PRODUCT MONOGRAPH

^{18}F-Fluorodeoxyglucose (^{18}F-FDG)

Parenteral Solution, > 0.5 GBq /mL

Diagnostic Radiopharmaceutical

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Table of Contents

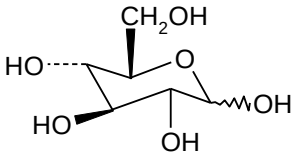
PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

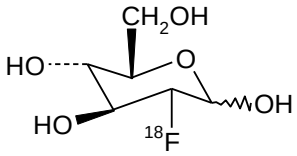
Route of Administration	Dosage Form / Strength	Clinically Relevant Non-medicinal Ingredients
Intravenous	Parenteral solution / > 0.5 GBq /mL in up to 30 mL	None

Fludeoxyglucose F 18 Injection is a positron-emitting radiopharmaceutical used as an accessory to Positron Emission Tomography (PET) for the assessment of abnormal glucose metabolism.

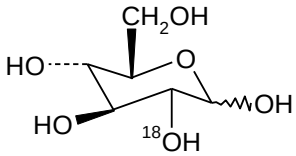
The active ingredient 2-deoxy-2-[^{18}F]fluoro-D-glucose, abbreviated [^{18}F]-FDG, differs from glucose only in having a radioactive fluorine (^{18}F) in the 2 position. The ^{18}F atom decays into ^{18}O, converting the molecule into D-[2-^{18}O]glucose , an isotopologue of glucose.



D-glucose



2-deoxy-2-[^{18}F]fluoro-D-glucose



D-[2-^{18}O]glucose

DESCRIPTION

Physical Characteristics

Fluorine F 18 decays by positron (β+) emission and has a half-life of 109.7 minutes. The fractions remaining at selected intervals after calibration are shown in Table 1.

Table 1. Physical Decay Chart for Fluorine ^{18}F

Time from Calibration	*15 min*	*30 min*	*45 min*	*60 min*	*75 min*	*90 min*	*120 min*	*150 min*	*180 min*	*210 min*	*240 min*
Fraction remaining	91%	83%	75%	68%	62%	57%	47%	39%	32%	27%	22%

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).

Table 2. Principal Emission Data for Fluorine ^{18}F

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

External Radiation

The specific gamma-ray constant for fluorine F 18 is 0.3 Gy/hr/kBq at 1cm. The narrow-beam attenuation half value layer is 4.1 mm for lead (and 3.4 cm for concrete). Broad-beam transmission factors at 511 keV for various thicknesses of lead are given in Table 3.

Table 3. Broad-beam transmission factors at 511 keV in lead

mm Pb	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*12*	*14*	*16*	*18*	*20*	*30*
Transmission	0.89	0.79	0.69	0.60	0.52	0.45	0.39	0.34	0.29	0.25	0.18	0.13	0.10	0.07	0.05	0.01

INDICATIONS AND CLINICAL USE

Fludeoxyglucose F 18 Injection is indicated as an accessory to positron emission tomography (PET) imaging, in patients with known or suspected abnormalities found by other testing modalities, for the assessment of abnormal glucose metabolism to assist in:

- The characterisation of solitary pulmonary nodules;
- The staging of lung cancer;
- The detection of recurrence in patients with previously diagnosed lung cancer; and
- The monitoring of the therapeutic response in patients with lung cancer.

The uptake of FDG is not cancer-specific. False-positives may occur in non-malignant areas of high metabolic activity, such as infection, inflammation, granulomatous reactions, and tissue repair. False negative results may occur in malignant tumors with low glycolytic activity, in tumors with large mucinous components, in some bronchioloalveolar carcinomas (*e.g.*, localized), in small-sized tumors (< 2 times system resolution), and in hyperglycemic states (See *Dosage and Administration, Image Interpretation*)

CONTRAINDICATIONS

^{18}F-FDG should not be administered to patients who are hypersensitive to fludeoxyglucose F18.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Radiopharmaceuticals should be used only by those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans.

^{18}F-FDG should not be administered to pregnant women unless it is considered that the benefits to be gained outweigh the potential hazards to the foetus.

There is little secretion of ^{18}F-FDG in breast milk but there is a high uptake of ^{18}F-FDG in a lactating, suckled breast. Where an assessment of the risk benefit ratio suggests the use of ^{18}F-FDG in nursing woman, breastfeeding should be discontinued, and close contact between mother and infant avoided, for a period of 12 hours following an FDG PET scan.

