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# Frequently Asked Questions about Medicare Reimbursement for Positron Emission Tomography

Answers for life.

### 1) What has changed as a result of the final decision memorandum on Positron Emission Tomography (PET) for Solid Tumors (CAG-00191R4)?

From the Final Decision Memorandum on Positron Emission Tomography (PET) for Solid Tumors (CAG-00191R4)<sup>1</sup>:

The Centers for Medicare and Medicaid Services (CMS) issued a final decision memorandum on Positron Emission Tomography (PET) for Solid Tumors (CAG-00191R4), effective for claims with dates of service on and after June 11, 2013. This decision memorandum was in response to the request made by the National Oncologic PET Registry (NOPR) to lift the requirement for Coverage with Evidence Development (CED) on subsequent PET scans for oncologic purposes.<sup>1</sup>

There were three specific elements of this decision:

1. CMS is ending the requirement for CED for <sup>18</sup>F fludeoxyglucose\* (FDG) PET for oncologic indications. This removes the requirement for prospective data collection by the NOPR for those cancers or cancer types that had been covered under CED.
2. CMS has determined that three (3) FDG PET scans are nationally covered when used to guide subsequent management of anti-tumor treatment strategy after completion of initial anticancer therapy. Coverage of any additional FDG PET scans (beyond three) used to guide subsequent management of anti-tumor treatment strategy after completion of initial anti-tumor therapy will be determined by local Medicare Administrative Contractors.

3. CMS reviewed additional evidence for the use of FDG PET for patients with cancer of the prostate. CMS proposes that use of FDG PET is reasonable and necessary and will nationally cover FDG PET when used to guide subsequent anti-tumor treatment strategy of prostate cancer.

FDG PET is often performed using a device that combines FDG PET with other imaging modalities. CMS includes integrated FDG PET/computerized tomography (FDG PET/CT) and integrated FDG PET/magnetic resonance imaging (FDG PET/MRI) in the term FDG PET as used in the decision unless context indicates otherwise.<sup>1</sup>

\*Indication and important safety information can be found below for fludeoxyglucose F 18 (<sup>18</sup>F FDG) injection, adult dose 5-10 mCi, administered by intravenous injection.

### 2) What is now covered based on the final decision memorandum on Positron Emission Tomography (PET) for Solid Tumors (CAG-00191R4)?

Effective for claims with dates of service on and after June 11, 2013, the chart below from Appendix C of the Final Decision Memorandum on PET for Solid Tumors (CAG-00191R4)<sup>2</sup> summarizes national FDG PET coverage for oncologic conditions.

For initial treatment strategy, one (1) scan is nationally covered, and for subsequent treatment strategies three (3) scans are nationally covered by Medicare, with additional scans being covered at the discretion of the local Medicare Administrative Contractors.

## FLUDEOXYGLUCOSE F 18 INJECTION

### INDICATIONS AND USAGE

Fludeoxyglucose F 18 injection (<sup>18</sup>F FDG) is indicated for positron emission tomography (PET) imaging in the following setting:

**Oncology:** For assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.

### IMPORTANT SAFETY INFORMATION

#### Radiation Risks

Radiation-emitting products, including fludeoxyglucose F 18 injection, may increase the risk for cancer, especially in pediatric patients. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker.

### Blood Glucose Abnormalities

In the oncology and neurology setting, suboptimal imaging may occur in patients with inadequately regulated blood glucose levels. In these patients, consider medical therapy and laboratory testing to assure at least two days of normoglycemia prior to fludeoxyglucose F18 injection administration.

### Adverse Reactions

Hypersensitivity reactions with pruritus, edema and rash have been reported; have emergency resuscitation equipment and personnel immediately available.

Full Prescribing Information for Fludeoxyglucose F 18 Injection can be found on page 10.

Fludeoxyglucose F 18 injection is manufactured by Siemens' PETNET Solutions, 810 Innovation Drive, Knoxville, TN 39732

Tumor Type	Initial Treatment Strategy (formerly "diagnosis" and "staging")	Subsequent Treatment Strategy (formerly "restaging" and "monitoring response to treatment")
All solid tumors not listed below	Covered	Covered
All cancers not listed below	Covered	Covered
Cervix	Covered with exceptions*	Covered
Prostate	Not covered	Covered
Breast (male and female)	Covered with exceptions*	Covered
Melanoma	Covered with exceptions*	Covered
Lung*	Covered	Covered

\*Cervix: Nationally non-covered for the initial diagnosis of cervical cancer related to initial anti-tumor treatment strategy. All other indications for initial anti-tumor treatment strategy for cervical cancer are nationally covered.

\*Breast: Nationally non-covered for initial diagnosis and/or staging of axillary lymph nodes. Nationally covered for initial staging of metastatic disease. All other indications for initial anti-tumor treatment strategy for breast cancer are nationally covered.

\*Melanoma: Nationally non-covered for initial staging of regional lymph nodes. All other indications for initial anti-tumor treatment strategy for melanoma are nationally covered.

\*Lung: Includes solitary pulmonary nodule (SPN).

### 3) What codes are used for billing <sup>18</sup>F FDG oncologic PET procedures?

The codes on the following tables are to be used to bill Medicare Part B, including hospital outpatient services paid under HOPPS (APC) and non-hospital outpatient services provided in a physician practice or IDTF paid under the Physician Fee Schedule (PFS).

To bill Medicare for PET- and PET/CT-covered procedures, providers should use the appropriate CPT® code based on the code description. The table below taken from the Medicare Claims Processing Manual revised July 2007<sup>3</sup> contains a complete listing of CPT codes for covered indications.

CPT Codes	Procedure Description
78459	Myocardial imaging, PET; metabolic evaluation
78491	Myocardial imaging, PET; perfusion; single study, at rest or stress
78492	Myocardial imaging, PET; perfusion; multiple studies, at rest &/or stress
78608	Brain imaging (PET); metabolic evaluation
78609*	Brain imaging (PET); perfusion evaluation*
78811	PET imaging; limited area (e.g., chest, head/neck)
78812	PET imaging; skull base to mid thigh
78813	PET imaging; whole body
78814	PET/CT imaging; limited area (e.g., chest, head/neck)
78815	PET/CT imaging; skull base to mid thigh
78816	PET/CT imaging; whole body

\*Not covered by Medicare.



#### 4) What is initial treatment strategy?

Initial treatment strategy includes diagnosis and initial staging.

CMS covers, with certain limitations for melanoma, breast and cervical cancers (see table on page 3), one FDG PET study, per patient per cancer type, for initial treatment strategy for all cancers (except prostate cancer, which is not covered) that are biopsy proven or strongly suspected based on other diagnostic testing when the beneficiary's treating physician determines that the FDG PET study is needed to determine the location and/or extent of the tumor for the following therapeutic purposes related to the initial treatment strategy:

- To determine whether or not the beneficiary is an appropriate candidate for an invasive diagnostic or therapeutic procedure; or,
- To determine the optimal anatomic location for an invasive procedure; or,
- To determine the anatomic extent of tumor when the recommended anti-tumor treatment reasonably depends on the extent of the tumor

Local Medicare Administrative Contractors have the discretion to cover or not cover within their jurisdictions

any additional FDG PET scans for initial treatment strategy as described above.<sup>4</sup>

#### 5) What is subsequent treatment strategy?

Subsequent treatment strategy includes monitoring tumor response to treatment during a planned course of therapy when a change in treatment is being considered and restaging after the completion of treatment to detect residual disease, or to detect suspected recurrence or to assess the extent of a known recurrence.

CMS nationally covers three FDG PET scans when used to guide subsequent management of anti-tumor treatment strategy after completion of initial anti-tumor therapy. Coverage of more than three FDG PET scans to guide subsequent management of anti-tumor treatment strategy after completion of initial anti-tumor therapy shall be determined by the local Medicare Administrative Contractors.<sup>2</sup>

#### 6) How do I identify a scan for initial treatment strategy or subsequent treatment strategy on my claim form?

Taken from the Medicare Claims Processing Manual revised July 2007<sup>5</sup>:

Effective for claims with dates of service on or after April 3, 2009, the following modifiers have been created for use to inform for the initial treatment strategy of biopsy-proven or strongly suspected tumors or subsequent treatment strategy of cancerous tumors:

**PI** – Positron Emission Tomography (PET) or PET/Computed Tomography (CT) to inform the initial treatment strategy of tumors that are biopsy proven or strongly suspected of being cancerous based on other diagnostic testing.

Short descriptor: PET tumor init tx strat

**PS** – Positron Emission Tomography (PET) or PET/Computed Tomography (CT) to inform the subsequent treatment strategy of cancerous tumors when the beneficiary's treatment physician determines that the PET study is needed to inform subsequent anti-tumor strategy.

Short descriptor: PS - PET tumor subseq tx strategy.

The transmittals can be found on the following Internet pages:

<http://www.cms.hhs.gov/transmittals/downloads/R1833CP.pdf>

<http://www.cms.hhs.gov/transmittals/downloads/R108NCD.pdf>

### 7) What is covered by Medicare for Sodium Fluoride F 18 (<sup>18</sup>F NaF) PET?

On February 26, 2010, CMS announced coverage for sodium fluoride F 18\* (<sup>18</sup>F NaF) PET imaging under Coverage with Evidence Development (CED) to: "assist initial antitumor treatment planning or to guide subsequent treatment strategy by the identification, location and quantification of bone metastases in beneficiaries in whom bone metastases

are strongly suspected based on clinical symptoms or the results of other diagnostic studies."<sup>6</sup>

Almost a year later, on February 7, 2011, the National Oncologic PET Registry (NOPR) began enrolling patients for <sup>18</sup>F NaF Bone PET studies and CMS began reimbursing <sup>18</sup>F NaF PET scans when the beneficiary is enrolled in, and the <sup>18</sup>F NaF PET provider and treating physician are participating in, the NOPR clinical study.

For more information, visit the NOPR website: [www.cancerpetregistry.org](http://www.cancerpetregistry.org)

\*Indication and important safety information can be found below for sodium fluoride F 18 (<sup>18</sup>F NaF) injection, adult dose 8-12 mCi, administered by intravenous injection.

### 8) How does the closing of <sup>18</sup>F FDG PET data collection impact NaF-NOPR?

CMS issued a final decision memorandum in June 2013, which called for the end of the prospective data collection requirements under CED for all oncologic indications for <sup>18</sup>F FDG PET. Please note that this decision applies to the <sup>18</sup>F FDG PET registry (NOPR-2009) only. Effective June 12, 2013, the NOPR-2009 registry will no longer accept new case registrations.

The sodium fluoride F 18 injection (<sup>18</sup>F NaF PET) registry will remain open. PET facilities that wish to continue participating in the <sup>18</sup>F NaF PET registry (or to begin participating) can continue to do so.

Check for updated information on the NOPR website at: <http://www.cancerpetregistry.org/index.htm>

## SODIUM FLUORIDE F 18 INJECTION

For Intravenous Use

### INDICATIONS AND USAGE

Sodium Fluoride F 18 Injection is a radioactive diagnostic agent for positron emission tomography (PET) indicated for imaging of bone to define areas of altered osteogenic activity.

