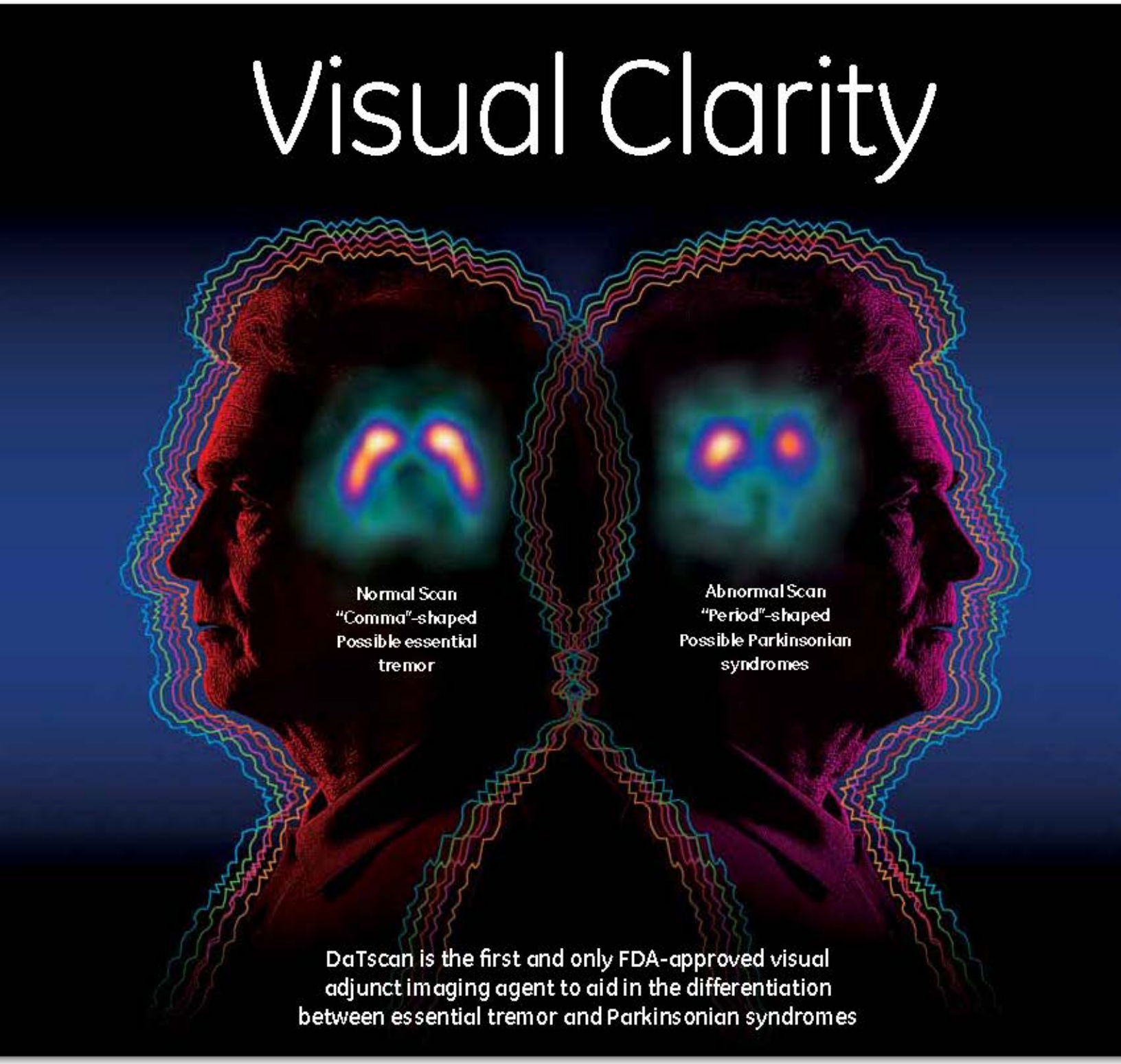
GE Healthcare

Visual Clarity



DaTscan is the first and only FDA-approved visual adjunct imaging agent to aid in the differentiation between essential tremor and Parkinsonian syndromes

Scans do not represent actual orientation within the patient's head.