General

Precautions related to the handling of radioactive material must be observed in the handling and utilisation of this product including those concerning radioactive patients. Only those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans shall use radiopharmaceuticals.

The product should be administered under the supervision of a health professional who is experienced in the use of radiopharmaceuticals. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

The radiopharmaceutical product may be received, used and administered only by authorized persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of local competent official organizations.

As in the use of any other radioactive material, care should be taken to minimize radiation exposure to patients consistent with proper patient management, and to minimize radiation exposure to occupational workers.

Carcinogenesis and Mutagenesis

Studies with Fludeoxyglucose F 18 Injection have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility (see also *Pregnant women*, below).

Contamination

The following measures should be taken for up to 12 hours after receiving the radiopharmaceutical product: Toilet should be used instead of urinal. Toilet should be flushed several times after use.

Special precautions such as bladder catheterization should be taken following administration to incontinent patients to minimize the risk of radioactive contamination of clothing, bed linen and the patient's environment.

Endocrine and Metabolism

Use in patients with diabetes or hyperglycemia has not been well studied. It is recommended that patients be normoglycemic when undergoing PET imaging with Fludeoxyglucose F 18 Injection.

Transport of Fludeoxyglucose F 18 into cells may be affected by fasting or by blood glucose changes associated with diabetes mellitus. Diabetic patients may need stabilization of blood glucose levels on the day before and on the day of administration of Fludeoxyglucose F 18 Injection.

Special Populations

Pregnant Women: Ideally examinations using radiopharmaceuticals, especially those elective in nature of women of childbearing capability should be performed during the first ten days following the onset of menses.

Since adequate reproduction studies have not been performed in animals to determine whether this drug affects fertility in males or females, has teratogenic potential, or has other adverse reactions on the fetus, this radiopharmaceutical preparation should not be administered to pregnant women unless it is considered that the potential benefits outweigh the potential hazards to the fetus.

The fetus would receive a radiation dose of 10 mGy* from a 455 MBq maternal dose (7.5 MBq/kg to a 60 kg women). This level of radiation can increase the risk of leukemia and other cancers by 40%.[1] The use of a lower dose of [^{18}F]-FDG, maternal hydration, and frequent voiding can reduce the radiation dose to the fetus.

Nursing Women: There is little secretion of Fludeoxyglucose F 18 in breast milk but there is a high uptake of Fludeoxyglucose F 18 in a lactating, suckled breast[2]. A higher radiation dose is received by the infant from close contact with the breast than from ingestion of radioactive milk. Breastfeeding should be discontinued, and close contact between mother and infant avoided, for a period of 12 hours following an FDG PET scan.

Pediatrics: The safety and effectiveness of Fludeoxyglucose F 18 Injection in the approved indication has not been established in pediatric patients. Fludeoxyglucose F 18 injection has been safely and effectively used in pediatric patients for the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

Geriatrics: Geriatric patients were included in the studies demonstrating the efficacy and safety of [^{18}F]-FDG in the approved indication. There are no known limitations on the clinical use of Fludeoxyglucose F 18 Injection in geriatric patients.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

A systematic review of the published literature, publicly available reference sources, and adverse drug reaction reporting systems indicated that adverse reactions have not been reported for Fludeoxyglucose F 18 Injection.

In a large published study in 22 PET centres, no adverse reactions to positron-emitting radiopharmaceuticals, primarily ^{18}F-FDG, were reported retrospectively for 33,295 doses and prospectively for 47,876 doses.[3]

Clinical Trial Adverse Drug Reactions

> *Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates*.

In a 7,710-patient prospective clinical trial, no adverse reactions attributable to FDG were reported.

Less Common Clinical Trial Adverse Drug Reactions (<1%)

In a 7,710-patient prospective clinical trial, there were 6 reports of skin rash (6/7710; 0.08%), without pruritus or other accompanying signs or symptoms, all reported 24 hours after the procedure. A relationship to FDG can neither be inferred nor denied.

* Fetal dose is estimated at 2.2 x 10^{-2} mGy/MBq; see Radiation Dosimetry below

Abnormal Hematologic and Clinical Chemistry Findings
Not applicable.

Post-Market Adverse Drug Reactions
Not applicable.

DRUG INTERACTIONS

Interactions with drugs, food, herbs, and laboratory tests have not been established.