### IMPORTANT SAFETY INFORMATION

- **Allergic Reactions:** As with any injectable drug product, allergic reactions and anaphylaxis may occur. Emergency resuscitation equipment and personnel should be immediately available.

- **Cancer Risk:** Sodium Fluoride F 18 Injection may increase the risk of cancer. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker.

### ADVERSE REACTIONS

No adverse reactions have been reported for Sodium Fluoride F 18 Injection based on a review of the published literature, publicly available reference sources, and adverse drug reaction reporting system.

Full Prescribing Information for Sodium Fluoride F 18 Injection can be found on page 18.

Sodium Fluoride F 18 injection is manufactured by Siemens' PETNET Solutions, 810 Innovation Drive, Knoxville, TN 39732

### 9) What codes and modifiers apply to billing <sup>18</sup>F NaF scans?

Taken from Medicare Claims Processing Manual revised July 2007<sup>7</sup>:

Medicare covered PET procedures for bone scans should be reported using CPT<sup>®</sup> codes as well as the applicable Healthcare Procedure Coding System (HCPCS) Level II code for the radiopharmaceutical. According to CMS, effective for claims with dates of service on or after February 26, 2010, contractors shall accept PET oncologic claims billed with modifier 26 and modifier KX to inform the initial treatment strategy or strategy or subsequent treatment strategy for bone metastasis that include the following:

- PI or PS modifier AND
- PET or PET/CT CPT code (78811, 78812, 78813, 78814, 78815, 78816) AND
- ICD-9 cancer diagnosis code AND
- Q0 modifier – Investigational clinical service provided in a clinical research study, are present on the claim.

#### NOTE:

1. If modifier KX is present on the professional component service, Contractors shall process the service as <sup>18</sup>F NaF PET rather than <sup>18</sup>F FDG PET.
2. Contractors shall also return as unprocessable <sup>18</sup>F NaF PET oncologic professional component claims (e.g., claims billed with modifiers 26 and KX).

### 10) What are the NDC numbers for <sup>18</sup>F FDG, <sup>18</sup>F NaF and <sup>13</sup>N NH<sub>3</sub>?

The National Drug Code (NDC) is a unique 10-digit, 3-segment numeric identifier assigned to each medication listed under Section 510 of the US Federal Food, Drug, and Cosmetic Act. The segments identify the labeler or vendor, product (within the scope of the labeler), and trade package (of this product).<sup>8</sup>

The NDC number for sodium fluoride F 18 injection is 40028-512-30

The NDC number for fludeoxyglucose F 18 injection 30 ml vial is 40028-511-30

The NDC number for fludeoxyglucose F 18 injection 50 ml vial is 40028-511-50

The NDC number for ammonia N 13 injection is 40028-513-30

NDC listings may be found at the following Internet page: <http://www.accessdata.fda.gov/scripts/cder/ndc/packagecode.cfm>

### 11) What codes are used for billing radiopharmaceuticals?

The chart below is taken from Medicare Claims Processing Manual revised July 2007<sup>9</sup>:

HCPCS Codes	Procedure Description
A9552	<sup>18</sup> F FDG, diagnostic, per study dose
A9555	<sup>82</sup> Rb Rubidium, diagnostic, per study dose
A9526	<sup>13</sup> N Ammonia,* diagnostic, per study dose
A9580	<sup>18</sup> F Sodium Fluoride, diagnostic, per study dose

\*Indication and important safety information can be found on page 8 for ammonia N 13 (<sup>13</sup>N NH<sub>3</sub>) injection, adult dose 10-20 mCi, administered by intravenous injection.

### 12) Who is responsible for determining and documenting medical necessity?

The referring physician is responsible for determining and documenting medical necessity. Documentation that qualifying conditions are met should be maintained by the referring physician in the beneficiary's medical record, as is normal business practice. Information may be needed from the referring physician to support insurer reimbursement for the procedure and ensure that certain conditions detailed in Medicare's National Coverage Determination for PET are met.<sup>10</sup>

### 13) What is covered by Medicare for neurology with FDG?

PET's ability to measure cerebral metabolism and blood flow makes it valuable in certain neurological applications, such as refractory epilepsy.

#### Refractory Seizures

Since July 1, 2001, Medicare covers FDG PET for the pre-surgery evaluation for the purpose of localization of a focus of refractory seizure activity.<sup>9</sup>

- 78608 – Brain imaging, PET, metabolic evaluation for pre-surgical evaluation of refractory seizure
- A9552 – Fluorodeoxyglucose F18, FDG, diagnostic, per study dose

#### Brain Tumor

Brain tumors are covered under the decision memorandum on PET for Solid Tumors (see FAQ 2).<sup>2,9</sup>

- 78608 – Brain imaging, PET, metabolic evaluation for brain tumor
- A9552 – Fluorodeoxyglucose F18, FDG, diagnostic, per study dose

## 14) What is covered by Medicare for cardiology?

### Myocardial Viability with <sup>18</sup>F FDG

The information below is taken from Medicare National Coverage Determinations Manual<sup>13</sup>:

The identification of patients with partial loss of heart muscle movement or hibernating myocardium is important in selecting candidates with compromised ventricular function to determine appropriateness for revascularization. Diagnostic tests such as FDG PET distinguish between dysfunctional but viable myocardial tissue and scar tissue in order to affect management decisions in patients with ischemic cardiomyopathy and left ventricular dysfunction.

Medicare covers FDG PET for the determination of myocardial viability as a primary or initial diagnostic study prior to revascularization, or following an inconclusive SPECT.

Limitations: In the event a patient receives a SPECT test with inconclusive results, a PET scan may be covered. However, if a patient receives a FDG PET study with inconclusive results, a follow up SPECT test is not covered.

Documentation that these conditions are met should be maintained by the referring physician in the beneficiary's medical record, as is normal business practice.<sup>13</sup>

Medicare covers FDG PET to assess myocardial viability following an inconclusive SPECT or as a primary or initial diagnostic study prior to revascularization.<sup>9</sup>

- 78459 – Myocardial imaging, PET, metabolic evaluation
- A9552 – <sup>18</sup>F FDG, per dose

### Myocardial Perfusion Imaging with <sup>82</sup>Rubidium

The information below is taken from Medicare National Coverage Determinations Manual<sup>14</sup>:

Effective for services performed on or after March 14, 1995, PET scans performed at rest or with pharmacological stress used for noninvasive imaging of the perfusion of the heart for the diagnosis and management of patients with known or suspected coronary artery disease using the FDA-approved radiopharmaceutical Rubidium 82 (Rb 82) are covered, provided the requirements below are met:

- The PET scan, whether at rest alone, or rest with stress, is performed in place of, but not in addition to, a single photon emission computed tomography (SPECT); or
- The PET scan, whether at rest alone or rest with stress, is used following a SPECT that was found to be inconclusive. In these cases, the PET scan must have been considered necessary in order to determine what medical or surgical intervention is required to treat the patient. (For purposes of this requirement, an inconclusive test is a test(s) whose results are equivocal, technically uninterpretable, or discordant with a patient's other clinical data and must be documented in the beneficiary's file.)

- For any PET scan for which Medicare payment is claimed for dates of services prior to July 1, 2001, the claimant must submit additional specified information on the claim form (including proper codes and/or modifiers), to indicate the results of the PET scan. The claimant must also include information on whether the PET scan was performed after an inconclusive noninvasive cardiac test. The information submitted with respect to the previous noninvasive cardiac test must specify the type of test performed prior to the PET scan and whether it was inconclusive or unsatisfactory. These explanations are in the form of special G codes used for billing PET scans using Rb 82. Beginning July 1, 2001, claims should be submitted with the appropriate codes.

### Myocardial Perfusion Imaging with <sup>13</sup>N Ammonia

The information below is taken from Medicare National Coverage Determinations Manual<sup>14</sup>:

Effective for services performed on or after October 1, 2003, PET scans performed at rest or with pharmacological stress used for noninvasive imaging of the perfusion of the heart for the diagnosis and management of patients with known or suspected coronary artery disease using the FDA-approved radiopharmaceutical ammonia N-13 are covered, provided the requirements below are met:

- The PET scan, whether at rest alone, or rest with stress, is performed in place of, but not in addition to, a SPECT; or
- The PET scan, whether at rest alone or rest with stress, is used following a SPECT that was found to be inconclusive. In these cases, the PET scan must have been considered necessary in order to determine what medical or surgical intervention is required to treat the patient. (For purposes of this requirement, an inconclusive test is a test whose results are equivocal, technically uninterpretable, or discordant with a patient's other clinical data and must be documented in the beneficiary's file.)<sup>14</sup>

Medicare covers PET exams to assess myocardial perfusion in place of, but not in addition to SPECT or following an inconclusive SPECT.<sup>9</sup>

- 78491 – Myocardial imaging, PET, perfusion; single study at rest or stress
- 78492 – Myocardial imaging, PET, perfusion; multiple studies at rest or stress
- A9555 – <sup>82</sup>Rubidium, diagnostic, per study dose, up to 60 millicuries
- A9526 – <sup>13</sup>N Ammonia, diagnostic, per study dose, up to 40 millicuries

## **AMMONIA N 13 INJECTION**

### **INDICATIONS AND USAGE**

Ammonia N 13 Injection is a radioactive diagnostic agent for Positron Emission Tomography (PET) indicated for diagnostic PET imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease.

### **IMPORTANT SAFETY INFORMATION**

Ammonia N 13 Injection may increase the risk of cancer. Use the smallest dose necessary for imaging and ensure

safe handling to protect the patient and health care worker.

### **ADVERSE REACTIONS**

No adverse reactions have been reported for Ammonia N 13 Injection based on a review of the published literature, publicly available reference sources, and adverse drug reaction reporting system.