NEW

DaTscan™ (II)

Ioflupane I 123 Injection

See the Difference

Differentiate With Visual Clarity

Visualization of dopamine transporter (DaT) distribution within the striatum can aid in the clinical diagnosis of Parkinsonian syndromes (PS)[1]

The diagnostic challenge: differentiating between PS and essential tremor (ET)

- Signs and symptoms of PS can be misleading or mimic other conditions, especially during early stages of disease and in the elderly[2-4]

Single photon emission computerized tomography (SPECT) images with DaTscan may provide a reliable assessment of striatal DaT receptor distribution

- DaTscan™ (Ioflupane I 123 Injection) is a radiopharmaceutical indicated for striatal dopamine transporter visualization using SPECT brain imaging to assist in the evaluation of adult patients with suspected PS[5]

DaTscan may be used as an adjunct to other diagnostic evaluations to help differentiate essential tremor from tremor due to PS, including[5]:

Idiopathic Parkinson's disease (PD)

Multiple system atrophy (MSA)

Progressive supranuclear palsy (PSP)

- These three conditions have been associated with dopaminergic neurodegeneration
- 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
- Differentiation of a disease such as idiopathic PD from a condition with similar symptoms (ET) may help improve disease management[1,6,7]

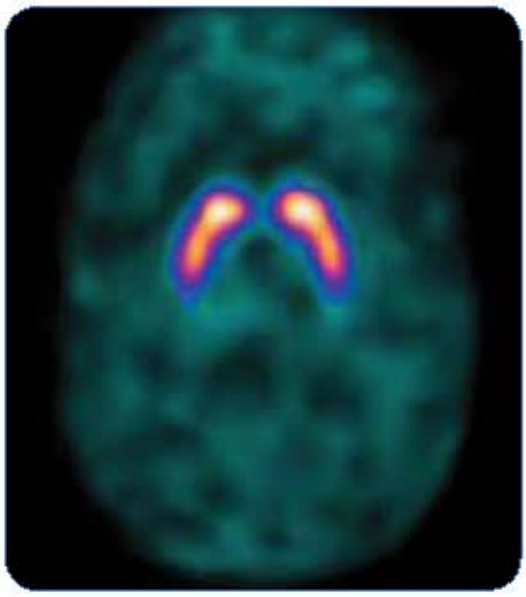
Important Risk and Safety Information About DaTscan

DaTscan is a DEA Schedule II controlled substance. A DEA license is required for handling or administering this controlled substance. **CONTRAINDICATIONS:** DaTscan is contraindicated in patients with known hypersensitivity to the active substance, any of the excipients, or iodine.

DaTscan Reveals the Difference

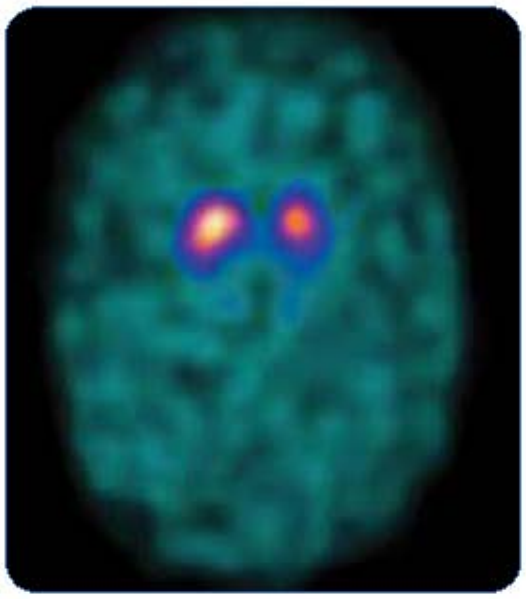
Differentiation between normal and abnormal scans is assessed by the extent (as indicated by shape) and intensity of the striatal signal following DaTscan administration[5,8-9]