DOSAGE AND ADMINISTRATION

Dosing considerations

Patients should fast for at least 4 hours prior to dosing. Blood glucose should be assessed prior to dosing. Hyperglycemic patients should have their blood glucose level normalized prior to dosing.

Patients should be well hydrated and should be encouraged to drink sufficient amounts of water to permit frequent bladder emptying, especially immediately prior to and after the PET examination.

Patients should avoid all strenuous physical activity prior to the examination and remain at rest between the injection and examination.

Dosage

The optimal dose of [^{18}F]-FDG has not been systematically investigated and may vary according to the imaging equipment used, the delay from administration to imaging, and to patient characteristics. The usual recommended adult dose is 7.5 MBq/kg (370 to 740 MBq).

Administration

The dose of [^{18}F]-FDG should be measured by a suitable radioactivity calibration system prior to intravenous administration. The intravenous injection should be on the contralateral side to the site of concern.

Image Acquisition and Interpretation

Image acquisition parameters and procedures will vary depending upon the clinical question and the type of equipment available.

The optimal time from dosing to imaging has not been systematically investigated. Images are generally acquired 30 to 60 minutes after the administration of ^{18}F-FDG but later imaging times are also frequently used.

Only experienced nuclear medicine physicians familiar with the normal and condition-specific physiological and anatomical variants of ^{18}F-FDG biodistribution should interpret ^{18}F-FDG-PET images.

Physicians should be aware of patient preparation anomalies (*e.g.*, marginally acceptable blood glucose level and heightened anxiety state), and relevant patient history (*e.g.* recent and current health problems, recent surgeries and radiation treatments, menstrual and lactation status).

The uptake of [^{18}F]-FDG is not cancer-specific. False positive findings may occur in non-malignant areas of high metabolic activity, such as infection (mycobacterial, fungal, bacterial infection), inflammatory and especially granulomatous reactions (*e.g.*, bronchiectasis, sarcoidosis, pleurodesis, radiotherapy sites, and active atheromas) and tissue repair (trauma, post- surgery).

False-negatives have been reported in tumors with low glycolytic activity (*e.g.*, adenomas; bronchioloalveolar, mucinous, and lobular carcinomas; carcinoid tumors, and fibroadenoma), and in small-sized tumors (< 1 cm). [^{18}F]-FDG competes with blood glucose for uptake; increased levels of blood glucose can interfere with the uptake of [^{18}F]-FDG by malignant cells and result in false negative findings.

Instructions for Preparation and Use

The components of the vial are sterile and non-pyrogenic. It is essential that the user follows the directions carefully and adheres to strict aseptic technique. Use aseptic technique and wear waterproof gloves throughout the entire preparation procedure. Make all transfers of radioactive solutions with an adequately shielded syringe and maintain adequate shielding around the vial during the useful life of the radioactive product.

Directions for Quality Control

The required quality control testing has been performed on the product prior to release.

RADIATION DOSIMETRY

Based on ICRP 80, the effective dose resulting from the administration of 555 MBq of ^{18}F-FDG is 10.5 mSv. The whole-body dose, based on MIRD dose estimates, is 6.7 mGy.

For the critical organs bladder, heart, and brain, the (MIRD) estimated absorbed radiation doses from 555 MBq of ^{18}F-FDG are, respectively, 41 mGy, 38 mGy, and 26 mGy.

The estimated absorbed radiation doses are shown in Table 4.

Table 4. Estimated Absorbed Radiation Doses after IV ^{18}FDG

Target organ	mGy/MBq	rad/mCi
Brain	0.046± 0.012	0.170± 0.044
Heart wall	0.068± 0.036	0.250± 0.130
Kidneys	0.021± 0.0059	0.078± 0.022
Liver	0.024± 0.0085	0.088± 0.031
Lungs	0.015± 0.0084	0.056± 0.031
Pancreas	0.014± 0.0016	0.052± 0.0060
Red marrow	0.011± 0.0017	0.040± 0.0062
Spleen	0.015± 0.0021	0.056± 0.0078
Urinary bladder wall	0.073± 0.042	0.270± 0.160
Ovaries	0.011± 0.0015	0.041± 0.0055
Testes	0.011± 0.0016	0.041± 0.0057
Whole body	0.012± 0.00077	0.043± 0.0023

MIRD Dose Estimate Report No. 19[4]