Full Prescribing Information for Ammonia N 13 Injection can be found on page 24

Ammonia N 13 Injection is manufactured by Siemens' PETNET Solutions, 810 Innovation Drive, Knoxville, TN 39732

## Disclaimers

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## References:

1. Final Decision Memorandum on Positron Emission Tomography (PET) for Solid Tumors (CAG-00191R4)  
<http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=263>
2. Appendix C of the Final Decision Memorandum on Positron Emission Tomography (PET) for Solid Tumors (CAG-00191R4)  
<http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=263>
3. Medicare Claims Processing Manual revised July 2007, Chapter 13, Section 60.3.1 Appropriate CPT Codes Effective for PET Scans for Services Performed on or After January 28, 2005 (Rev. 1301, Issued: 07-20-07, Effective: 01-28-05 CPT Code 78609/01-01-08 HCPCS Code A4641, Implementation: 01-07-08)  
<http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/clm104c13.pdf>
4. Transmittal 120.  
<http://www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/downloads/R120NCD.pdf>
5. Medicare Claims Processing Manual revised July 2007, Chapter 13, Section 60.16 Billing and Coding for PET Scans Effective for Services on or After April 3, 2009. (Rev. 1888, Issued: 01-06-10, Effective: 11-10-09, Implementation: 01-04-10)  
<http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/clm104c13.pdf>
6. Medicare National Coverage Determinations Manual Chapter 1, Part 4 Section 220.6.19 Positron Emission Tomography (NaF-18 PET) to Identify Bone Metastases of Cancer (Effective February 26, 2010) (Rev. 119, Issued 03-26-10, Effective 02-26-10, Implementation 07-06-10)  
[http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1\\_part4.pdf](http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1_part4.pdf)
7. Medicare Claims Processing Manual revised July 2007, Chapter 13, Section 60.18 Billing and Coverage Changes for PET (NaF-18) Scans to Identify Bone Metastases of Cancer Effective for Claims with Dates of Services on or After February 26, 2010 (Rev. 2096, Issued: 11-19-10, Effective: 02-26-10, Implementation: 02-22-11)  
<http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/clm104c13.pdf>
8. National Drug Code Directory. US Food and Drug Administration  
<http://www.accessdata.fda.gov/scripts/cder/ndc/packagecode.cfm>
9. Medicare Claims Processing Manual revised July 2007, Chapter 13, Section 60.3.2 Tracer Codes Required for PET Scans. (Rev. 2096, Issued: 11-19-10, Effective: 02-26-10, Implementation: 02-22-11) can be found at: <http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/clm104c13.pdf>
10. Medicare National Coverage Determinations Manual Chapter 1, Part 4 (Section 220.6 Positron Emission Tomography) (Rev. 154, 06-10-13)  
[http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1\\_part4.pdf](http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1_part4.pdf)
11. Medicare National Coverage Determinations Manual Chapter 1, Part 4 Section 220.6.13 FDG PET for Dementia and Neurodegenerative Diseases (Effective September 15, 2004) (Rev. 120; Issued: 05-06-10; Effective Date: 04-03-09; Implementation Date: 10-30-09)  
[http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1\\_part4.pdf](http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1_part4.pdf)
12. Medicare Claims Processing Manual revised July 2007, Chapter 13, Section 60.12 Coverage for PET Scans for Dementia and Neurodegenerative Diseases. (Rev. 956, Issued: 05-19-06, Effective: 01-28-05, Implementation: 06-19-06) can be found at: <http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/clm104c13.pdf>
13. Medicare National Coverage Determinations Manual Chapter 1, Part 4 (Section 220.6.8 FDG PET for Myocardial Viability (Various Effective Dates) (Rev. 31; Issued: 04-04-05; Effective Date: 01-28-05; Implementation Date: 04-18-05)  
[http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1\\_part4.pdf](http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1_part4.pdf)
14. Medicare National Coverage Determinations Manual Chapter 1, Part 4 (Section 220.6.1 PET for Perfusion of the Heart (Various Effective Dates) (Rev. 120; Issued: 05-06-10; Effective Date: 04-03-09; Implementation Date: 10-30-09)  
[http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1\\_part4.pdf](http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/ncd103c1_part4.pdf)

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Fludeoxyglucose F 18 Injection safely and effectively. See full prescribing information for Fludeoxyglucose F 18 Injection.

### Fludeoxyglucose F 18 Injection, USP

For intravenous use

Initial U.S. Approval: 2005

#### -----RECENT MAJOR CHANGES-----

Warnings and Precautions (5.1, 5.2) 7/2010  
Adverse Reactions (6) 7/2010

#### -----INDICATIONS AND USAGE-----

Fludeoxyglucose F18 Injection is indicated for positron emission tomography (PET) imaging in the following settings:

- Oncology: For assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.
- Cardiology: For the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.
- Neurology: For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures (1).

#### -----DOSAGE AND ADMINISTRATION-----

Fludeoxyglucose F18 Injection emits radiation. Use procedures to minimize radiation exposure. Screen for blood glucose abnormalities.

- In the oncology and neurology settings, instruct patients to fast for 4 to 6 hours prior to the drug's injection. Consider medical therapy and laboratory testing to assure at least two days of normoglycemia prior to the drug's administration (5.2).
- In the cardiology setting, administration of glucose-containing food or liquids (e.g., 50 to 75 grams) prior to the drug's injection facilitates localization of cardiac ischemia (2.3).

Aseptically withdraw Fludeoxyglucose F18 Injection from its container and administer by intravenous injection (2).

The recommended dose:

- for adults is 5 to 10 mCi (185 to 370 MBq), in all indicated clinical settings (2.1).
  - for pediatric patients is 2.6 mCi in the neurology setting (2.2).
- Initiate imaging within 40 minutes following drug injection; acquire static emission images 30 to 100 minutes from time of injection (2).

#### -----DOSAGE FORMS AND STRENGTHS-----

Multi-dose 30mL and 50mL glass vial containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL) Fludeoxyglucose F18 Injection and 4.5mg of sodium chloride with 0.1 to 0.5% w/w ethanol as a stabilizer (approximately 15 to 50 mL volume) for intravenous administration (3).

#### -----CONTRAINDICATIONS-----

None

#### -----WARNINGS AND PRECAUTIONS-----

- Radiation risks: use smallest dose necessary for imaging (5.1).
- Blood glucose abnormalities: may cause suboptimal imaging (5.2).

#### -----ADVERSE REACTIONS-----

Hypersensitivity reactions have occurred; have emergency resuscitation equipment and personnel immediately available (6).

**To report SUSPECTED ADVERSE REACTIONS, contact PETNET Solutions, Inc. at 877-473-8638 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

#### -----USE IN SPECIFIC POPULATIONS-----

- Pregnancy Category C: No human or animal data. Consider alternative diagnostics; use only if clearly needed (8.1).
- Nursing mothers: Use alternatives to breast feeding (e.g., stored breast milk or infant formula) for at least 10 half-lives of radioactive decay, if Fludeoxyglucose F 18 Injection is administered to a woman who is breast-feeding (8.3).
- Pediatric Use: Safety and effectiveness in pediatric patients have not been established in the oncology and cardiology settings (8.4).

#### See 17 for PATIENT COUNSELING INFORMATION

Revised: 1/2011

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Fludeoxyglucose F18 Injection is indicated for positron emission tomography (PET) imaging in the following settings:

#### 1.1 Oncology

For assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.

#### 1.2 Cardiology

For the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.

#### 1.3 Neurology

For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

### 2 DOSAGE AND ADMINISTRATION

Fludeoxyglucose F18 Injection emits radiation. Use procedures to minimize radiation exposure. Calculate the final dose from the end of synthesis (EOS) time using proper radioactive decay factors. Assay the final dose in a properly calibrated dose calibrator before administration to the patient [see Description (11.2)].

#### 2.1 Recommended Dose for Adults

Within the oncology, cardiology and neurology settings, the recommended dose for adults is 5 to 10 mCi (185 to 370 MBq) as an intravenous injection.

#### 2.2 Recommended Dose for Pediatric Patients

Within the neurology setting, the recommended dose for pediatric patients is 2.6 mCi, as an intravenous injection. The optimal dose adjustment on the basis of body size or weight has not been determined [see Use in Special Populations (8.4)].

#### 2.3 Patient Preparation

- To minimize the radiation absorbed dose to the bladder, encourage adequate hydration. Encourage the patient to drink water or other fluids (as tolerated) in the 4 hours before their PET study.
- Encourage the patient to void as soon as the imaging study is completed and as often as possible thereafter for at least one hour.
- Screen patients for clinically significant blood glucose abnormalities by obtaining a history and/or laboratory tests [see Warnings and Precautions (5.2)]. Prior to Fludeoxyglucose F 18 PET imaging in the oncology and neurology settings, instruct patient to fast for 4 to 6 hours prior to the drug's injection.
- In the cardiology setting, administration of glucose-containing food or liquids (e.g., 50 to 75 grams) prior to Fludeoxyglucose F 18 Injection facilitates localization of cardiac ischemia

## 2.4 Radiation Dosimetry

The estimated human absorbed radiation doses (rem/mCi) to a newborn (3.4 kg), 1-year old (9.8 kg), 5-year old (19 kg), 10-year old (32 kg), 15-year old (57 kg), and adult (70 kg) from intravenous administration of Fludeoxyglucose F 18 Injection are shown in Table 1. These estimates were calculated based on human<sup>2</sup> data and using the data published by the International Commission on Radiological Protection<sup>4</sup> for Fludeoxyglucose <sup>18</sup>F. The dosimetry data

show that there are slight variations in absorbed radiation dose for various organs in each of the age groups. These dissimilarities in absorbed radiation dose are due to developmental age variations (e.g., organ size, location, and overall metabolic rate for each age group). The identified critical organs (in descending order) across all age groups evaluated are the urinary bladder, heart, pancreas, spleen, and lungs.

**Table 1. Estimated Absorbed Radiation Doses (rem/mCi) After Intravenous Administration of Fludeoxyglucose F 18 Injection<sup>a</sup>**

Organ	Newborn (3.4 kg)	1-year old (9.8 kg)	5-year old (19 kg)	10-year old (32 kg)	15-year old (57 kg)	Adult (70 kg)
Bladder wall <sup>b</sup>	4.3	1.7	0.93	0.60	0.40	0.32
Heart wall	2.4	1.2	0.70	0.44	0.29	0.22
Pancreas	2.2	0.68	0.33	0.25	0.13	0.096
Spleen	2.2	0.84	0.46	0.29	0.19	0.14
Lungs	0.96	0.38	0.20	0.13	0.092	0.064
Kidneys	0.81	0.34	0.19	0.13	0.089	0.074
Ovaries	0.80	0.8	0.19	0.11	0.058	0.053
Uterus	0.79	0.35	0.19	0.12	0.076	0.062
LLI wall*	0.69	0.28	0.15	0.097	0.060	0.051
Liver	0.69	0.31	0.17	0.11	0.076	0.058
Gallbladder wall	0.69	0.26	0.14	0.093	0.059	0.049
Small intestine	0.68	0.29	0.15	0.096	0.060	0.047
ULI wall**	0.67	0.27	0.15	0.090	0.057	0.046
Stomach wall	0.65	0.27	0.14	0.089	0.057	0.047
Adrenals	0.65	0.28	0.15	0.095	0.061	0.048
Testes	0.64	0.27	0.14	0.085	0.052	0.041
Red marrow	0.62	0.26	0.14	0.089	0.057	0.047
Thymus	0.61	0.26	0.14	0.086	0.056	0.044
Thyroid	0.61	0.26	0.13	0.080	0.049	0.039
Muscle	0.58	0.25	0.13	0.078	0.049	0.039
Bone surface	0.57	0.24	0.12	0.079	0.052	0.041
Breast	0.54	0.22	0.11	0.068	0.043	0.034
Skin	0.49	0.20	0.10	0.060	0.037	0.030
Brain	0.29	0.13	0.09	0.078	0.072	0.070
Other tissues	0.59	0.25	0.13	0.083	0.052	0.042

<sup>a</sup> MIRDOSE 2 software was used to calculate the radiation absorbed dose. Assumptions on the biodistribution based on data from Gallagher et al.1 and Jones et al.2

<sup>b</sup> The dynamic bladder model with a uniform voiding frequency of 1.5 hours was used. \*LLI = lower large intestine; \*\*ULI = upper large intestine

## 2.5 Radiation Safety – Drug Handling

- Use waterproof gloves, effective radiation shielding, and appropriate safety measures when handling Fludeoxyglucose F18 Injection to avoid unnecessary radiation exposure to the patient, occupational workers, clinical personnel and other persons.
- Radiopharmaceuticals should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radionuclides, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.
- Calculate the final dose from the end of synthesis (EOS) time using proper radioactive decay factors. Assay the final dose in a properly calibrated dose calibrator before administration to the patient [see Description (11.2)].
- The dose of Fludeoxyglucose F18 used in a given patient should be minimized consistent with the objectives of the procedure, and the nature of the radiation detection devices employed.