Normal Scan —
Possible essential tremor



DaTscan will be distributed in the striata and appear as mirrored "comma" or crescent shapes if dopaminergic neurons are intact or not affected[5,10]

Abnormal Scan —
Possible Parkinsonian syndromes



A decrease in DaTscan activity will result in a circular "period" or oval shape(s) and reduced image intensity on one or both sides[5,10]

Important Risk and Safety Information About DaTscan

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 upon DaTscan imaging results has not been established. **Please see Important Risk and Safety Information on page 14 and Full Prescribing Information enclosed.**

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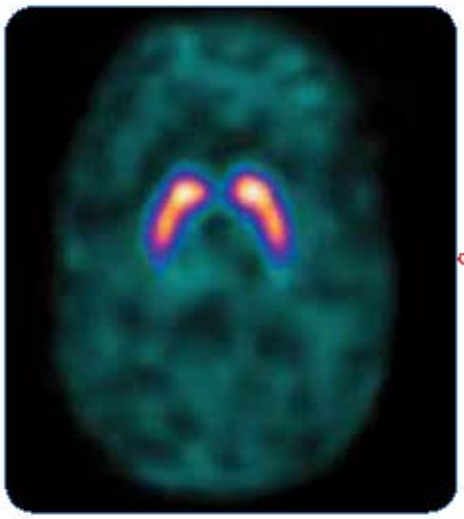
Image Interpretation With DaTscan

The uptake of DaTscan indicates either a normal "comma" scan, indicative of possible essential tremor, or an abnormal "period" scan, indicative of possible Parkinsonian syndromes

Example of normal "comma"-shaped scan[5]:



- In transaxial images, normal images are characterized by **two symmetric comma- or crescent-shaped focal regions** of activity mirrored about the median plane. Striatal activity is distinct, relative to surrounding brain tissue

Image interpretation with DaTscan[5]

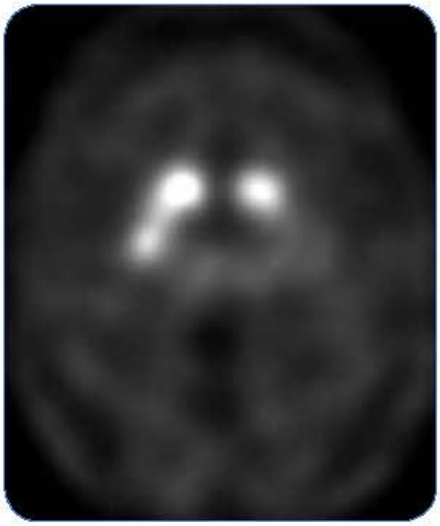
DaTscan images are interpreted visually, based upon the appearance of the striata. Determination of whether an image is normal or abnormal is made by assessing the extent (as indicated by shape) and intensity of the striatal signal. Image interpretation does not involve integration of the striatal image appearance with clinical signs and/or symptoms.

Important Risk and Safety Information About DaTscan

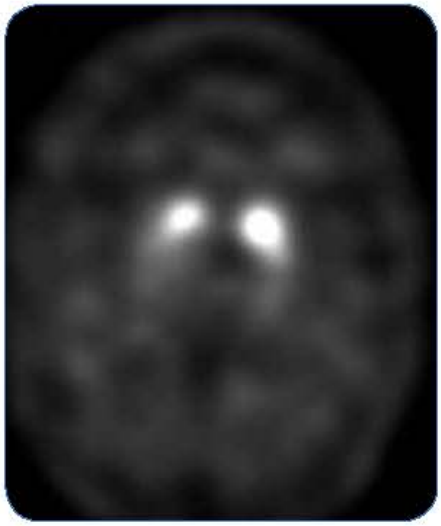
INDICATIONS AND USAGE: DaTscan is a radiopharmaceutical indicated for striatal dopamine transporter visualization using single photon emission computed tomography (SPECT) brain imaging to assist in the evaluation of adult patients with suspected Parkinsonian syndromes (PS). DaTscan may be used to help 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.

