SIEMENS Healthineers

Left supraclavicular lymph node metastases from recurrent uterine carcinoma defined on ultra-fast* ^{18}F-FDG PET/CT performed on Biograph Vision Quadra

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Data and images courtesy of EMC Grha Kedoya Hospital, Jakarta, Indonesia



1 **MIP image of ^{18}F-FDG PET/CT scanned on Biograph Vision Quadra with head-to-toe acquisition of only 4 minutes shows multiple lymph node metastases from bilateral common iliac to para-aortic, mediastinal to left supraclavicular lymph nodes. These findings reflect nodal spread of metastases from uterine cancer from pelvis to thorax and cervical nodes via the thoracic duct.**

History

65-year-old woman with history of uterine carcinoma treated total hysterectomy with bilateral salpingo-oophorectomy, followed by chemo-radiation presented with suspected recurrence. Patient underwent Flude-oxyglucose F 18 Injection (^{18}F-FDG) PET/CT evaluation for metastatic spread and local recurrence.

Study was acquired 60 minutes following intravenous injection of 3.3 mCi F-FDG (0.05 mCi/kg)** on the Biograph Vision Quadra long axial field of view (aFOV) PET/CT scanner (106 cm aFOV). Total scan time was approximately 4 minutes (229 seconds) for head-to-toe acquisition. Low-dose, noncontrast CT was performed for attenuation correction. PET image reconstruction parameters were 4i5s, 440x440 matrix, all-pass.

* *Measured value, based on phantom studies performed on a single system. Biograph Vision Quadra has ≤249 ps based on acceptance values. Data on file.*

** *Based on bench testing (e.g. improved sensitivity and ToF per NEMA NU-2:2018). Please refer to the approved PET drug prescribing information for dosing and administration instructions.*

Fludeoxyglucose F 18 injection

Indications and usage

Fludeoxyglucose F 18 injection (^{18}F-FDG) 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.

IMPORTANT SAFETY INFORMATION

- **Radiation Risk:** 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 ensure at least two days of normoglycemia prior to Fludeoxyglucose F 18 injection administration.

- **Adverse Reactions:** Hypersensitivity reactions with pruritus, edema, and rash have been reported. Have emergency resuscitation equipment and personnel immediately available.

- **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.

DOSAGE FORMS AND STRENGTHS

Multiple-dose 30 mL and 50 mL glass vial containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL) 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.

- **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.