## 2.6 Drug Preparation and Administration

- Calculate the necessary volume to administer based on calibration time and dose.
- Aseptically withdraw Fludeoxyglucose F18 Injection from its container.
- Inspect Fludeoxyglucose F18 Injection visually for particulate matter and discoloration before administration, whenever solution and container permit.
- Do not administer the drug if it contains particulate matter or discoloration; dispose of these unacceptable or unused preparations in a safe manner, in compliance with applicable regulations.
- Use Fludeoxyglucose F 18 Injection within 12 hours from the EOS.

## 2.7 Imaging Guidelines

- Initiate imaging within 40 minutes following Fludeoxyglucose F 18 Injection administration.
- Acquire static emission images 30 to 100 minutes from the time of injection.

## 3 DOSAGE FORMS AND STRENGTHS

Multiple-dose 30mL and 50mL glass vial containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL) of Fludeoxyglucose F 18 Injection and 4.5 mg of sodium chloride with 0.1 to 0.5% w/w ethanol as a stabilizer (approximately 15 to 50 mL volume) for intravenous administration.

## 4 CONTRAINDICATIONS

None

## 5 WARNINGS AND PRECAUTIONS

## 5.1 Radiation Risks

Radiation-emitting products, including Fludeoxyglucose F 18 Injection, may increase the risk for cancer, especially in pediatric patients. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker [see Dosage and Administration (2.5)].

## 5.2 Blood Glucose Abnormalities

In the oncology and neurology setting, suboptimal imaging may occur in patients with inadequately regulated blood glucose levels. In these patients, consider medical therapy and laboratory testing to assure at least two days of normoglycemia prior to Fludeoxyglucose F 18 Injection administration.

## 6 ADVERSE REACTIONS

Hypersensitivity reactions with pruritus, edema and rash have been reported in the post-marketing setting. Have emergency resuscitation equipment and personnel immediately available.

## 7 DRUG INTERACTIONS

The possibility of interactions of Fludeoxyglucose F 18 Injection with other drugs taken by patients undergoing PET imaging has not been studied.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### *Pregnancy Category C*

Animal reproduction studies have not been conducted with Fludeoxyglucose F 18 Injection. It is also not known whether Fludeoxyglucose F 18 Injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Consider alternative diagnostic tests in a pregnant woman; administer Fludeoxyglucose F 18 Injection only if clearly needed.

### 8.3 Nursing Mothers

It is not known whether Fludeoxyglucose F 18 Injection is excreted in human milk. Consider alternative diagnostic tests in women who are breast-feeding. Use alternatives to breast feeding (e.g., stored breast milk or infant formula) for at least 10 half-lives of radioactive decay, if Fludeoxyglucose F 18 Injection is administered to a woman who is breast-feeding.

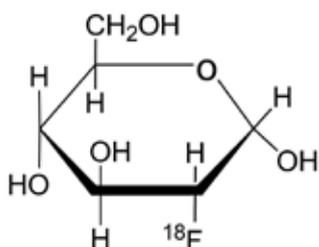
### 8.4 Pediatric Use

The safety and effectiveness of Fludeoxyglucose F 18 Injection in pediatric patients with epilepsy is established on the basis of studies in adult and pediatric patients. In pediatric patients with epilepsy, the recommended dose is 2.6 mCi. The optimal dose adjustment on the basis of body size or weight has not been determined. In the oncology or cardiology settings, the safety and effectiveness of Fludeoxyglucose F 18 Injection have not been established in pediatric patients.

## 11 DESCRIPTION

### 11.1 Chemical Characteristics

Fludeoxyglucose F 18 Injection is a positron emitting radiopharmaceutical that is used for diagnostic purposes in conjunction with positron emission tomography (PET) imaging. The active ingredient 2-deoxy-2-[<sup>18</sup>F]fluoro-D-glucose has the molecular formula of C<sub>6</sub>H<sub>11</sub>18FO<sub>5</sub> with a molecular weight of 181.26, and has the following chemical structure:



Fludeoxyglucose F 18 Injection is provided as a ready to use sterile, pyrogen free, clear, colorless solution. Each mL contains between 0.740 to 7.40GBq (20.0 to 200 mCi) of 2-deoxy-2-[<sup>18</sup>F]fluoro-D-glucose at the EOS, 4.5 mg of sodium chloride and 0.1 to 0.5% w/w ethanol as a stabilizer. The pH of the solution is between 4.5 and 7.5. The solution is packaged in a multiple-dose glass vial and does not contain any preservative.

### 11.2 Physical Characteristics

Fluorine F 18 decays by emitting positron to Oxygen O 16 (stable) and has a physical half-life of 109.7 minutes. The principal photons useful for imaging are the dual 511 keV gamma photons, that are produced and emitted simultaneously in opposite direction when the positron interacts with an electron (Table 2).

Radiation/Emission	% Per Disintegration	Mean Energy
Positron( $\beta^+$ )	96.73	249.8 keV
Gamma( $\pm$ )*	193.46	511.0 keV

\*Produced by positron annihilation  
From: Kocher, D.C. Radioactive Decay Tables DOE/TIC-1 1026, 89 (1981)

The specific gamma ray constant (point source air kerma coefficient) for fluorine F 18 is 5.7 R/hr/mCi ( $1.35 \times 10^{-6}$  Gy/hr/kBq) at 1 cm. The half-value layer (HVL) for the 511 keV photons is 4 mm lead (Pb). The range of attenuation coefficients for this radionuclide as a function of lead shield thickness is shown in Table 3. For example, the interposition of an 8 mm thickness of Pb, with a coefficient of attenuation of 0.25, will decrease the external radiation by 75 percent.

Shield thickness (Pb) mm	Coefficient of attenuation
0	0.00
4	0.50
8	0.25
13	0.10
26	0.01
39	0.001
52	0.0001

For use in correcting for physical decay of this radionuclide, the fractions remaining at selected intervals after calibration are shown in Table 4.

Minutes	Fraction Remaining
0*	1.000
15	0.909
30	0.826
60	0.683
110	0.500
220	0.250

\*calibration time

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Fludeoxyglucose F 18 is a glucose analog that concentrates in cells that rely upon glucose as an energy source, or in cells whose dependence on glucose increases under pathophysiological conditions. Fludeoxyglucose F 18 is transported through the cell membrane by facilitative glucose transporter proteins and is phosphorylated within the cell to [<sup>18</sup>F] FDG-6-phosphate by the enzyme hexokinase. Once phosphorylated it cannot exit until it is dephosphorylated by glucose-6-phosphatase. Therefore, within a given tissue or pathophysiological process, the retention and clearance of Fludeoxyglucose F 18 reflect a balance involving glucose transporter, hexokinase and glucose-6-phosphatase activities. When allowance is made for the kinetic differences between glucose and Fludeoxyglucose F 18 transport and phosphorylation (expressed as the "lumped constant" ratio), Fludeoxyglucose F 18 is used to assess glucose metabolism.

In comparison to background activity of the specific organ or tissue type, regions of decreased or absent uptake of Fludeoxyglucose F 18 reflect the decrease or absence of glucose metabolism. Regions of increased uptake of Fludeoxyglucose F 18 reflect greater than normal rates of glucose metabolism.

## 12.2 Pharmacodynamics

Fludeoxyglucose F 18 Injection is rapidly distributed to all organs of the body after intravenous administration. After background clearance of Fludeoxyglucose F 18 Injection, optimal PET imaging is generally achieved between 30 to 40 minutes after administration.

In cancer, the cells are generally characterized by enhanced glucose metabolism partially due to (1) an increase in activity of glucose transporters, (2) an increased rate of phosphorylation activity, (3) a reduction of phosphatase activity or, (4) a dynamic alteration in the balance among all these processes. However, glucose metabolism of cancer as reflected by Fludeoxyglucose F 18 accumulation shows considerable variability. Depending on tumor type, stage, and location, Fludeoxyglucose F 18 accumulation may be increased, normal, or decreased. Also, inflammatory cells can have the same variability of uptake of Fludeoxyglucose F 18.

In the heart, under normal aerobic conditions, the myocardium meets the bulk of its energy requirements by oxidizing free fatty acids. Most of the exogenous glucose taken up by the myocyte is converted into glycogen. However, under ischemic conditions, the oxidation of free fatty acids decreases, exogenous glucose becomes the preferred myocardial substrate, glycolysis is stimulated, and glucose taken up by the myocyte is metabolized immediately instead of being converted into glycogen. Under these conditions, phosphorylated Fludeoxyglucose F 18 accumulates in the myocyte and can be detected with PET imaging.

In the brain, cells normally rely on aerobic metabolism. In epilepsy, the glucose metabolism varies. Generally, during a seizure, glucose metabolism increases. Interictally, the seizure focus tends to be hypometabolic.

## 12.3 Pharmacokinetics

**Distribution:** In four healthy male volunteers, receiving an intravenous administration of 30 seconds in duration, the arterial blood level profile for Fludeoxyglucose F 18 decayed triexponentially. The effective half-life ranges of the three phases were 0.2 to 0.3 minutes, 10 to 13 minutes with a mean and standard deviation (STD) of 11.6 ( $\pm$ ) 1.1 min, and 80 to 95 minutes with a mean and STD of 88 ( $\pm$ ) 4 min.

Plasma protein binding of Fludeoxyglucose F 18 has not been studied.

**Metabolism:** Fludeoxyglucose F 18 is transported into cells and phosphorylated to [ $^{18}$ F]FDG-6-phosphate at a rate proportional to the rate of glucose utilization within that tissue. [F 18]-FDG-6-phosphate presumably is metabolized to 2-deoxy-2-[F 18]fluoro-6-phospho-D-mannose([F 18]FDM-6-phosphate).

Fludeoxyglucose F 18 Injection may contain several impurities (e.g., 2-deoxy-2-chloro-D-glucose (CIDG)). Biodistribution and metabolism of CIDG are presumed to be similar

to Fludeoxyglucose F 18 and would be expected to result in intracellular formation of 2-deoxy-2-chloro-6-phospho-D-glucose (CIDG-6-phosphate) and 2-deoxy-2-chloro-6-phospho-D-mannose (CIDM-6-phosphate). The phosphorylated deoxyglucose compounds are dephosphorylated and the resulting compounds (FDG, FDM, CIDG, and CIDM) presumably leave cells by passive diffusion. Fludeoxyglucose F 18 and related compounds are cleared from non-cardiac tissues within 3 to 24 hours after administration. Clearance from the cardiac tissue may require more than 96 hours. Fludeoxyglucose F 18 that is not involved in glucose metabolism in any tissue is then excreted in the urine.