The fetal dose estimates are: 2.2 x 10^{-2} mGy/MBq in early pregnancy and at 3-months gestation, and 1.7 x 10^{-2} mGy/MBq at 6 and 9 months gestation.[5]

OVERDOSAGE

Cases of overdose are not known to have occurred with Fludeoxyglucose F 18. In case of overdose, the patient should be monitored and managed as clinically indicated.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

^{18}F-FDG is transported in a manner similar to glucose from blood to tissue where it is phosphorylated by hexokinase to ^{18}F-FDG-6-phosphate. As ^{18}F-FDG-6-phosphate is not a substrate for subsequent glycolytic pathways, and has very low membrane permeability, ^{18}F-FDG becomes trapped in tissue in proportion to the rate of glycolysis or glucose utilisation of that tissue. Imaging of the subject using a positron emission tomography (PET) scanner takes advantage of the positron decay of ^{18}F to identify those tissues that have an abnormal accumulation of the radioisotope.

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

Pharmacodynamics

At the concentrations used for diagnostic examinations, [^{18}F]-FDG does not have any pharmacodynamic activity.

Pharmacokinetics

Distribution:

FDG is widely distributed in the body following intravenous administration and equilibrates quickly between plasma and erythrocytes.[6] The brain, heart, and liver show the highest accumulation. The brain contains 3.9% of injected activity 33 minutes after dosing[7] and 6.9% of cumulated activity.[8] Other cumulated activities are urinary bladder, 6.3%; liver, 4.4%; heart, 3.3%; kidney, 1.3%; lung, 0.9%; spleen 0.4%; and pancreas 0.3%. Based on these results, cumulated activities have been estimated for red marrow, 1.7%; testes, 0.4%; and ovaries, 0.01%. The majority of FDG distribution at 90 minutes is in tissues other than the blood, brain, heart and liver. These other tissues (probably the skeletal muscle and gut) become increasingly important with time and account for approximately 75% of the cumulated activity.[6]

Mean residence times have been calculated from human data for plasma, 0.17 ± 0.06; erythrocytes, 0.10 ± 0.03; heart, 0.13 ± 0.06; lungs, 0.08 ± 0.03; liver, 0.16 ± 0.06; whole brain, 0.24 ± 0.09; and bladder, 0.04 ± 0.017, with voids at 0.5, 1, 2, then every 2 hours. Whole body residence time is 2.41 ± 0.09.[6]

Metabolism:

^{18}F-FDG is phosphorylated to ^{18}F-FDG-6-phosphate by hexokinase, with no further metabolism taking place.

Excretion:

^{18}F-FDG is mostly excreted unchanged in the urine; approximately 20% of the administered activity is recovered in the urine within the first 2 hours.[7,8]

Special Populations and Conditions

No data available.

STORAGE AND STABILITY

Fludeoxyglucose F 18 Injection should be stored upright in a lead shielded container at controlled room temperature. Fludeoxyglucose F 18 Injection should be used within 12 hours from the time of the end of synthesis.

SPECIAL HANDLING INSTRUCTIONS

As in the use of any other radioactive material, care should be taken to minimize radiation exposure to

patients consistent with proper patient management, and to minimize radiation exposure to occupational workers.

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 radionuclide, and whose experience and training have been approved by the appropriate governmental agency authorised to license the use of radionuclides.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Fludeoxyglucose F 18 Injection is supplied in a multi-dose, septum-caped, 30 mL, glass vial containing at least 0.5 GBq /mL (>18.5 mCi)) of no carrier added 2-deoxy-2-[^{18}F]fluoro-D-glucose, at end of synthesis, in up to 30 mL.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

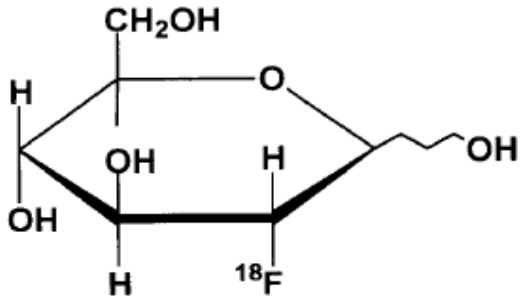
Proper name: Fludeoxyglucose ^{18}F

Chemical name: 2-Deoxy-2-fluoro-D-glucose

Molecular formula: $C_6H_{11}{}^{18}FO_5$

Molecular mass: 181.26 daltons

Structural formula:



Physicochemical properties: clear, colorless solution.