Three Distinct Abnormal Images With DaTscan[5]

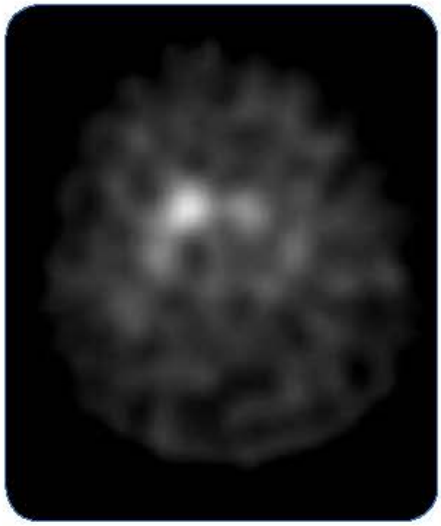
Abnormal "period" scans fall into at least one of the following three categories (all are considered abnormal)



Activity is **asymmetric**, eg, 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



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

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Reporting DaTscan Results

DaTscan results can be used as a visual adjunct to clinical evaluation by referring physicians, which may aid in the determination of patient treatment

In NDA clinical trials, DaTscan demonstrated agreement among readers[5]

- DaTscan images were evaluated by readers blinded to clinical information[5]

Positive and negative percent agreements for NDA studies 1 and 2[5]

	Positive percent agreement (95% CI) (% patients with an abnormal DaTscan image among patients with PS)	Negative percent agreement (95% CI) (% patients with a normal DaTscan image among patients with non-PS)
Study 1 (patients with early signs and/or symptoms of PS)		
Reader A, n = 99	77 (66, 87)	96 (82, 100)
Reader B, n = 96	78 (66, 87)	96 (82, 100)
Reader C, n = 98	79 (67, 87)	96 (82, 100)
Study 2 (patients with established diagnoses of PS or ET)		
Reader A, n = 185	93 (88, 97)	96 (81, 100)
Reader B, n = 185	97 (93, 99)	74 (54, 89)
Reader C, n = 185	96 (92, 99)	85 (66, 96)
Reader D, n = 185	92 (87, 96)	93 (76, 99)
Reader E, n = 185	94 (90, 97)	93 (76, 99)

Study Design[5]: Two multicenter, single-arm studies (Study 1 and Study 2) evaluated 284 adult patients with tremor. DaTscan image outcomes were compared to a reference clinical diagnostic standard of "PS" or "non-PS." The reference clinical diagnostic standard for "PS" was diagnoses for PD, MSA, and PSP. The reference clinical diagnostic standard for "non-PS" was an ET diagnosis or other non-PS diagnosis. Study 1 consisted of patients with early features of Parkinsonism; patients with features suggestive of MSA or PSP were excluded. Study 2 consisted of patients with clinically established diagnosis of PS (PD, MSA, PSP) or ET.

DaTscan images were evaluated by readers blinded to clinical information. Study 1 readers had no other role in patient assessment; Study 2 readers included site investigators. The reference clinical diagnostic standards were the clinical diagnoses established by a consensus panel of movement disorder specialists that evaluated data inclusive through 36 months of follow-up (Study 1) or the investigator-determined baseline clinical diagnosis (Study 2).

Among the 99 patients in Study 1, 44% were female, 42% were aged 65 or over, and all were Caucasian; among the 185 patients in Study 2, 35% were female, 48% were aged 65 or over, and 99% were Caucasian. Among the patients in Study 1, the baseline clinical diagnoses consisted of: probable PD (44%), possible PD (31%), "benign" PD (6%), possible ET (11%), and other diagnoses (7%). Among the patients in Study 2, the baseline clinical diagnoses consisted of: PD (70%), ET (15%), MSA (10%), and PSP (5%).

Important Risk and Safety Information About DaTscan

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 upon DaTscan imaging results has not been established.