**Elimination:** Fludeoxyglucose F 18 is cleared from most tissues within 24 hours and can be eliminated from the body unchanged in the urine. Three elimination phases have been identified in the reviewed literature. Within 33 minutes, a mean of 3.9% of the administered radioactive dose was measured in the urine. The amount of radiation exposure of the urinary bladder at two hours post-administration suggests that 20.6% (mean) of the radioactive dose was present in the bladder.

**Special Populations:** The pharmacokinetics of Fludeoxyglucose F 18 Injection have not been studied in renally-impaired, hepatically impaired or pediatric patients. Fludeoxyglucose F 18 is eliminated through the renal system. Avoid excessive radiation exposure to this organ system and adjacent tissues.

The effects of fasting, varying blood sugar levels, conditions of glucose intolerance, and diabetes mellitus on Fludeoxyglucose F 18 distribution in humans have not been ascertained [see Warnings and Precautions (5.2)].

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been performed to evaluate the Fludeoxyglucose F 18 Injection carcinogenic potential, mutagenic potential or effects on fertility.

## 14 CLINICAL STUDIES

### 14.1 Oncology

The efficacy of Fludeoxyglucose F 18 Injection in positron emission tomography cancer imaging was demonstrated in 16 independent studies. These studies prospectively evaluated the use of Fludeoxyglucose F 18 in patients with suspected or known malignancies, including non-small cell lung cancer, colo-rectal, pancreatic, breast, thyroid, melanoma, Hodgkin's and non-Hodgkin's lymphoma, and various types of metastatic cancers to lung, liver, bone, and axillary nodes. All these studies had at least 50 patients and used pathology as a standard of truth. The Fludeoxyglucose F 18 Injection doses in the studies ranged from 200 MBq to 740 MBq with a median and mean dose of 370 MBq.

In the studies, the diagnostic performance of Fludeoxyglucose F 18 Injection varied with the type of cancer, size of cancer, and other clinical conditions. False negative and false positive scans were observed. Negative Fludeoxyglucose F 18 Injection PET scans do not exclude the diagnosis of cancer. Positive Fludeoxyglucose F 18 Injection PET scans can not replace pathology to establish a diagnosis of cancer. Non-malignant conditions such as fungal infections, inflammatory processes and benign tumors have patterns of increased glucose metabolism that may give rise to false-positive scans. The efficacy of Fludeoxyglucose F 18 Injection PET imaging in cancer screening was not studied.

#### 14.2 Cardiology

The efficacy of Fludeoxyglucose F 18 Injection for cardiac use was demonstrated in ten independent, prospective studies of patients with coronary artery disease and chronic left ventricular systolic dysfunction who were scheduled to undergo coronary revascularization. Before revascularization, patients underwent PET imaging with Fludeoxyglucose F 18 Injection (74 to 370 MBq, 2 to 10 mCi) and perfusion imaging with other diagnostic radiopharmaceuticals. Doses of Fludeoxyglucose F 18 Injection ranged from 74 to 370 MBq (2 to 10 mCi). Segmental, left ventricular, wall-motion assessments of asynergic areas made before revascularization were compared in a blinded manner to assessments made after successful revascularization to identify myocardial segments with functional recovery.

Left ventricular myocardial segments were predicted to have reversible loss of systolic function if they showed Fludeoxyglucose F 18 accumulation and reduced perfusion (i.e., flow-metabolism mismatch). Conversely, myocardial segments were predicted to have irreversible loss of systolic function if they showed reductions in both Fludeoxyglucose F 18 accumulation and perfusion (i.e., matched defects).

Findings of flow-metabolism mismatch in a myocardial segment may suggest that successful revascularization will restore myocardial function in that segment. However, false-positive tests occur regularly, and the decision to have a patient undergo revascularization should not be based on PET findings alone. Similarly, findings of a matched defect in a myocardial segment may suggest that myocardial function will not recover in that segment, even if it is successfully revascularized. However, false-negative tests occur regularly, and the decision to recommend against coronary revascularization, or to recommend a cardiac transplant, should not be based on PET findings alone. The reversibility of segmental dysfunction as predicted with Fludeoxyglucose F 18 PET imaging depends on successful coronary revascularization. Therefore, in patients with a low likelihood of successful revascularization, the diagnostic usefulness of PET imaging with Fludeoxyglucose F 18 Injection is more limited.

#### 14.3 Neurology

In a prospective, open label trial, Fludeoxyglucose F 18 Injection was evaluated in 86 patients with epilepsy. Each patient received a dose of Fludeoxyglucose F 18 Injection in the range of 185 to 370 MBq (5 to 10 mCi). The mean age was 16.4 years (range: 4 months to 58 years; of these, 42 patients were less than 12 years and 16 patients were less than 2 years old). Patients had a known diagnosis of complex partial epilepsy and were under evaluation for surgical treatment of their seizure disorder. Seizure foci had been previously identified on ictal EEGs and sphenoidal EEGs. Fludeoxyglucose F 18 Injection PET imaging confirmed previous diagnostic findings in 16% (14/87) of the patients; in 34% (30/87) of the patients, Fludeoxyglucose F 18 Injection PET images provided new findings. In 32% (27/87), imaging with Fludeoxyglucose F 18 Injection was inconclusive. The impact of these imaging findings on clinical outcomes is not known.

Several other studies comparing imaging with Fludeoxyglucose F 18 Injection results to subsphenoidal EEG, MRI and/or surgical findings supported the concept that the degree of hypometabolism corresponds to areas of confirmed epileptogenic foci. The safety and effectiveness of Fludeoxyglucose F 18 Injection to distinguish idiopathic epileptogenic foci from tumors or other brain lesions that may cause seizures have not been established.

### 15 REFERENCES

1. Gallagher B.M., Ansari A., Atkins H., Casella V., Christman D.R., Fowler J.S., Ido T., MacGregor R.R., Som P., Wan C.N., Wolf A.P., Kuhl D.E., and Reivich M. "Radiopharmaceuticals XXVII. 18F-labeled 2-deoxy-2-fluoro-d-glucose as a radiopharmaceutical for measuring regional myocardial glucose metabolism in vivo: tissue distribution and imaging studies in animals," *J Nucl Med*, 1977; 18, 990-6.
2. Jones S.C., Alavi, A., Christman D., Montanez, I., Wolf, A.P., and Reivich M. "The radiation dosimetry of 2 [F-18] fluoro-2-deoxy-D-glucose in man," *J Nucl Med*, 1982; 23, 613-617.
3. Kocher, D.C. "Radioactive Decay Tables: A handbook of decay data for application to radiation dosimetry and radiological assessments," 1981, DOE/TIC-I 1026, 89.
4. ICRP Publication 53, Volume 18, No. I-4, 1987, pages 75-76.

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## 16 HOW SUPPLIED/STORAGE AND DRUG HANDLING

Fludeoxyglucose F 18 Injection is supplied in a multi-dose, capped 30 mL and 50 mL glass vial containing between 0.740 to 7.40GBq/mL (20 to 200 mCi/mL), of no carrier added 2deoxy-2-[F 18] fluoro-D-glucose, at end of synthesis, in approximately 15 to 50 mL. The contents of each vial are sterile, pyrogen-free and preservative-free.

NDC 40028-511-30; 40028-511-50

Receipt, transfer, handling, possession, or use of this product is subject to the radioactive material regulations and licensing requirements of the U.S. Nuclear Regulatory Commission, Agreement States or Licensing States as appropriate.

Store the Fludeoxyglucose F 18 Injection vial upright in a lead shielded container at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Store and dispose of Fludeoxyglucose F 18 Injection in accordance with the regulations and a general license, or its equivalent, of an Agreement State or a Licensing State.

The expiration date and time are provided on the container label. Use Fludeoxyglucose F 18 Injection within 12 hours from the EOS time.

## 17 PATIENT COUNSELING INFORMATION

Instruct patients in procedures that increase renal clearance of radioactivity. Encourage patients to:

- drink water or other fluids (as tolerated) in the 4 hours before their PET study.
- void as soon as the imaging study is completed and as often as possible thereafter for at least one hour.

Manufactured by: PETNET Solutions Inc.  
810 Innovation Drive  
Knoxville, TN 37932

Distributed by: PETNET Solutions Inc.  
810 Innovation Drive  
Knoxville, TN 37932

**PETNET** Solutions

PN0002262 Rev. A  
March 1, 2011

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## SODIUM FLUORIDE F 18 INJECTION

### HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Sodium Fluoride F 18 Injection safely and effectively. See full prescribing information for Sodium Fluoride F 18 Injection.

#### SODIUM FLUORIDE F 18 INJECTION

##### For Intravenous Use

Initial U.S. Approval: January 2011

#### -----INDICATIONS AND USAGE-----

Sodium Fluoride F 18 Injection is a radioactive diagnostic agent for positron emission tomography (PET) indicated for imaging of bone to define areas of altered osteogenic activity (1).

#### -----DOSAGE AND ADMINISTRATION-----

- Sodium Fluoride F18 Injection emits radiation and must be handled with appropriate safety measures (2.1).
- Administer 300-450 MBq (8–12 mCi) as an intravenous injection in adults (2.4).
- Administer approximately 2.1 MBq/kg in children with a minimum of 19 MBq (0.5 mCi) and a maximum of 148 MBq (4 mCi) as an intravenous injection (2.5).
- Imaging can begin 1–2 hours after administration; optimally at one hour post administration (2.7).
- Encourage patients to void immediately prior to imaging the lumbar spine and bony pelvis (2.7).

#### -----DOSAGE FORMS AND STRENGTHS-----

Multiple-dose vial containing 370–7,400 MBq/mL (10–200 mCi/mL) of no-carrier-added sodium fluoride F18 at the end of synthesis (EOS) reference time in aqueous 0.9% sodium chloride solution (3). Sodium Fluoride F 18 Injection is a clear, colorless, sterile, pyrogen-free and preservative-free solution for intravenous administration.

#### -----CONTRAINDICATIONS-----

None (4).

#### -----WARNINGS AND PRECAUTIONS-----

- Allergic Reactions: As with any injectable drug product, allergic reactions and anaphylaxis may occur. Emergency resuscitation equipment and personnel should be immediately available (5.1).
- Cancer Risk: Sodium Fluoride F 18 Injection may increase the risk of cancer. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker (5.2).

#### -----ADVERSE REACTIONS-----

No adverse reactions have been reported for Sodium Fluoride F 18 Injection based on a review of the published literature, publicly available reference sources, and adverse drug reaction reporting systems (6).