Product Characteristics

Fludeoxyglucose F18 Injection is provided as a ready to use sterile, clear, colorless solution. Each mL contains at least 0.5 GBq (18.5 mCi) of 2-deoxy-2-[^{18}F]fluoro-D glucose at the end of synthesis (EOS). The pH of the solution is between 4.5 to 7.5. The solution is packaged in a multiple-dose glass vial and does not contain any preservative.

CLINICAL TRIALS

Isologic conducted a single clinical trial in over 7,700 patients in a variety of oncology, neurology, and cardiovascular indications. The most common indications were the characterization of solitary pulmonary nodules (SPN), the staging and localization of lung cancer, and the diagnosis of relapse of lung cancer.

A sub-group of 138 patients who underwent [^{18}]-FDG-PET for investigation of solitary pulmonary nodules was selected for 'efficacy' analysis. The criteria for selection were that there be an acceptable "truth standard" to support the diagnosis, and that the patient's clinical follow-up be at the same institution.

The mean (± sd) dose of ^{18}FDG was 524 ± 114 MBq, or 7.5 ± 0.6 MBq/kg. The mean time from dosing to imaging was 87.1 ± 20.8 minutes. The pulmonary nodules assessed had a mean (±sd) size of 2.6 ± 1.7

cm. The smallest nodule was 0.8 cm and the largest was 8.3 cm. The overall prevalence of malignancy in this patient population was 71.0%.

The "truth standard" was established by histopathology in 77% of patients; CT follow-up in 15%; X-ray follow-up in 4%, and clinical follow-up in 4%. X-ray, CT, and clinical follow-up of negative cases were generally for a period of 2 or more years.

FDG-PET was 98% sensitive for the detection of malignancy in patients with solitary pulmonary nodules. There were only two false negatives in this sample of 138 patients. One lesion was a 1.1 cm metastasis of an adenocarcinoma and the other was a 2.0 cm bronchoalveolar cell carcinoma.

Specificity was 77.5%. The nine false positives included one case each of bronchiolitis obliterans with organizing pneumonia (BOOP); lipid pneumonia; granulotamous inflammation; silico-anthracotic nodules; non-necrotizing granuloma and bronchiectasis; and pulmonary granulomatous reaction. In the two remaining cases, the pathology was either non-existent or not described.

Table 4. Diagnostic Performance

	Mean	$CI_{95\%}$ LL	$CI_{95\%}$ UL
Sensitivity	98.0% (96/98)	92.1%	99.6%
Specificity	77.5% (31/40)	61.1%	88.6%
PPV	91.4%	83.9%	95.8%
NPV	93.9%	78.4%	98.9%
Accuracy	92.0%	85.9%	95.8%

These results are essentially identical to the results of a meta-analysis published by Gould, of 31 studies of FDG-PET in a total of 1474 focal pulmonary lesions[9]. Gould concluded: "In current practice, FDG-PET operates at a point on the summary receiver operating characteristic curve that corresponds approximately to a sensitivity and specificity of 96.8% and 77.8%.

An earlier tabulated summary of the FDG-PET literature was compiled by Gambhir.[10] For the diagnosis of lung disease, Ghambir's review included 23 publications in a total of 1255 patients. He reported an overall sensitivity of 96% and a specificity of 73%.

DETAILED PHARMACOLOGY

The hydroxyl group of the second carbon of glucose can be substituted by a group such as hydrogen or fluorine without seriously compromising the kinetic and biochemical ability of the molecule to be actively transported through the cell membrane and to act as a substrate for the hexokinase enzyme. The 2-deoxy analogues of glucose are transported into the cell and metabolized quantitatively exactly like D-glucose up the point in the glycolytic pathway where its anomalous structure prevents the final conversion of the 2-deoxyglucose-6-phosphate by phosphohexoseixomeriase.[11]

In mice, ^{18}F-FDG distributes uniformly to the kidneys, heart, brain, lungs and liver initially and clears rapidly from all tissue except the heart where it remains constant for at least 2 hours and, to a lesser extent, in the brain where it decreases slowly from 1 to 2 hours.[12,13] The rapid clearance of ^{18}F-FDG from the liver, lungs and kidneys, and its retention by the heart and brain is a result of metabolic trapping within these organs and is reflective of glucose utilisation. Urinary excretion of intact ^{18}F-FDG was 15-25% of injected dose at 90 minutes.