Patient Preparation Steps

Helping patients prepare for the SPECT process with DaTscan

1 Prior to administering DaTscan, review current medications to determine possible drug interactions

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

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

4 Thyroid-blocking agent administered at least one hour before DaTscan administration

5 Patient will receive DaTscan via slow intravenous injection and wait three to six hours before SPECT imaging

DaTscan™ Ioflupane I 123 Injection

6 Patient will lie still for an approximately 30-minute SPECT procedure

7 Patient will be instructed 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 pruritis. Injection site pain also has been reported.

Please see Important Risk and Safety Information on page 14 and Full Prescribing Information enclosed.

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Optimal Patient Positioning and Camera Setup for DaTscan

Patient positioning is critical to acquiring interpretable images with DaTscan

Proper head tilt:
A lateral head tilt may make a normal image appear abnormal. Always use a headrest to help avoid abnormal images[5]

Subject with no tilt

Subject with lateral tilt

- **Small camera radius:** Place the camera as close to the patient's head as physically possible without touching. The best image resolution occurs with a radius of rotation of 11-15 cm; the ideal radius is 13 cm[5]
- **Minimal patient motion:** Decrease excess motion with head, arm, and leg straps

Each SPECT camera requires its own specific setup parameters for acquiring DaTscan images

- Specific camera parameters available at **www.datscan.com**

Recommended camera acquisition parameters

- High-resolution or fan beam collimator
- 159 KeV ±10% energy window (20% total window width)
- Matrix size 128 x 128
- Double- or triple-head SPECT gamma camera
  - Triple-head camera – 45 sec/frame
  - Double-head camera – 30 sec/frame
- Circular 360° orbit
- Camera radius of 11-15 cm; 13 cm is ideal
- Minimum imaging time 30 minutes
- Minimum of 1.5 million counts required for optimal image quality
- Always image with DaTscan using the same camera parameters

DaTscan Dosing Protocol

To minimize thyroid uptake of radioactive iodine, administer a thyroid-blocking agent at least one hour prior to DaTscan injection[5]

Thyroid Blocking—Commonly Used Protocols[5]

- Potassium iodide/iodate
- Potassium perchlorate
- Lugol's Solution

Dosing Instructions

- The recommended adult dose is 3-5 mCi, administered intravenously[5]
- This dose must be measured using a suitable radioactivity calibration system immediately prior to administration[5]

Patient Counseling

Instruct patients to inform you if they[5]:

- Have reduced renal or hepatic function
- Are sensitive to DaTscan
- Are sensitive to Potassium Iodide Oral Solution or Lugol's Solution
- 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 48 hours following DaTscan administration.[5]

Important Risk and Safety Information About DaTscan

Radiation safety[5]: 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 14 and Full Prescribing Information enclosed.

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DaTscan Administration and Storage

DaTscan Administration

DaTscan should be administered via a slow intravenous (IV) injection in an arm vein (no less than 15-20 seconds)[5]

- Be sure the location of the IV will not interfere with positioning the patient for the scan
- SPECT imaging should be performed within three to six hours post-injection[5]
- It is recommended to keep imaging times post-injection as consistent as possible for all patient studies

DaTscan Storage

- Store DaTscan in its original lead container (or an equivalent radiation shielding) at 68°-77°F (20°-25°C) in a securely locked, substantially constructed cabinet [5,11]

DaTscan Safety Profile[5,12]

In NDA clinical studies in 942 patients, no serious adverse reactions were reported[5]

The most common mild-to-moderate adverse reactions[5]:

Headache | Nausea | Vertigo | Dry mouth | Dizziness

Occurrence rate

≤1%

- Radiation exposure less than most CT scans: 3.94 mSv[5,13]
- In the postmarketing experience, hypersensitivity reactions have been reported, generally consisting of skin erythema and pruritis. Injection site pain also has been reported

Worldwide clinical experience

DaTscan™ Ioflupane I 123 Injection

Used in Europe for >10 years[12]

Administered to >300,000 patients[12]

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. 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 14 and Full Prescribing Information enclosed.