**To report SUSPECTED ADVERSE REACTIONS, contact NCI/ DCTD/CIP at 1-301-496-9531 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

#### -----USE IN SPECIFIC POPULATIONS-----

- Pregnancy: No human or animal data. Any radiopharmaceutical, including Sodium Fluoride F18 injection, may cause fetal harm. Use only if clearly needed (8.1)
- Nursing: A decision should be made whether to interrupt nursing after Sodium Fluoride F 18 Injection administration or not to administer Sodium Fluoride F 18 Injection taking into consideration the importance of the drug to the mother. (8.3)
- Pediatrics: Children are more sensitive to radiation and may be at higher risk of cancer from Sodium Fluoride F18 injection (8.4).

**See 17 for PATIENT COUNSELING INFORMATION**

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Sodium Fluoride F 18 Injection is indicated for diagnostic positron emission tomography (PET) imaging of bone to define areas of altered osteogenic activity.

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Radiation Safety – Drug Handling

- Wear waterproof gloves and effective shielding when handling Sodium Fluoride F 18 Injection. Use appropriate safety measures, including shielding, consistent with proper patient management to avoid unnecessary radiation exposure to the patient, occupational workers, clinical personnel, and other persons.
- Radiopharmaceuticals should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radionuclides, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.
- Use aseptic technique to maintain sterility during all operations involved in the manipulation and administration of Sodium Fluoride F 18 Injection.
- The dose of Sodium Fluoride F 18 Injection should be minimized consistent with the objectives of the procedure, and the nature of the radiation detection devices employed.
- The final dose for the patient should be calculated using proper decay factors from the time of End of Synthesis (EOS), and measured by a suitable radioactivity calibration system before administration [see Description (11.2)].

#### 2.2 Radiation Safety - Patient Preparation

- To minimize the radiation-absorbed dose to the bladder, encourage adequate hydration. Encourage the patient to ingest at least 500 mL of fluid immediately prior and subsequent to the administration of Sodium Fluoride F 18 Injection.
- Encourage the patient to void one-half hour after administration of Sodium Fluoride F 18 Injection and as frequently thereafter as possible for the next 12 hours.

#### 2.3 Drug Preparation and Administration

- Calculate the necessary volume to administer based on calibration time and dose.
- Inspect Sodium Fluoride F 18 Injection visually for particulate matter and discoloration before administration, whenever solution and container permit.
- Do not administer Sodium Fluoride F 18 Injection containing particulate matter or discoloration; dispose of these unacceptable or unused preparations in a safe manner, in compliance with applicable regulations.
- Aseptically withdraw Sodium Fluoride F 18 Injection from its container.

#### 2.4 Recommended Dose for Adults

- Administer 300–450 MBq (8–12 mCi) as an intravenous injection.

#### 2.5 Recommended Dose for Pediatric Patients

In reported clinical experience in approximately 100 children, weight based doses (2.1 MBq/kg) ranging from 19 MBq–148 MBq (0.5 mCi–4 mCi) were used.

## 2.6 Radiation Dosimetry

The age/weight-based estimated absorbed radiation doses (mGy/MBq) from intravenous injection of Sodium Fluoride F 18 Injection are shown in Table 1. These estimates were calculated based on human data and using the data published by the Nuclear Regulatory Commission [1] and the International Commission on Radiological Protection for Sodium Fluoride Injection [2]. The bone, bone marrow and urinary bladder are considered target and critical organs.

## 2.7 Imaging Guidelines

- Imaging of Sodium Fluoride F 18 Injection can begin 1–2 hours after administration; optimally at 1 hour post administration.
- Encourage the patient to void immediately prior to imaging the fluoride F18 radioactivity in the lumbar spine or bony pelvis.

**Table 1: Estimated Absorbed Radiation Doses after Intravenous Administration of Sodium Fluoride F 18 Injection**

Organ	Estimated Radiation Dose mGy/MBq					
	Adult 70 kg <sup>1</sup>	15 year 56.8 kg <sup>2</sup>	10 year 33.2 kg <sup>2</sup>	5 year 19.8 kg <sup>2</sup>	1 year 9.7 kg <sup>2</sup>	
Adrenals	0.0062	0.012	0.018	0.028	0.052	
Brain	0.0056	N/A	N/A	N/A	N/A	
Bone surfaces	0.060	0.050	0.079	0.13	0.30	
GI	Breasts	0.0028	0.0061	0.0097	0.015	0.030
	Gallbladder wall	0.0044	N/A	N/A	N/A	N/A
	Stomach wall	0.0038	0.008	0.013	0.019	0.036
	Small intestine	0.0066	0.012	0.018	0.028	0.052
	Upper large intestine wall	0.0058	0.010	0.016	0.026	0.046
	Lower large intestine wall	0.012	0.016	0.025	0.037	0.063
Heart wall	0.0039	N/A	N/A	N/A	N/A	
Kidneys	0.019	0.025	0.036	0.053	0.097	
Liver	0.0040	0.0084	0.013	0.021	0.039	
Lungs	0.0041	0.0084	0.013	0.020	0.039	
Muscle	0.0060	N/A	N/A	N/A	N/A	
Ovaries	0.011	0.016	0.023	0.036	0.063	
Pancreas	0.0048	0.0096	0.015	0.023	0.044	
Red marrow	0.028	0.053	0.088	0.18	0.38	
Skin	0.0040	N/A	N/A	N/A	N/A	
Spleen	0.0042	0.0088	0.014	0.021	0.041	
Testes	0.0078	0.013	0.021	0.033	0.062	
Thymus	0.0035	N/A	N/A	N/A	N/A	
Thyroid	0.0044	0.0084	0.013	0.020	0.036	
Urinary bladder wall	0.25	0.27	0.4	0.61	1.1	
Uterus	0.019	0.023	0.037	0.057	0.099	
Other tissue	N/A	0.010	0.015	0.024	0.044	
Effective Dose Equivalent mSv/MBq	0.027	0.034	0.052	0.086	0.17	

1 Data from Nuclear Regulatory Commission Report, *Radiation Dose Estimates for Radiopharmaceuticals*, NUREG/CR-6345, page 10, 1996.

2 Data from ICRP publication 53, *Radiation Dose to Patients from Radiopharmaceuticals*, Ann ICRP, Volume 18, pages 15 and 74, 1987

### 3 DOSAGE FORMS AND STRENGTHS

Multiple-dose vial containing 370–7,400 MBq/mL (10–200 mCi/mL) at EOS reference time of no-carrier-added sodium fluoride F 18 in aqueous 0.9% sodium chloride solution. Sodium Fluoride F 18 Injection is a clear, colorless, sterile, pyrogen-free and preservative-free solution for intravenous administration.

### 4 CONTRAINDICATIONS

None.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Allergic Reactions

As with any injectable drug product, allergic reactions and anaphylaxis may occur. Emergency resuscitation equipment and personnel should be immediately available.

#### 5.2 Radiation Risks

Sodium Fluoride F 18 Injection may increase the risk of cancer. Carcinogenic and mutagenic studies with Sodium Fluoride F 18 injection have not been performed. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker [see Dosage and Administration (2.1)].

### 6 ADVERSE REACTIONS

No adverse reactions have been reported for Sodium Fluoride F 18 Injection based on a review of the published literature, publicly available reference sources, and adverse drug reaction reporting systems. However, the completeness of these sources is not known.

### 7 DRUG INTERACTIONS

The possibility of interactions of Sodium Fluoride F 18 Injection with other drugs taken by patients undergoing PET imaging has not been studied.

### 8 USE IN SPECIFIC POPULATIONS

#### 8.1 Pregnancy Pregnancy Category C

Any radiopharmaceutical including Sodium Fluoride F 18 Injection has a potential to cause fetal harm. The likelihood of fetal harm depends on the stage of fetal development, and the radionuclide dose. Animal reproductive and developmental toxicity studies have not been conducted with Sodium Fluoride F 18 Injection. Prior to the administration of Sodium Fluoride F 18 Injection to women of childbearing potential, assess for presence of pregnancy. Sodium Fluoride F 18 Injection should be given to a pregnant woman only if clearly needed.

#### 8.3 Nursing Mothers

It is not known whether Sodium Fluoride F 18 Injection is excreted into human milk. Because many drugs are excreted in 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 Sodium Fluoride F 18 Injection or not

to administer Sodium Fluoride F 18 Injection, taking into account the importance of the drug to the mother. The body of scientific information related to radioactivity decay, drug tissue distribution and drug elimination shows that less than 0.01% of the radioactivity administered remains in the body after 24 hours (10 half-lives). To minimize the risks to a nursing infant, interrupt nursing for at least 24 hours.

#### 8.4 Pediatric Use

In reported clinical experience in approximately 100 children, weight based doses (2.1 MBq/kg) ranging from 19 MBq–148 MBq (0.5 mCi – 4 mCi) were used. Sodium Fluoride F18 was shown to localize to areas of bone turnover including rapidly growing epiphyses in developing long bones. Children are more sensitive to radiation and may be at higher risk of cancer from Sodium Fluoride F18 injection.

### 11 DESCRIPTION

#### 11.1 Chemical Characteristics

Sodium Fluoride F 18 Injection is a positron emitting radiopharmaceutical, containing no carrier-added, radioactive fluoride F18 that is used for diagnostic purposes in conjunction with PET imaging. It is administered by intravenous injection. The active ingredient, sodium fluoride F18, has the molecular formula Na[<sup>18</sup>F] with a molecular weight of 40.99, and has the following chemical structure:  
**Na + <sup>18</sup>F**

Sodium Fluoride F 18 Injection is provided as a ready-to-use, isotonic, sterile, pyrogen-free, preservative-free, clear and colorless solution. Each mL of the solution contains between 370 MBq to 7,400 MBq (10 mCi to 200 mCi) sodium fluoride F18, at the EOS reference time, in 0.9% aqueous sodium chloride. The pH of the solution is between 4.5 and 8. The solution is presented in 30 mL multiple-dose glass vials with variable total volume and total radioactivity in each vial.

#### 11.2 Physical Characteristics

Fluoride F 18 decays by positron ( $\beta^+$ ) emission and has a half-life of 109.7 minutes. Ninety-seven percent of the decay results in emission of a positron with a maximum energy of 633 keV and 3% of the decay results in electron capture with subsequent emission of characteristic X-rays of oxygen. The principal photons useful for diagnostic imaging are the 511 keV gamma photons, resulting from the interaction of the emitted positron with an electron (Table 2). Fluorine F18 atom decays to stable <sup>18</sup>O-oxygen.

Radiation/Emission	% per Disintegration	Mean Energy
Positron ( $\beta^+$ )	96.73	249.8 keV
Gamma ( $\pm$ ) <sup>*</sup>	193.46	511.0 keV

<sup>\*</sup>Produced by positron annihilation

[3] Kocher, D.C. Radioactive Decay Data Tables DOE/TIC-11026, 69, 1981.