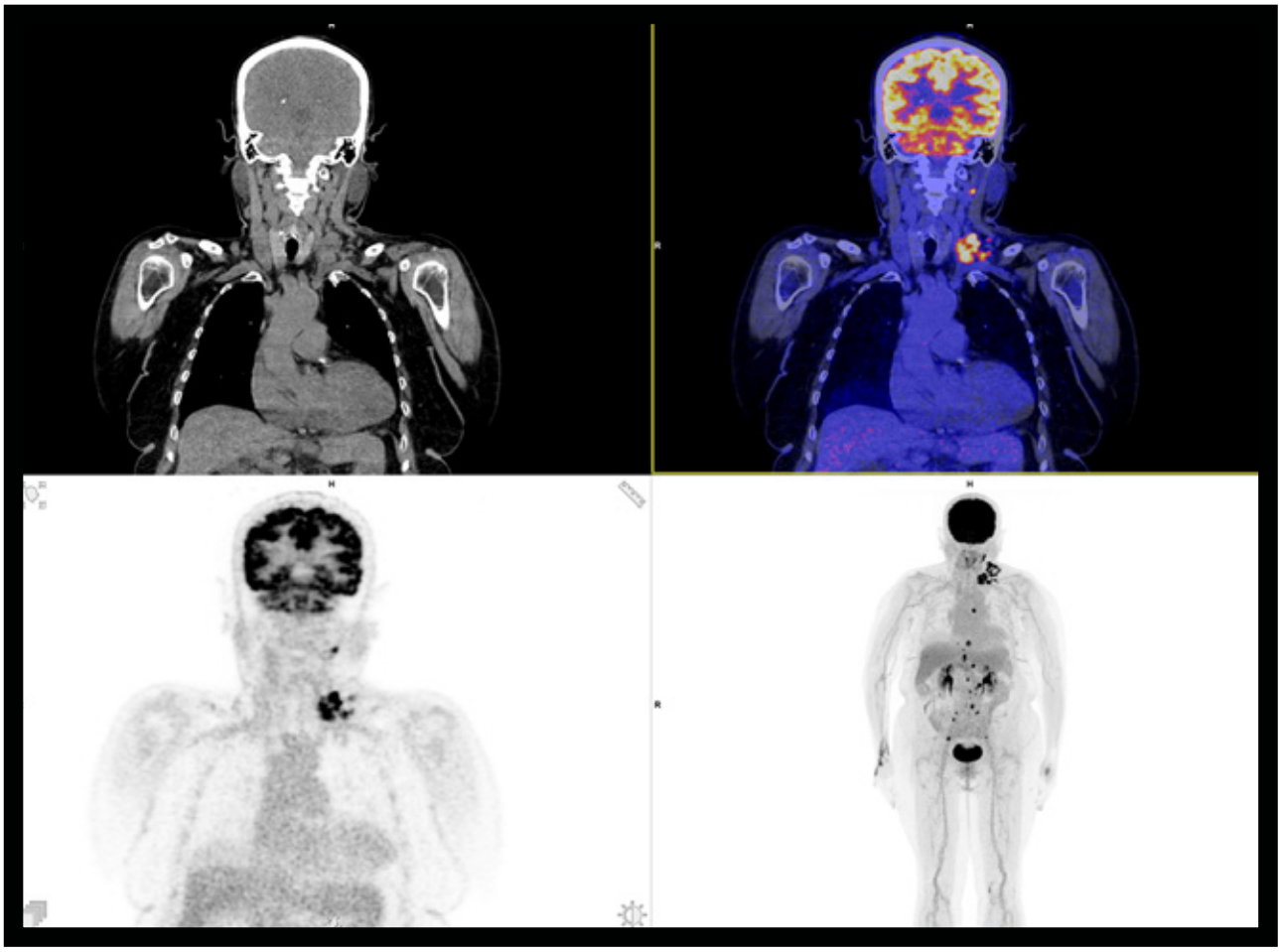
Fludeoxyglucose F 18 injection is manufactured and distributed by:
PETNET Solutions, Inc.
810 Innovation Drive
Knoxville, Tennessee 37932

Findings

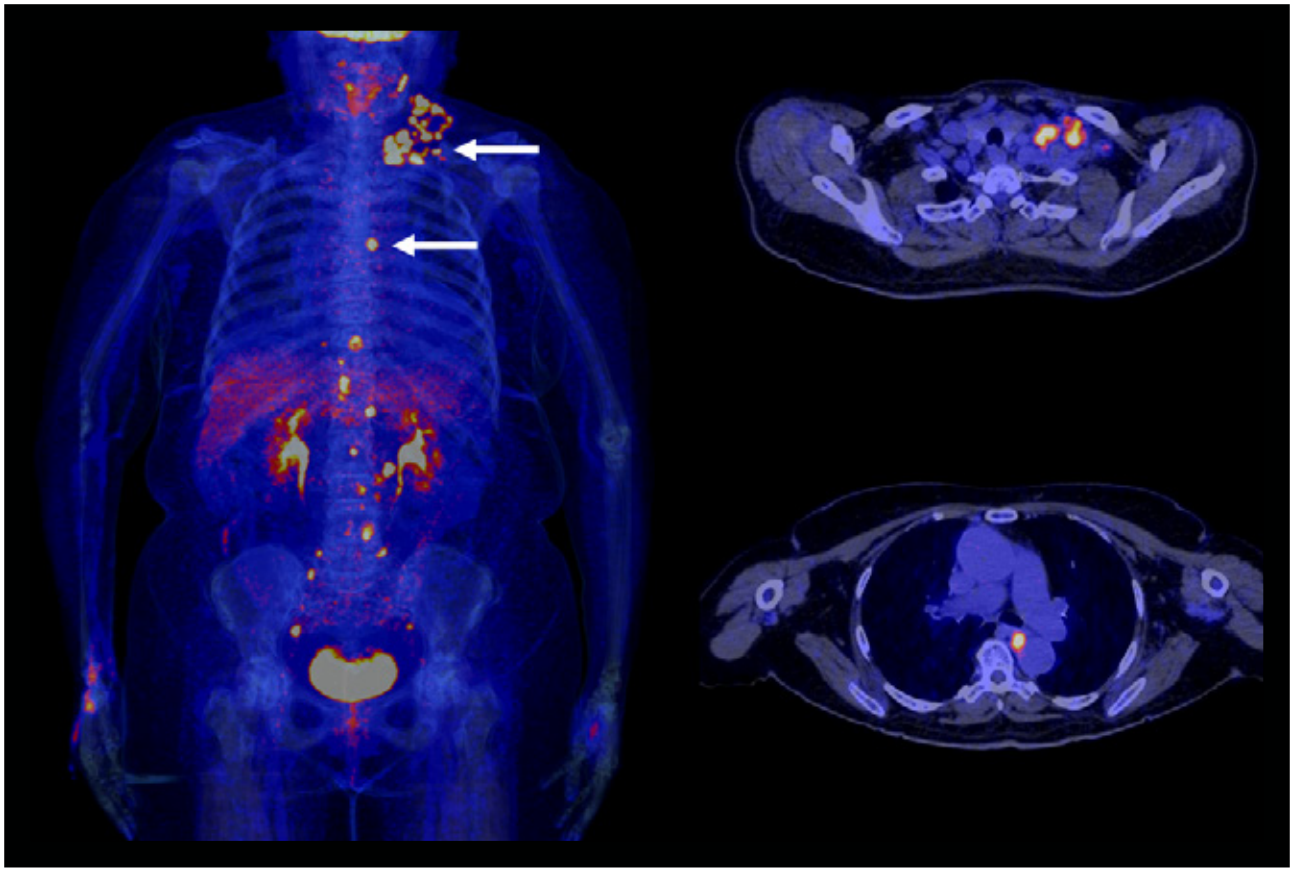
MIP image (Figure 1) shows high ^{18}F-FDG uptake in hypermetabolic lymph nodal mass in the left supraclavicualar and upper jugular region. Multiple ^{18}F-FDG-avid lymph nodes (SUV 5.1) are visualized in the left upper jugular region (level II, measuring approximately 1.7 × 0.6 cm), left lower jugular region (level IV, largest measuring approximately 1.5 × 1.3 cm), and most prominently, in the left posterior triangle (level V, largest measuring approximately 1.5 × 1.3 cm) (Figures 2 and 3).

