing women may consider interrupting nursing and pump and discard breast milk for six days after DaTscan administration to minimize risks to a nursing infant. **Pediatric Use:** The safety and efficacy of DaTscan have not been established in pediatric patients. **Geriatric Use:** There were no differences in responses between the elderly and younger patients that would require a dose adjustment. **Renal and Hepatic Impairment:** The effect of renal or hepatic impairment on DaTscan imaging has not been established. The kidney excretes DaTscan; patients with severe renal impairment may have increased radiation exposure and altered DaTscan images. **DRUG ABUSE AND DEPENDENCE:** Ioflupane I 123 Injection is a DEA Schedule II controlled substance. A DEA license is required for handling or administering this controlled substance. **OVERDOSAGE:** It is unknown whether or not ioflupane is dialyzable. The major risks of overdose relate to increased radiation exposure and long-term risk for neoplasia. In case of radioactivity overdosage, frequent urination and defecation should be encouraged to minimize radiation exposure to the patient. **PROCEDURE — Radiation Safety:** DaTscan emits radiation and must be handled with safety measures to minimize radiation exposure to clinical personnel and patients.

Please read Full Prescribing Information at the end of this document prior to administration.
GE Healthcare’s Commitment to You

If you have a question regarding DaTscan, please refer to the numbers below for assistance:

Customer Service
To place an order, call 800 292 8514

Medical Affairs
For technical or product-related questions, call 800 654 0118
(option 2, then option 3)

Reimbursement Hotline
For reimbursement-related questions (eg, appropriate coding), call our Hotline at 800 767 6664

For more information about DaTscan, visit www.datscan.com.

Please see Important Risk and Safety Information on page 32 and Full Prescribing Information at the end of this document prior to administration.

INDICATIONS AND USAGE
DaTscan (Iof lupane 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, DaTscan may be used to help differentiate essential tremor from tremor due to PD (idiopathic Parkinson's disease, multiple system atrophy and progressive supranuclear palsy). DaTscan is an adjunct to other diagnostic evaluations. (1)

DOSE AND ADMINISTRATION
• DaTscan 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 DaTscan. (2.2)
• The recommended DaTscan dose is 111 to 185 MBq (3 to 5 mCi). (2.4)
• Begin SPECT imaging between 3 and 6 hours post-injection. (2.6)

DOSE FORMS AND STRENGTHS
2.5 mL of sterile solution for intravenous injection in a single-use 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 DaTscan administration. Have anaphylactic and hypersensitivity treatment measures available prior to DaTscan administration. (5.1)
• Administer a thyroid-blocking agent before DaTscan administration. (5.2)

ADVERSE REACTIONS
Hypersensitivity and injection site reactions have been reported following DaTscan 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 GE Healthcare at 1-800-654-0118 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS
Aloxapine, amphetamine, benzotropine, buPROPion, butpine, cocaine, m AZindol, methamphetamine, methylphenidate, norephedrine, phentermine, phenylpropanolamine, selegiline, sertraline, citalopram and paroxetine may interfere with DaTscan imaging. (7) The effects of dopamine agonists and antagonists on DaTscan imaging have not been established.

USE IN SPECIFIC POPULATIONS
• Pregnancy: No human or animal data. Any radiopharmaceutical, including DaTscan, may cause fetal harm. Use only if clearly needed. (8.1)
• Nursing Mothers: A decision should be made whether to interrupt nursing after DaTscan administration or not to administer DaTscan, taking into consideration the importance of the drug to the mother. (8.3)
• Pediatric: Safety and effectiveness have not been established. (8.4)

See 17 for PATIENT COUNSELING INFORMATION.

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Revised: 4/2011

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
DaTscan 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, DaTscan may be used to help differentiate essential tremor from tremor due to PS (idiopathic Parkinson’s disease, multiple system atrophy and progressive supranuclear palsy). DaTscan is an adjunct to other diagnostic evaluations.