The specific gamma ray constant for fluoride F18 is 5.7 R/hr/mCi ( $1.35 \times 10^{-6}$  Gy/hr/kBq) at 1 cm. The half-value layer (HVL) for the 511 keV photons is 4.1 mm lead (Pb). A range of values for the attenuation of radiation results from the interposition of various thickness of Pb. The range of attenuation coefficients for this radionuclide is shown in Table 3. For example, the interposition of an 8.3 mm thickness of Pb with a coefficient of attenuation of 0.25 will decrease the external radiation by 75%.

Shield Thickness (Pb) mm	Coefficient of Attenuation
0	0.00
4	0.50
8	0.25
13	0.10
26	0.01
39	0.001
52	0.0001

Table 4 lists the fraction of radioactivity remaining at selected time intervals for the calibration time. This information may be used to correct for physical decay of the radionuclide.

Time Since Calibration	Fraction Remaining
0*	1.00
15 minutes	0.909
30 minutes	0.826
60 minutes	0.683
110	0.500
220 minutes	0.250
440 minutes	0.060
12 hours	0.011
24 hours	0.0001

\* Calibration time

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Fluoride F18 ion normally accumulates in the skeleton in an even fashion, with greater deposition in the axial skeleton (e.g. vertebrae and pelvis) than in the appendicular skeleton and greater deposition in the bones around joints than in the shafts of long bones.

### 12.2 Pharmacodynamics

Increased fluoride F18 ion deposition in bone can occur in areas of increased osteogenic activity during growth, infection, malignancy (primary or metastatic) following trauma, or inflammation of bone.

### 12.3 Pharmacokinetics

After intravenous administration, fluoride F18 ion is rapidly cleared from the plasma in a biexponential manner. The first phase has a half-life of 0.4 h, and the second phase has a half-life of 2.6 h. Essentially all the fluoride F18 that is delivered to bone by the blood is retained in the bone. One hour after administration of fluoride, F18 only about 10% of the injected dose remains in the blood. Fluoride F18 diffuses through capillaries into bone extracellular fluid space, where it becomes bound by chemisorption at the surface of bone crystals, preferentially at sites of newly mineralizing bone. Deposition of fluoride F18 in bone appears to be primarily a function of blood flow to the bone and the efficiency of the bone in extracting the fluoride F18. Fluoride F18 does not appear to be bound to serum proteins. In patients with normal renal function, 20% or more of the fluorine ion is cleared from the body in the urine within the first 2 hours after intravenous administration.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies to assess reproductive toxicity, mutagenesis and carcinogenesis potential of Sodium Fluoride F 18 Injection have not been performed.

## 14 CLINICAL STUDIES

### 14.1 Metastatic Bone Disease

The doses used in reported studies ranged from 2.7 mCi to 20 mCi (100 MBq to 740 MBq), with an average median dose of 10 mCi (370 MBq) and an average mean dose of 9.2 mCi (340 MBq). In PET imaging of bone metastases with Sodium Fluoride F 18 Injection, focally increased tracer uptake is seen in both osteolytic and osteoblastic bone lesions. Negative PET imaging results with Sodium Fluoride F 18 Injection do not preclude the diagnosis of bone metastases. Also, as benign bone lesions are also detected by Sodium Fluoride F 18 Injection, positive PET imaging results cannot replace biopsy to confirm a diagnosis of cancer.

### 14.2 Other Bone Disorders

The doses used in reported studies ranged from 2.43 mCi to 15 mCi (90 MBq to 555 MBq), with an average median dose of 8.0 mCi (300 MBq) and an average mean dose of 7.6 mCi (280 MBq).

## 15 REFERENCES

1. Stabin, M.G., Stubbs, J.B. and Toohey R.E., Radiation Dose Estimates for Radiopharmaceuticals, U.S. Nuclear Regulatory Commission report NUREG/CR-6345, page 10, 1996.
2. Radiation Dose to Patients from Radiopharmaceuticals, ICRP publication 53, Ann ICRP, 18 pages 15 and 74, 1987
3. Kocher, D.C., "Radioactive Decay Data Tables: A Handbook of decay data for application to radiation dosimetry and radiological assessments" DOE/TIC-11026, page 69, 1981.

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## 16 HOW SUPPLIED/STORAGE AND HANDLING

Sodium Fluoride F 18 Injection is supplied in a multiple-dose Type I glass vial with elastomeric stopper and aluminum crimp seal containing between 370 and 7,400 MBq/mL (10–200 mCi/mL) of no carrier-added sodium fluoride F18, at the EOS reference time, in aqueous 0.9% sodium chloride solution. The total volume and total radioactivity per vial are variable. Each vial is enclosed in a shielded container of appropriate thickness. The product is available in a 30 mL vial configuration with a variable fill volume. The NDC number is: 40028-512-30 (30 mL)

### Storage

Store at 25°C (77°F) in a shielded container; excursions permitted to 15–30°C (59–86°F). Use the solution within 12 hours of the EOS reference time.

### Handling

Receipt, transfer, handling, possession, or use of this product is subject to the radioactive material regulations and licensing requirements of the U.S. Nuclear Regulatory Commission, Agreement States or Licensing States as appropriate.

## 17 PATIENT COUNSELING INFORMATION

### 17.1 Pre-study Hydration

Encourage patients to drink at least 500 mL of water prior to drug administration.

### 17.2 Post-study Voiding

To help protect themselves and others in their environment, patients should take the following precautions for 12 hours after injection: whenever possible, use a toilet and flush several times after each use; wash hands thoroughly after each voiding or fecal elimination. If blood, urine or feces soil clothing, wash the clothing separately.

**Manufactured by:** Siemens Molecular Imaging  
PETNET Solutions Inc.  
810 Innovation Drive, Knoxville, TN  
37932

**Distributed by:** Siemens Molecular Imaging  
PETNET Solutions Inc.  
810 Innovation Drive, Knoxville, TN  
37932

**AMMONIA N 13 - ammonia n-13 injection**  
**PETNET Solutions, Inc.**

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**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use Ammonia N 13 Injection safely and effectively. See full prescribing information for Ammonia N 13 Injection. Ammonia N 13 Injection for intravenous use Initial U.S. Approval: 2007

**INDICATIONS AND USAGE**

Ammonia N 13 Injection is a radioactive diagnostic agent for Positron Emission Tomography (PET) indicated for diagnostic PET imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease (1).

**DOSAGE AND ADMINISTRATION**

Rest Imaging Study (2.1):

- Aseptically withdraw Ammonia N 13 Injection from its container and administer 10-20 mCi (0.368 – 0.736 GBq) as a bolus through a catheter inserted into a large peripheral vein.
- Start imaging 3 minutes after the injection and acquire images for a total of 10-20 minutes.

Stress Imaging Study (2.2):

- If a rest imaging study is performed, begin the stress imaging study 40 minutes or more after the first Ammonia N13 injection to allow sufficient isotope decay.
- Administer a pharmacologic stress-inducing drug in accordance with its labeling.
- Aseptically withdraw Ammonia N 13 Injection from its container and administer 10-20 mCi (0.368 – 0.736 GBq) of Ammonia N 13 Injection as a bolus at 8 minutes after the administration of the pharmacologic stress-inducing drug.
- Start imaging 3 minutes after the Ammonia N 13 Injection and acquire images for a total of 10-20 minutes.

Patient Preparation (2.3):

- To increase renal clearance of radioactivity and to minimize radiation dose to the bladder, hydrate the patient before the procedure and encourage voiding as soon as each image acquisition is completed and as often as possible thereafter for at least one hour.

**DOSAGE FORMS AND STRENGTHS**

Glass vial containing 0.138-1.387 GBq (3.75-37.5 mCi/mL) of Ammonia N 13 Injection in aqueous 0.9 % sodium chloride solution (The total volume in the vial will vary) (3).

**CONTRAINDICATIONS**

None (4)

**WARNINGS AND PRECAUTIONS**

Ammonia N 13 Injection may increase the risk of cancer. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker (5).

**ADVERSE REACTIONS**

No adverse reactions have been reported for Ammonia N 13 Injection based on a review of the published literature, publicly available reference sources, and adverse drug reaction reporting system ( 6).6).

To report SUSPECTED ADVERSE REACTIONS, contact PETNET Solutions, Inc. at 877-473-8638 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### USE IN SPECIFIC POPULATIONS

- It is not known whether this drug is excreted in human milk. Alternatives to breastfeeding (e.g. using stored breast milk or infant formula) should be used for 2 hours (>10 half-lives of radioactive decay for N 13 isotope) after administration of Ammonia N 13 Injection (8.3).
- The safety and effectiveness of Ammonia N 13 Injection has been established in pediatric patients (8.4).

See 17 for Patient Counseling Information, Patient Counseling Information, Patient Counseling Information, and Patient Counseling Information

Revised: 01/2011

### FULL PRESCRIBING INFORMATION: CONTENTS\*

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#### Drug Product Label

\*

Sections or subsections omitted from the full prescribing information are not listed

## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Ammonia N 13 Injection is indicated for diagnostic Positron Emission Tomography (PET) imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease.

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Rest Imaging Study

- Aseptically withdraw Ammonia N 13 Injection from its container and administer 10-20 mCi (0.368 – 0.736 GBq) as a bolus through a catheter inserted into a large peripheral vein.
- Start imaging 3 minutes after the injection and acquire images for a total of 10-20 minutes.

#### 2.2 Stress Imaging Study

- If a rest imaging study is performed, begin the stress imaging study 40 minutes or more after the first Ammonia N 13 injection to allow sufficient isotope decay.
- Administer a pharmacologic stress-inducing drug in accordance with its labeling.
- Aseptically withdraw Ammonia N 13 Injection from its container and administer 10-20 mCi (0.368 – 0.736 GBq) of Ammonia N 13 Injection as a bolus at 8 minutes after the administration of the pharmacologic stress-inducing drug.
- Start imaging 3 minutes after the Ammonia N 13 Injection and acquire images for a total of 10-20 minutes.

#### 2.3 Patient Preparation

To increase renal clearance of radioactivity and to minimize radiation dose to the bladder, ensure that the patient is well hydrated before the procedure and encourage voiding as soon as a study is completed and as often as possible thereafter for at least one hour.