MIP images also show focal hypermetabolic metastatic lymph nodes in the mediastinum, including the subcarinal (station 7, measuring approximately 1.5 × 1.2 cm) and paraesophageal region (station 8, largest measuring approximately 2.2 × 1.2 cm) (Figure 3). Multiple hypermetabolic nodal metastases are also visualized in the para-aortic region extending to bilateral common iliac arteries. Enlarged ^{18}F-FDG-avid lymph nodes (SUV 4.6) are defined in the retrocrural, para-aortic, aortocaval, and bilateral para-iliac regions (Figures 4 and 5), the largest node measuring approximately 1.3 × 1.1 cm in the para-aortic region.

No focal ^{18}F-FDG-avid lesion is visualized in the pelvis in the hysterectomy bed or pelvic wall or obturator nodes.



2 **CT, PET, and fused coronal images showing high ^{18}F-FDG uptake in the left supraclavicular lymph node mass as well as focal uptake in left upper jugular lymph node metastases. High lesion contrast within the small left upper jugular lymph nodal lesion reflects high system resolution, sensitivity, and time-of-flight performance of the Biograph Vision Quadra.**

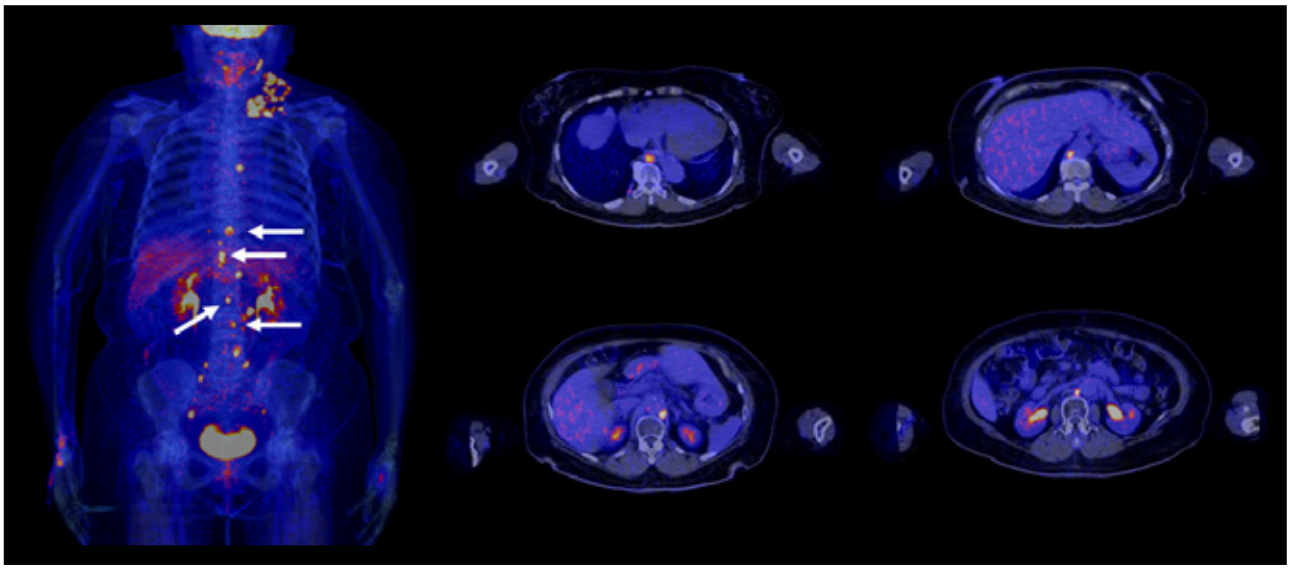


3 **Volume rendered fused PET/CT image as well as axial fused slices at the level of left supraclavicular and para-aortic thoracic lymph node metastases (white arrows) demonstrate high lesion contrast within small nodal lesions.**

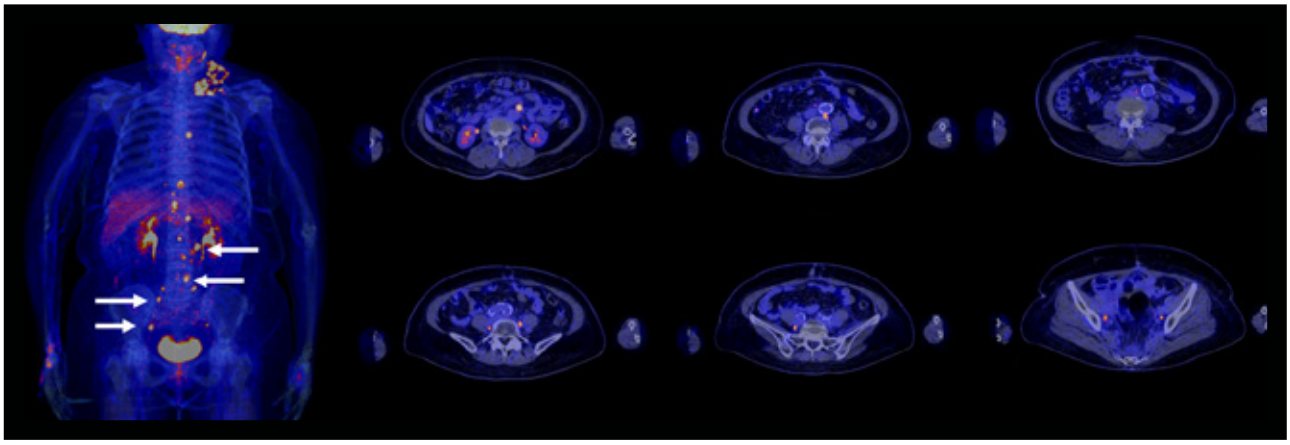
Discussion

The ^{18}F-FDG PET/CT images clearly show multiple lymph node metastases involving bilateral internal iliac nodes; para-aortic nodes in the abdomen and lower thorax; subcarinal and para-esophageal nodes in the thorax; and finally, in the metastatic lymph nodal mass in left supraclavicular and upper and mid jugular nodes in the neck. This reflects the pattern of lymph nodal metastatic spread from primary uterine malignancy to para-aortic, mediastinal, and left supraclavicular node (historically known as **Virchow's nodes**) via the thoracic duct.

As depicted in Figure 6, uterine tumor malignant spread initially via lymphatic channels to the iliac lymph nodes and subsequently, to the para-aortic and lumbar nodes and also the cisterna chyli. Subsequently, the malignant cells spread via the thoracic lymphatics which predominantly involve the thoracic duct. The thoracic duct connects to the systemic venous system in the neck at the junction of the left subclavian and internal jugular veins. Because of this connection, remote cancer cells often deposit in the left supraclavicular lymph nodes, as apparent from the PET images in this example. The high uptake of ^{18}F-FDG within the enlarged matted lymph nodal mass in the left supraclavicular region reflects the enlarged Virchow's node. Palpable left supraclavicular mass is often associated with advanced abdominal and pelvic malignancies like uterine and gastric carcinoma typically associated with Virchow's nodal metastasis presentation.