To minimize radiation dose to the bladder, encourage hydration prior to and following DaTscan administration in order to permit frequent voiding. Encourage the patient to void frequently for the first 48 hours following DaTscan administration (see Dosage and Administration [2.5]).

2.2 Thyroid Blockade Before DaTscan Injection
Before administration of DaTscan, 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 DaTscan (see Warnings and Precautions [5.2]).

2.3 Preparation and Administration
Use aseptic procedures and radiation shielding during preparation and administration. Inspect the DaTscan vial prior to administration and do not use it if the seal is ruptured or particulate matter or discoloration (see Description [11]). Administer DaTscan 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 DaTscan 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).
Activity of one or both is generally reduced (Figure 4).

- 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).

2.6 Imaging Guidelines

Begin SPECT imaging 3 to 6 hours following DaTscan administration. Acquire images using a gamma camera fitted with high-resolution collimators and set to a photoshoot of 120 keV with ±10% energy window. Angular sampling should not exceed 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

DaTscan 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 foci of activity mirrored about the median plane. Striatal activity is distinct, relative to surrounding brain tissue (Figure 1).

Abnormal:
Abnormal DaTscan 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).

Table 1
Estimated Radiation Absorbed Doses from DaTscan

<table>
<thead>
<tr>
<th>ORGAN / TISSUE</th>
<th>ABSORBED DOSE PER UNIT ADMINISTERED ACTIVITY (µSv/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenals</td>
<td>12.9</td>
</tr>
<tr>
<td>Brain</td>
<td>17.8</td>
</tr>
<tr>
<td>Striata</td>
<td>230.0</td>
</tr>
<tr>
<td>Breasts</td>
<td>7.8</td>
</tr>
<tr>
<td>Esophagus</td>
<td>10.0</td>
</tr>
<tr>
<td>Gallbladder Wall</td>
<td>26.4</td>
</tr>
<tr>
<td>Stomach Wall</td>
<td>11.2</td>
</tr>
<tr>
<td>Small Intestine Wall</td>
<td>21.2</td>
</tr>
<tr>
<td>Colon Wall</td>
<td>39.8</td>
</tr>
<tr>
<td>Upper Large Intestine Wall</td>
<td>38.1</td>
</tr>
<tr>
<td>Lower Large Intestine Wall</td>
<td>42.0</td>
</tr>
<tr>
<td>Heart Wall</td>
<td>12.9</td>
</tr>
<tr>
<td>Kidneys</td>
<td>10.9</td>
</tr>
<tr>
<td>Liver</td>
<td>27.9</td>
</tr>
<tr>
<td>Lungs</td>
<td>41.2</td>
</tr>
<tr>
<td>Muscle</td>
<td>9.4</td>
</tr>
<tr>
<td>Osteogenic Cells</td>
<td>28.2</td>
</tr>
<tr>
<td>Ovaries</td>
<td>16.8</td>
</tr>
<tr>
<td>Pancreas</td>
<td>13.0</td>
</tr>
<tr>
<td>Red Marrow</td>
<td>9.2</td>
</tr>
<tr>
<td>Skin</td>
<td>6.0</td>
</tr>
<tr>
<td>Spleen</td>
<td>10.4</td>
</tr>
<tr>
<td>Testes</td>
<td>8.5</td>
</tr>
<tr>
<td>Thymus</td>
<td>10.0</td>
</tr>
<tr>
<td>Thyroid</td>
<td>9.0</td>
</tr>
<tr>
<td>Urinary Bladder Wall</td>
<td>53.1</td>
</tr>
<tr>
<td>Uterus</td>
<td>16.1</td>
</tr>
<tr>
<td>Total Body</td>
<td>11.3</td>
</tr>
</tbody>
</table>

**EFFECTIVE DOSE PER UNIT ADMINISTERED ACTIVITY (µSv/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, \( D_{\text{colon}} = 0.57D_{\text{ULI}} + 0.43D_{\text{LLI}} \) (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 DaTscan administration with an administered activity of 185 MBq (5 mCi) is 3.94 mSv in an adult.