#### 2.4 Radiation Dosimetry

The converted radiation absorbed doses in rem/mCi are shown in Table 1. These estimates are calculated from the Task Group of Committee 2 of the International Commission on Radiation Protection.<sup>1</sup>

**Table 1: N 13 Absorbed Radiation Dose Per Unit Activity (rem/mCi) for Adults and Pediatric Groups.**

Organ	Adult	15 - year old	10 - year old	5 - year old	1 - year old
Adrenals	0.0085	0.0096	0.016	0.025	0.048
Bladder wall	0.030	0.037	0.056	0.089	0.17
Bone surfaces	0.0059	0.0070	0.011	0.019	0.037
Brain	0.016	0.016	0.017	0.019	0.027
Breast	0.0067	0.0067	0.010	0.017	0.033
Stomach wall	0.0063	0.0078	0.012	0.019	0.037
Small intestine	0.0067	0.0081	0.013	0.021	0.041
*ULI	0.0067	0.0078	0.013	0.021	0.037
**LLI	0.0070	0.0078	0.013	0.020	0.037
Heart	0.0078	0.0096	0.015	0.023	0.041
Kidneys	0.017	0.021	0.031	0.048	0.089
Liver	0.015	0.018	0.029	0.044	0.085

Lungs	0.0093	0.011	0.018	0.029	0.056
Ovaries	0.0063	0.0085	0.014	0.021	0.041
Pancreas	0.0070	0.0085	0.014	0.021	0.041
Red marrow	0.0063	0.0078	0.012	0.020	0.037
Spleen	0.0093	0.011	0.019	0.030	0.056
Testes	0.0067	0.0070	0.011	0.018	0.035
Thyroid	0.0063	0.0081	0.013	0.021	0.041
Uterus	0.0070	0.0089	0.014	0.023	0.041
Other tissues	0.0059	0.0070	0.011	0.018	0.035

\*Upper large intestine, \*\*Lower large intestine

## 2.5 Drug Handling

- Inspect Ammonia N 13 Injection visually for particulate matter and discoloration before administration, whenever solution and container permit.
- Do not administer Ammonia N 13 Injection containing particulate matter or discoloration; dispose of these unacceptable or unused preparations in a safe manner, in compliance with applicable regulations.
- Wear waterproof gloves and effective shielding when handling Ammonia N 13 Injection.
- Use aseptic technique to maintain sterility during all operations involved in the manipulation and administration of Ammonia N 13 Injection. The contents of each vial are sterile and non-pyrogenic.
- Use appropriate safety measures, including shielding, consistent with proper patient management to avoid unnecessary radiation exposure to the patient, occupational workers, clinical personnel, and other persons.
- Radiopharmaceuticals should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radionuclides, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.
- Before administration of Ammonia N 13 Injection, assay the dose in a properly calibrated dose calibrator.

## 3 DOSAGE FORMS AND STRENGTHS

Glass vial (30 mL) containing 0.138-1.387 GBq (3.75-37.5 mCi/mL) of Ammonia N 13 Injection in aqueous 0.9 % sodium chloride solution (the total volume in the vial will vary) that is suitable for intravenous administration.

## 4 CONTRAINDICATIONS

None

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Radiation Risks

Ammonia N 13 Injection may increase the risk of cancer. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker. [see *Dosage and Administration (2.4)*].

## 6 ADVERSE REACTIONS

No adverse reactions have been reported for Ammonia N 13 Injection based on a review of the published literature, publicly available reference sources, and adverse drug reaction reporting systems. However, the completeness of these sources is not known.

## 7 DRUG INTERACTIONS

The possibility of interactions of Ammonia N 13 Injection with other drugs taken by patients undergoing PET imaging has not been studied.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Pregnancy Category C

Animal reproduction studies have not been conducted with Ammonia N 13 Injection. It is also not known whether Ammonia N 13 Injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Ammonia N 13 Injection should be given to a pregnant woman only if clearly needed.

### 8.3 Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for radiation exposure to nursing infants from Ammonia N 13 Injection, use alternative infant nutrition sources (e.g. stored breast milk or infant formula) for 2 hours (>10 half-lives of radioactive decay for N 13 isotope) after administration of the drug or avoid use of the drug, taking into account the importance of the drug to the mother.

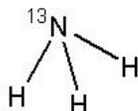
### 8.4 Pediatric Use

The safety and effectiveness of Ammonia N 13 Injection has been established in pediatric patients based on known metabolism of ammonia, radiation dosimetry in the pediatric population, and clinical studies in adults. [see *Dosage and Administration (2.4)*].

## 11 DESCRIPTION

### 11.1 Chemical Characteristics

Ammonia N 13 Injection is a positron emitting radiopharmaceutical that is used for diagnostic purposes in conjunction with positron emission tomography (PET) imaging. The active ingredient, [13N] ammonia, has the molecular formula of  $^{13}\text{NH}_3$  with a molecular weight of 16.02, and has the following chemical structure:



Ammonia N 13 Injection is provided as a ready to use sterile, pyrogen-free, clear and colorless solution. Each mL of the solution contains between 0.138 GBq to 1.387 GBq (3.75 mCi to 37.5mCi) of [13N] ammonia, at the end of synthesis (EOS) reference time, in 0.9% aqueous sodium chloride. The pH of the solution is between 4.5 to 7.5. The recommended dose of radioactivity (10-20 mCi) is associated with a theoretical mass dose of 0.05-0.1 picomoles (8.47-16.94 picograms) of ammonia.

## 11.2 Physical Characteristics

Nitrogen N13 decays by emitting positron to Carbon C13 (stable) and has a physical half-life of 9.96 minutes. The principal photons useful for imaging are the dual 511 keV gamma photons that are produced and emitted simultaneously in opposite direction when the positron interacts with an electron (Table 2).

**Table 2: Principal Radiation Emission Data for Nitrogen 13**

Radiation/Emission	% Per Disintegration	Energy
Positron( $\beta^+$ )	100	1190 keV (Max.)
Gamma( $\pm$ )*	200	511 keV

\*Produced by positron annihilation

The specific gamma ray constant (point source air kerma coefficient) for nitrogen N13 is 5.9 R/hr/mCi ( $1.39 \times 10^{-6}$  Gy/hr/kBq) at 1 cm. The half-value layer (HVL) of lead (Pb) for 511 keV photons is 4 mm. Selected coefficients of attenuation are listed in Table 3 as a function of lead shield thickness. For example, the use of 39 mm thickness of lead will attenuate the external radiation by a factor of about 1000.

**Table 3: Radiation Attenuation of 511 keV Photons by lead (Pb) shielding**

Shield Thickness (Pb) mm	Coefficient of Attenuation
4	0.5
8	0.25
13	0.1
26	0.01
39	0.001
52	0.0001

Table 4 lists fractions remaining at selected time intervals from the calibration time. This information may be used to correct for physical decay of the radionuclide.

**Table 4: Physical Decay Chart for Nitrogen N 13**

Minutes	Fraction Remaining
0*	1.000
5	0.706
10	0.499
15	0.352
20	0.249
25	0.176
30	0.124

\*Calibration time

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Ammonia N 13 Injection is a radiolabeled analog of ammonia that is distributed to all organs of the body after intravenous administration. It is extracted from the blood in the coronary capillaries into the myocardial cells where it is metabolized to glutamine N 13 and retained in the cells. The presence of ammonia N 13 and glutamine N 13 in the myocardium allows for PET imaging of the myocardium.

## 12.2 Pharmacodynamics

Following intravenous injection, ammonia N 13 enters the myocardium through the coronary arteries. The PET technique measures myocardial blood flow based on the assumption of a three-compartmental disposition of intravenous ammonia N 13 in the myocardium. In this model, the value of the rate constant, which represents the delivery of blood to myocardium, and the fraction of ammonia N 13 extracted into the myocardial cells, is a measure of myocardial blood flow. Optimal PET imaging of the myocardium is generally achieved between 10 to 20 minutes after administration.

## 12.3 Pharmacokinetics

Following intravenous injection, Ammonia N 13 Injection is cleared from the blood with a biologic half-life of about 2.84 minutes (effective half-life of about 2.21 minutes). In the myocardium, its biologic half-life has been estimated to be less than 2 minutes (effective half-life less than 1.67 minutes).

The mass dose of Ammonia N 13 Injection is very small as compared to the normal range of ammonia in the blood (0.72-3.30 mg) in a healthy adult man. [see *Description (11.1)*]

Plasma protein binding of ammonia N 13 or its N 13 metabolites has not been studied.

Ammonia N 13 undergoes a five-enzyme step metabolism in the liver to yield urea N 13 (the main circulating metabolite). It is also metabolized to glutamine N 13 (the main metabolite in tissues) by glutamine synthesis in the skeletal muscles, liver, brain, myocardium, and other organs. Other metabolites of ammonia N 13 include small amounts of N 13 amino acid anions (acidic amino acids) in the forms of glutamate N 13 or aspartate N 13.

Ammonia N 13 is eliminated from the body by urinary excretion mainly as urea N 13.

The pharmacokinetics of Ammonia N 13 Injection have not been studied in renally impaired, hepatically impaired, or pediatric patients.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long term animal studies have not been performed to evaluate the carcinogenic potential of Ammonia N 13 Injection. Genotoxicity assays and impairment of male and female fertility studies with Ammonia N 13 Injection have not been performed.

## 14 CLINICAL STUDIES

In a descriptive, prospective, blinded image interpretation study<sup>2</sup> of adult patients with known or suspected coronary artery disease, myocardial perfusion deficits in stress and rest PET images obtained with Ammonia N 13 (N=111) or Rubidium 82 (N=82) were compared to changes in stenosis flow reserve (SFR) as determined by coronary angiography. The principal outcome of the study was the evaluation of PET defect severity relative to SFR.

PET perfusion defects at rest and stress for seven cardiac regions (anterior, apical, anteroseptal, posteroseptal, anterolateral, posterolateral, and inferior walls) were graded on a 0 to 5 scale defined as normal (0), possible (1), probable (2), mild (3), moderate (4), and severe (5) defects. Coronary angiograms were used to measure absolute and relative stenosis dimensions and to calculate stenosis flow reserve defined as the maximum value of flow at maximum coronary vasodilatation relative to rest flow under standardized hemodynamic conditions. SFR scores ranged from 0 (total occlusion) to 5 (normal).

With increasing impairment of flow reserve, the subjective PET defect severity increased. A PET defect score of 2 or higher was positively correlated with flow reserve impairment (SFR<3).

## 15 REFERENCES

1. Annals of the ICRP. Publication 53. Radiation dose to patients from radiopharmaceuticals. New York: Pergamon Press, 1988.
2. Demer, L.L.K.L.Gould, R.A.Goldstein, R.L.Kirkeeide, N.A.Mullani, R.W. Smalling, A.Nishikawa, and M.E.Merhige. Assessment of coronary artery disease severity by PET: Comparison with quantitative arteriography in 193 patients. Circulation 1989; 79: 825-35.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

Ammonia N 13 Injection is packaged in 30 mL multiple dose glass vial containing between 1.11 GBq to 11.1 GBq (30 mCi to 300 mCi) of [13N] ammonia, at the end of synthesis (EOS) reference time, in 0.9% sodium chloride injection solution. The total volume in the vial will vary. The recommended dose of radioactivity (10-20 mCi) is associated with a theoretical mass dose of 0.05-0.1 picomoles (8.47-16.94 picograms) of Ammonia.

### Storage

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). Use the solution within 30 minutes of the End of Synthesis (EOS) calibration.

## 17 PATIENT COUNSELING INFORMATION

### 17.1 Pre-study Hydration

Instruct patients to drink plenty of water or other fluids (as tolerated) in the 4 hours before their PET study.

### 17.2 Post-study Voiding

Instruct patients to void after completion of each image acquisition session and as often as possible for one hour after the PET scan ends.

### 17.3 Post-study Breastfeeding Avoidance

Instruct nursing patients to substitute stored breast milk or infant formula for breast milk for 2 hours after administration of Ammonia N 13 Injection.

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