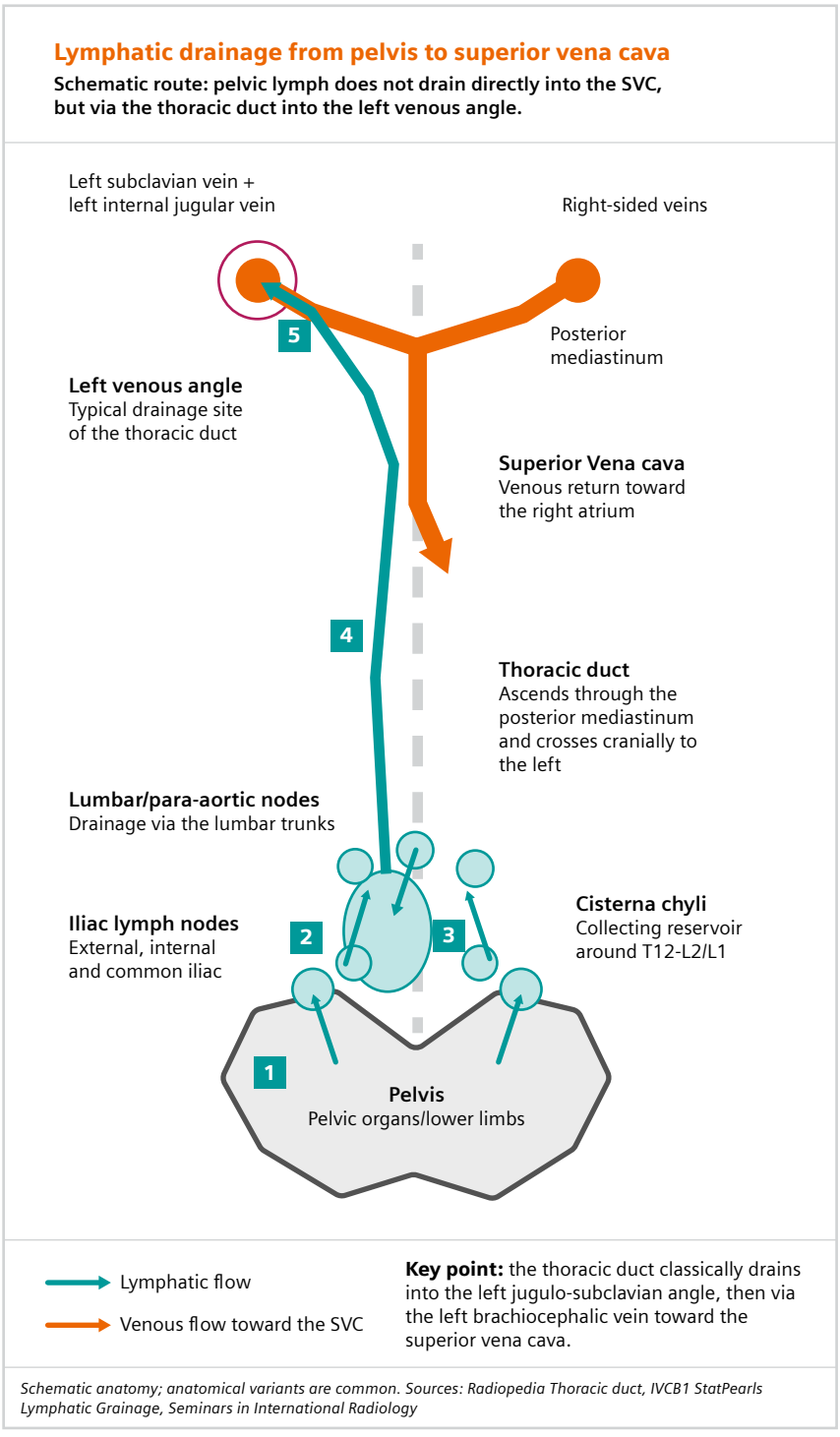
4 Axial fused slices at the level of lower thorax and upper abdomen show 4 separate hypermetabolic para-aortic nodal metastases which are indicated with white arrows in the volume rendered whole body image.