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DaTscan™ Ioflupane I 123 Injection

See the Difference

DaTscan Centers of Excellence

In order for a department to become a DaTscan Imaging Center of Excellence, a GE Healthcare Clinical Applications Specialist must train department personnel on proper image acquisition and necessary license requirements. Before a department can order and handle DaTscan, a Schedule II radiopharmaceutical, the necessary licensing and storage facilities must be in place.

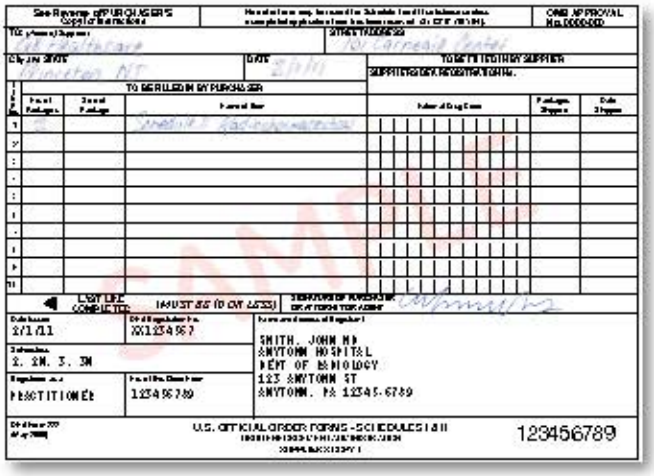
The following checklist summarizes the licensing requirements and GE Healthcare's shipping requirements for a Schedule II product:

☐ 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 Using DEA Form 222

- Schedule II radiopharmaceuticals like DaTscan must be ordered using DEA Form 222 (sample form on right)
- DaTscan can be ordered by:
  - Hospital Central Pharmacy
  - Nuclear Medicine Department



☐ Delivery and Storage

- Secure storage
  - Upon receipt, DaTscan must be stored in a securely locked, substantially constructed cabinet[11]
- Advance ordering
  - DaTscan must be ordered at least three business days in advance of planned administration to allow for Form 222 processing

Please call Medical Affairs at 800 654 0118 (option 2) to make an appointment with your GE Healthcare Clinical Applications Specialist to set up your department as a DaTscan Imaging Center of Excellence

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.

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 (option 4)

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

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

GE Healthcare Sales or Clinical Applications Specialist
To contact your local sales representative or Clinical Applications Specialist, call Medical Affairs at 800 654 0118 (option 2)

Local Radiopharmacy
To locate a radiopharmacy in your area, call 800 242 8004

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Important Risk and Safety Information About DaTscan

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). 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. **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 pruritis, 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 DaTscan administration. 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 upon DaTscan imaging results has not been established. **SPECIFIC POPULATIONS: Pregnancy:** It is unknown whether DaTscan can cause fetal harm or increase 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. Radioactive iodine products cross the placenta and can permanently impair fetal thyroid function. **Nursing Mothers:** It is unknown 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. 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 upon DaTscan imaging has not been established. DaTscan is excreted by the kidney; 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.

Prior to DaTscan administration, please see Full Prescribing Information enclosed.

References

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Visual Clarity With DaTscan

Become a DaTscan Imaging Center of Excellence

The DaTscan Readiness Initiative is a program designed to ensure that your first—and every—experience with DaTscan is a positive one.

As part of this initiative, a GE Healthcare Clinical Applications Specialist is ready to guide your lab through acquiring high-quality images with DaTscan—from start to finish.

To schedule your department's hands-on DaTscan tutorial with a GE Healthcare Clinical Applications Specialist, call Medical Affairs at 800 654 0118 (option 2).

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Go to www.datscan.com for more information

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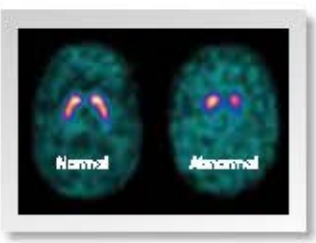
www.gehealthcare.com



NEW

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See the Difference

imagination at work

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