3 DOSAGE FORMS AND STRENGTHS

Single-use 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

DaTscan 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 DaTscan 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 DaTscan. If the patient is known or strongly suspected of having had a hypersensitivity reaction to DaTscan, the decision to administer DaTscan 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 DaTscan administration and, following administration, observe patients for symptoms or signs of a hypersensitivity reaction.

5.2 Thyroid Accumulation

The DaTscan injection may contain up to 6% of free iodine (iodine 123). To decrease thyroid accumulation of iodine 123, block the thyroid gland before administration of DaTscan (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 DaTscan 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 DaTscan 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 DaTscan 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 DaTscan binds to the dopamine transporter. Drugs that bind to the dopamine transporter with high affinity may interfere with the image obtained following DaTscan administration. These potentially interfering drugs consist of: amoxapine, amphetamine, benztrapine, bupropion, buspirone, cocaine, mazindol, metamphetamine, methylenephedrine, 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 DaTscan administration may minimize the interference with a DaTscan image is unknown.

The impact of dopamine agonists and antagonists upon DaTscan imaging results has not been established.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Pregnancy Category C: It is not known whether DaTscan can cause fetal harm or increase the risk of pregnancy loss when administered to a pregnant woman. Animal reproductive and developmental toxicity studies have not been conducted with DaTscan. Prior to the administration of DaTscan to women of childbearing potential, assess for the presence of pregnancy. DaTscan should be given to a pregnant woman only if clearly needed.

Like all radiopharmaceuticals, DaTscan has a potential to cause fetal harm. The likelihood of fetal harm depends on the stage of fetal development, and the magnitude of the radionuclide dose. Administration of DaTscan at a dose of 185 MBq (5 mCi) results in an absorbed radiation dose to the uterus of 0.3 rad (3.0 mGy). Radiation doses greater than 15 rad (150 mGy) have been associated with congenital anomalies but doses under 5 rad (50 mGy) generally have not. Radioactive iodine products cross the placenta and can permanently impair fetal thyroid function.

8.3 Nursing Mothers
It is not known whether DaTscan is excreted into human milk. However, iodine 123 is excreted into human milk. Because many drugs are excreted into human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to interrupt nursing after administration of DaTscan or not to administer DaTscan, taking into account the importance of the drug to the mother. Based on the physical half-life of iodine 123 (13.2 hours), nursing women may consider interrupting nursing and pumping and discarding breast milk for 6 days after DaTscan administration in order to minimize risks to a nursing infant.

8.4 Pediatric Use
DaTscan is not indicated for use in children. The safety and efficacy of DaTscan 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 DaTscan imaging has not been established. DaTscan is excreted by the kidney and patients with severe renal impairment may have increased radiation exposure and altered DaTscan images.

9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
Ioflupane I 123 Injection is a Schedule II controlled substance under the Controlled Substances Act. A DEA license is required for handling or administering this controlled substance.

10 OVERDOSAGE
The clinical consequence of overdose with DaTscan has not been reported. It is unknown whether or not ioflupane is dialyzable. Due to the small quantity of ioflupane in each vial, overdose 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 overdose 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
DaTscan (Ioflupane I 123 Injection) is a sterile, pyrogen-free radiopharmaceutical for intravenous injection. The clear and colorless solution is supplied in single-use vials in which each milliliter contains 0.07 to 0.13 µg 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>
<thead>
<tr>
<th>Radiation</th>
<th>Energy Level (keV)</th>
<th>Abundance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma</td>
<td>159</td>
<td>83</td>
</tr>
</tbody>
</table>

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 2 (e.g., the use of 2.16 cm Pb will decrease the external radiation exposure by a factor of about 1,000).