5 Multiple hypermetabolic lymph node metastases in abdominal para-aortic and bilateral common iliac group of lymph nodes visualized on axial fused image with corresponding lesions indicated with white arrows in the volume rendered whole body fused PET/CT image.

This clinical example shows hypermetabolic nodal lesions at every stage of the lymphatic metastatic spread. This includes lesions in bilateral common iliac, para-aortic, para-esophageal, left supraclavicular, and left upper jugular nodes, defining the spread from the uterine primary to the thorax and neck via thoracic duct.

^{18}F-FDG PET/CT shows high lesion contrast in hypermetabolic lymph nodal metastases despite ultra-fast acquisition time of just 4 minutes for a head-to-toe PET study (FlowMotion AI enables continuous movement and region-specific acquisition speeds; in this case, two zones with 3-minute acquisition for head-to-mid-thigh and 1 minute for lower extremities). The low injected dose (3.3 mCi)* achieved high lesion contrast, low background, and sharp vascular definition, reflecting the high sensitivity and resolution of the Biograph Vision Quadra. ●



6 **Illustration of lymphatic spread of uterine carcinoma metastases from tumor to iliac lymph nodes with subsequent spread to lumbar and para-aortic nodes with further spread into thorax and left supraclavicular region via the thoracic duct which drains into the left subclavian vein.**

* *Based on bench testing (e.g. improved sensitivity and ToF per NEMA NU-2:2018). Please refer to the approved PET drug prescribing information for dosing and administration instructions.*

Examination protocol

Scanners: Biograph Vision Quadra

PET	
Injected dose	122 MBq (3.3 mCi) ^{18}F-FDG
Post-injection delay	60 minutes
Acquisition time	Head to toe FlowMotion acquisition – 3.8 min total scan time
Reconstruction	UltraHD PET (PSF+TOF) 4i5s Gauss 2.0

CT	
Tube voltage	140 KvP Sn

The outcomes achieved by the Siemens Healthineers customers described herein were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption) there can be no guarantee that others will achieve the same results.

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

----------INDICATIONS AND USAGE----------
Fludeoxyglucose F 18 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 F 18 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 F 18 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 (96.2 MBq) 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 50 mL and 100 mL glass vial containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL) Fludeoxyglucose F 18 Injection, USP and 4.5 mg of sodium chloride with 0.1 to 0.5% w/w ethanol as a stabilizer (approximately 15 to 100 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.

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

- Lactation: Temporarily discontinue breastfeeding. A lactating woman should pump and discard breastmilk for 9 hours after Fludeoxyglucose F 18 Injection (8.2).
- 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: 07/2026

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Fludeoxyglucose F 18 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 F 18 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[2] data and using the data published by the International Commission on Radiological Protection[4] for Fludeoxyglucose ^{18}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[a]

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[b]	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

[a] MIRDOSE 2 software was used to calculate the radiation absorbed dose.
[b] 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 F 18 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 F 18 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 F 18 Injection from its container.
- Inspect Fludeoxyglucose F 18 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 50 mL and 100 mL glass vial containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL) of Fludeoxyglucose F 18 Injection, USP and 4.5 mg of sodium chloride with 0.1 to 0.5% w/w ethanol as a stabilizer (approximately 15 to 100 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 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

Risk Summary

Data from published case series and case reports describe Fludeoxyglucose F 18 Injection crossing the placenta with uptake by the fetus (see Data). All radiopharmaceuticals have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of the radiation dose. However, published studies that describe Fludeoxyglucose F 18 Injection use in pregnant women have not identified a risk of drug-associated major birth defects, miscarriage, or adverse maternal or fetal outcomes. If considering Fludeoxyglucose F 18 Injection administration to a pregnant woman, inform the patient about the potential for adverse pregnancy outcomes based on the radiation dose from Fludeoxyglucose F 18 Injection and the gestational timing of exposure.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies are 2-4% and 15-20%, respectively.

Data

Human Data

Data from published case series and case reports describe Fludeoxyglucose F 18 Injection crossing the placental barrier and visualization of radioactivity throughout the body of the fetus. The estimated fetal absorbed radiation dose from the maximum

labeled dose (370 MBq) of Fludeoxyglucose F 18 was 10 mGy with first trimester exposure to PET alone and 20 mGy with first trimester exposure to PET/CT scan combination. Long-term adverse radiation effects to a child exposed to Fludeoyxglucose F 18 Injection in utero are unknown. No adverse fetal effects or radiation-related risks have been identified for diagnostic procedures involving less than 50 mGy, which represents less than 20 mGy fetal doses.