In mice, FDG accumulates in organs and fluids as parent FDG (or FDG-6-phosphate) and FD-Mannose (or FD-Mannose-6-phosphate) and is excreted in the urine in both forms.[14]

In rats, the percentages of ^{18}F-FDG and ^{18}F-FDG-6-phosphate 45 minutes after injection were 68 and 33%, respectively in the liver; and 70 and 27%, respectively, in the kidney.[15]

In mice bearing C3H mammary carcinoma the predominant metabolite observed in the tumour at 180 minutes was ^{18}F-FDG-6-phosphate, with measurable quantities of other phosphorylated species. [16]

TOXICOLOGY

'Cold' 2-deoxy-2-fluoro-D-glucose had an LD_{50} of 600 mg/kg in both mice and rats when given by intraperitoneal injection in 5 or 6 consecutive daily doses.[17] .

Toxicity studies in mice given three doses of 14.3 mg/kg of FDG did not reveal any immediate or long-term effects as determined by routine observations, changes in body weight, and gross and histopathology of the internal organs. Toxicity studies in dogs injected with three doses of 0.72 mg/kg of FDG did not show any immediate or long-term effects. No significant abnormalities were detected in blood, urine, or CSF analyses, and no significant gross or microscopic abnormalities were detected in the heart, brain, spleen, liver, kidneys, lungs, ovaries, or intestines. [18].

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether ^{18}F-FDG affects fertility in males or females.

As with other radiopharmaceuticals that distribute intracellularly, there may be increased risk of chromosome damage from Auger electrons if nuclear uptake occurs.

REFERENCES

1 International Commission on Radiological Protection. Pregnancy and Medical Radiation. ICRP Publication 84. Annals of the ICRP 2000;30(1):1

2 Hicks RJ, Binns D, Stabin MG. Pattern of uptake and excretion of (18)F-FDG in the lactating breast. J Nucl Med. 2001 Aug;42(8):1238-42.

3 Silberstein EB. Prevalence of adverse reactions to positron emitting radiopharmaceuticals in nuclear medicine. Pharmacopeia Committee of the Society of Nuclear Medicine. J Nucl Med. 1998 Dec;39(12):2190-2

4 Hays MT, Watson EE, Thomas SR, Stabin M. MIRD dose estimate report no. 19: radiation absorbed dose estimates from (18)F-FDG. J Nucl Med 2002;43:210-4

5 Stabin MG. Proposed Addendum to Previously Published Fetal Dose Estimate Tables for ^{18}F-FDG. J Nucl Med 2004; 45:634–635

6 Hays MT, Segall GM. A mathematical model for the distribution of fluorodeoxyglucose in humans. J Nucl Med. 1999 Aug;40(8):1358-66.

7 Jones SC, Alavi A, Christman D, Montanez I, Wolf AP, Reivich M. The radiation dosimetry of 2 [F-18]fluoro-2-deoxy-D-glucose in man. J Nucl Med. 1982 Jul;23(7):613-7

8 Mejia AA, Nakamura T, Masatoshi I, Hatazawa J, Masaki M, Watanuki S. Estimation of absorbed doses in humans due to intravenous administration of fluorine-18-fluorodeoxyglucose in PET studies. J Nucl Med. 1991 Apr;32(4):699-706.

9 Gould MK, Maclean CC, Kuschner WG, Rydzak CE, Owens DK. Accuracy of positron emission tomography for diagnosis of pulmonary nodules and mass lesions: a meta-analysis. JAMA. 2001 Feb 21;285(7):914-24.

10 Gambhir SS, Czernin J, Schwimmer J, Silverman DH, Coleman RE, Phelps ME. A tabulated summary of the FDG PET literature. J Nucl Med. 2001 May;42(5 Suppl):1S-93S

11 Pauwels EKJ, Sturm EJC, Bombardieri E, Cleton FJ, Stokkel MPM. Positron-emission tomography with [18F]fluorodeoxyglucose: Part I. Biochemical uptake mechanism and its implication for clinical studies J Cancer Res Clin Oncol 2000;126:549-59.

12 Gallagher BM, Fowler JS, et al. Metabolic trapping as a principle of radiopharmaceuticals design: Some factors responsible for the biodistribution of [18F] 2-deoxy-2-fluoro-D-glucose. J Nucl Med 1978;19:1154-61.