<table>
<thead>
<tr>
<th>Shield Thickness (cm of lead (Pb))</th>
<th>Reduction in In-air Collision Kerma</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.04</td>
<td>0.5</td>
</tr>
<tr>
<td>0.13</td>
<td>10</td>
</tr>
<tr>
<td>0.77</td>
<td>10</td>
</tr>
<tr>
<td>2.16</td>
<td>10</td>
</tr>
<tr>
<td>3.67</td>
<td>10</td>
</tr>
</tbody>
</table>

*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 DaTscan is N-β-fluoropropyl-2β-carbomethoxy-3β-[123I]iodophenyl-nortropane or ioflupane I 123. In vitro, ioflupane binds reversibly to the human recombinant dopamine transporter (DaT) [Kd = 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 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 DaTscan 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 DaTscan 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 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 DaTscan; 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 DaTscan were evaluated in two multicenter, single-arm studies (Study 1 and Study 2) that evaluated 284 adult patients with tremor. In the studies, DaTscan images were evaluated by readers blinded to clinical information. To assess the carcinogenic potential of ioflupane, studies to assess the carcinogenic potential of ioflupane have not been performed.

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%), 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 (13%), MSA (10%), and PSP (5%).

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

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

<table>
<thead>
<tr>
<th>Study 1 (patients with early signs and/or symptoms of PS)</th>
<th>Positive percent agreement (95% CI) (% patients with an abnormal DaTscan image among patients with PS)</th>
<th>Negative percent agreement (95% CI) (% patients with a normal DaTscan image among patients with non-PS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reader A, n = 99</td>
<td>77 (66, 87)</td>
<td>96 (82, 100)</td>
</tr>
<tr>
<td>Reader B, n = 96</td>
<td>78 (66, 87)</td>
<td>96 (82, 100)</td>
</tr>
<tr>
<td>Reader C, n = 98</td>
<td>79 (67, 87)</td>
<td>96 (82, 100)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study 2 (patients with established diagnoses of PS or ET)</th>
<th>Positive percent agreement (95% CI) (% patients with an abnormal DaTscan image among patients with PS)</th>
<th>Negative percent agreement (95% CI) (% patients with a normal DaTscan image among patients with non-PS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reader A, n = 185</td>
<td>93 (88, 97)</td>
<td>96 (81, 100)</td>
</tr>
<tr>
<td>Reader B, n = 185</td>
<td>97 (93, 99)</td>
<td>74 (54, 89)</td>
</tr>
<tr>
<td>Reader C, n = 185</td>
<td>96 (92, 99)</td>
<td>85 (66, 96)</td>
</tr>
<tr>
<td>Reader D, n = 185</td>
<td>92 (87, 96)</td>
<td>93 (76, 99)</td>
</tr>
<tr>
<td>Reader E, n = 185</td>
<td>94 (90, 97)</td>
<td>93 (76, 99)</td>
</tr>
</tbody>
</table>

The effectiveness of DaTscan 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

DaTscan is supplied in 10-mL glass vials containing a total volume of 2.5 mL of solution with a total radioactivity of 185 MBq (5 mCi) at calibration time. Each vial is enclosed in a lead container of appropriate thickness.

Storage

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

Do not use DaTscan (Ioflupane I 123 injection) preparations after the expiration date and time stated on the label.

Handling

This preparation is approved for use by persons licensed by the Illinois Emergency Management Agency pursuant to 32 IL. Adm. Code Section 330.260(a) and 335.4010 or equivalent licenses of the Nuclear Regulatory Commission or an Agreement State.

17 PATIENT COUNSELING INFORMATION

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

1. have decreased renal or hepatic function.
2. are sensitive to DaTscan.
3. are sensitive to Potassium Iodide Oral Solution or Lugol’s Solution.
4. may be pregnant, are trying to become pregnant, or are breast feeding.

Instruct patients to increase their level of hydration prior to and after receiving DaTscan and to void frequently for the first 4 hours following DaTscan administration.