8.2 Lactation

Risk Summary

A published case report and case series show the presence of Fludeoxyglucose F 18 Injection in human milk following administration. There are no data on the effects of Fludeoxyglucose F 18 Injection on the breastfed infant or the effects on milk production. Exposure of Fludeoxyglucose F 18 Injection to a breastfed infant can be minimized by temporary discontinuation of breastfeeding (see Clinical Considerations). The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Fludeoxyglucose F 18 Injection, any potential adverse effects on the breastfed child from Fludeoxyglucose F 18 Injection or from the underlying maternal condition.

Clinical Considerations

To decrease radiation exposure to the breastfed infant, advise a lactating woman to pump and discard breastmilk and avoid close (breast) contact with the infant for at least 9 hours after the administration of Fludeoxyglucose F 18 Injection.

8.4 Pediatric Use

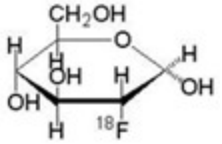
The safety and effectiveness of Fludeoxyglucose F 18 Injection in pediatric patients with epilepsy is established on the basis of studies in adult and pediatric patients. In pediatric patients with epilepsy, the recommended dose is 2.6 mCi. The optimal dose adjustment on the basis of body size or weight 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, USP 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-[^{18}F]fluoro-D-glucose has the molecular formula of $C_6H_{11}{}^{18}FO_5$ with a molecular weight of 181.26, and has the following chemical structure:



Fludeoxyglucose F 18 Injection, USP is provided as a ready to use sterile, pyrogen free, clear, colorless solution. Each mL contains between 0.740 to 7.40 GBq (20.0 to 200 mCi) of 2-deoxy-2-[^{18}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 has a physical half-life of 109.7 minutes and decays to Oxygen O 16 (stable) by positron decay. The principal photons useful for imaging are the dual 511 keV "annihilation" 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 Fluorine F 18

Radiation/Emission	% Per Disintegration	Mean Energy
Positron(β+)	96.73	249.8 keV
Gamma(±)*	193.46	511.0 keV

*Produced by positron annihilation
From: Kocher, D.C. Radioactive Decay Tables DOE/TIC-I 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 x 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%.

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

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.

Table 4. Physical Decay Chart for Fluorine F 18	
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 [^{18}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. 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 (±) 1.1 min, and 80 to 95 minutes with a mean and STD of 88 (±) 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. [^{18}F]-FDG-6-phosphate presumably is metabolized to 2-deoxy-2-[^{18}F]fluoro-6-phospho-D-mannose([^{18}F]FDM-6-phosphate).

Fludeoxyglucose F 18 Injection may contain several impurities (e.g., 2-deoxy-2-chloro-D-glucose (ClDG)). Biodistribution and metabolism of ClDG 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 (ClDG-6-phosphate) and 2-deoxy-2-chloro-6-phospho-D-mannose (ClDM-6-phosphate). The phosphorylated deoxyglucose compounds are dephosphorylated and the resulting compounds (FDG, FDM, ClDG, and ClDM) 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. Within 33 minutes, a mean of 3.9% of the administrated 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.

16 HOW SUPPLIED/STORAGE AND DRUG HANDLING

Fludeoxyglucose F 18 Injection, USP is supplied in a multi-dose, capped 50 mL and 100 mL

glass vial containing between 0.740 to 7.40 GBq/mL (20 to 200 mCi/mL), of no carrier added 2-deoxy-2-[^{18}F]-fluoro-D-glucose, at end of synthesis, in approximately 15 to 100 mL. The contents of each vial are sterile, pyrogen-free and preservative-free.

NDC 40028-511-50; 40028-511-99

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, USP 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, USP 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, USP 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.

Pregnancy: Advise pregnant women of the risk of fetal exposure to radiation with Fludeoxyglucose F 18 Injection [see Use in Specific Populations (8.1)].

Lactation: Advise lactating women that exposure to Fludeoxyglucose F 18 Injection through breast milk can be minimized by pumping and discarding breast milk and avoiding close (breast) contact with the infant for 9 hours after Fludeoxyglucose F 18 Injection [see Use in Specific Populations (8.2)].

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