13 Gallagher BM, Ansari A, Atkins H, et al., Radiopharmaceuticals XXVII. 18F-labelled 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.

14 Kanazawa Y, Momozono Y, Ishikawa M, et al. Metabolic pathway of 2-deoxy-2-fluoro-D-glucose studied by F-19 NMR. Life Sciences 1986;39:737-42

15 Suolinna E-M, Haaparanta M, Paul R, et al. Metabolism of 2-[18F]fluoro-2-deoxyglucose in tumor-bearing rats: Chromatographic and enzymatic studies. Nucl Med Biol 1986;13:577-81.

16 Kaarstad K, Bender D, Bentzen L, et al. Metabolic fate of 18F-FDG in mice bearing either SCCVII squamous cell carcinoma or C3H mammary carcinoma. J Nucl Med 2002; 43:940-7.

17 Bessell EM, Courtney VD, Foster AB, et al. Some in vivo and in vitro antitumor effects of the deoxyfluoro-D-glucopyranoses. Eur J Cancer 1973;9:463-70.

18 Reivich M, Kuhl D, Wolf A, Greenberg J, Phelps M, Ido T, Casella V, Fowler J, Hoffman E, Alavi A, Som P, Sokoloff L. The [18F]fluorodeoxyglucose method for the measurement of local cerebral glucose utilization in man. Circ Res. 1979 Jan;44(1):127-37.

PART III: CONSUMER INFORMATION

Fludeoxyglucose ^{18}F Injection

This leaflet is part III of a three-part "Product Monograph" published when Fludeoxyglucose ^{18}F Injection was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Fludeoxyglucose ^{18}F Injection. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
Fludeoxyglucose ^{18}F Injection, or FDG, is used to study how different tissues in your body are using blood sugar (glucose). The approved use is to study abnormalities found in the lung by other tests (e.g., chest x-ray).

What it does:
Fludeoxyglucose ^{18}F Injection behaves just like blood sugar (glucose) but because it has a radioactive atom, its behavior can be followed with a special camera (PET).

When it should not be used:
FDG should not be used in patients allergic to FDG.

What the medicinal ingredient is:
Fludeoxyglucose ^{18}F

What the important non-medicinal ingredients are:
There are no important non-medicinal ingredients.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions
Fludeoxyglucose 18F Injection should be used only by those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans.

^{18}F-FDG should not be administered to pregnant women unless it is considered that the benefits to be gained outweigh the potential hazards to the foetus.

Breastfeeding should be discontinued, and close contact between mother and infant avoided, for a period of 12 hours following an FDG PET scan.

BEFORE you receive Fludeoxyglucose ^{18}F Injection talk to your doctor or pharmacist if you think you might be pregnant or if you are diabetic.
^{18}F-FDG is not present in dangerous amounts in breast milk but high radioactivity is present in the breast tissue. Breastfeeding should be discontinued, and close contact between mother and infant avoided, for a period of 12 hours following an FDG PET scan.
To help eliminate Fludeoxyglucose ^{18}F Injection quickly after the procedure, you should drink a large glass of water and urinate frequently after you receive the injection. Males should use a toilet rather than a urinal. Toilets should be flushed several times. Hands should be thoroughly washed. If blood, urine or feces soil clothing, the clothing should be washed separately from other clothing.

INTERACTIONS WITH THIS MEDICATION

Drug-drug interactions with Fludeoxyglucose F 18 Injection have not been evaluated.

PROPER USE OF THIS MEDICATION

This product will be administered under the supervision of a health professional who is experienced in the use of radiopharmaceuticals.

Diabetic patients should ensure that their blood sugar levels are stable the day preceding and the day of the PET scan with 18F-FDG product.

You may be asked to eat nothing and drink only water for four hours before your scheduled PET scan with I8F-FDG product.

To decrease the radiation exposure to your bladder, you should drink plenty of water and urinate as often as possible when the PET scan is finished.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Fludeoxyglucose F 18 Injection is called a 'tracer' meaning that it is given in very small doses and has no activity of its own. Other than possible adverse reactions related to receiving an injection, adverse reactions have not been reported for Fludeoxyglucose F 18 Injection.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Reporting Side Effects
You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-

declaration/index-eng.php) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor, Isologic Innovative Radiopharmaceuticals Ltd at 877-636-5552.

This leaflet was prepared by Isologic Innovative Radiopharmaceuticals Ltd.

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