PRODUCT MONOGRAPH

FluGlucoScan™ Injection

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

Parenteral Solution / >0.5 GBq / vial

Diagnostic Radiopharmaceutical

Alberta Cancer Board
Standard Life Center
1220 – 10405 Jasper Avenue
Edmonton, AB T5J 3N4
Control #112722

Date of Approval :

October 2, 2007

Table of Contents

PART I: HEALTH PROFESSIONAL INFORMATION 3
SUMMARY PRODUCT INFORMATION 3
DESCRIPTION 3
INDICATIONS AND CLINICAL USE 5
CONTRAINDICATIONS 5
WARNINGS AND PRECAUTIONS 5
ADVERSE REACTIONS 7
DRUG INTERACTIONS 8
DOSAGE AND ADMINISTRATION 8
RADIATION DOSIMETRY 11
ACTION AND CLINICAL PHARMACOLOGY 12
OVERDOSAGE 14
STORAGE AND STABILITY 14
SPECIAL HANDLING INSTRUCTIONS 14
DOSAGE FORMS, COMPOSITION AND PACKAGING 14

PART II: SCIENTIFIC INFORMATION 15
PHARMACEUTICAL INFORMATION 15
CLINICAL TRIALS 17
DETAILED PHARMACOLOGY 23
TOXICOLOGY 24
REFERENCES 25

PART III: CONSUMER INFORMATION 26

FluGlucoScan ™[1] Injection

^{18}F - Fluorodeoxyglucose

PART I: HEALTH PROFESSIONAL INFORMATION

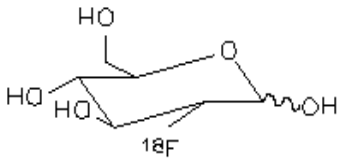
SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Intravenous	Parenteral Solution / > 0.5 GBq/vial	Citrate buffer and / or Sodium Chloride, Water

DESCRIPTION

FluGlucoScan (^{18}F - Fluorodeoxyglucose; ^{18}F - FDG) Injection is an intravenous diagnostic radiopharmaceutical for Positron Emission Tomography (PET).

The chemical name of the active ingredient in FluGlucoScan Injection is 2-deoxy-2-^{18}F-fluoro-D-glucose, which has a molecular formula of $C_6H_{11}{}^{18}FO_5$ with a molecular weight of 181.1 daltons and the following chemical structure:



FluGlucoScan Injection is supplied as a multi-dose (20 mL), sterile, non-pyrogenic injection vial containing a calibrated amount of ^{18}F - FDG in approximately 16 mL of citrate buffer and / or saline without preservatives. The pH of the solution is between 4.5 and 7.5.

[1] FluGlucoScan™ is a trademark owned by the Alberta Cancer Board.

Physical Characteristics

The radionuclide present in the drug substance is fluorine-18 (^{18}F), which decays by positron ($ß^{+}$) emission with a half life of 109.7 minutes. The daughter product of this process is the stable radionuclide, oxygen-18 (^{18}O). The physical radiation emission data for fluorine-18 are summarised in Table 1.

Table 1 Principle Emission Data for Fluorine-18

Radiation Emission	Percentage per Disintegration	Mean Energy (keV)
Positron ($ß^{+}$)	96.9	249.8
Gamma (γ)*	193.8	511.0

* produced by positron annihilation

External Radiation

The specific gamma ray constant for Fluorine F18 is 0.3 (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 listed in Table 2. To correct for the physical decay of this radionuclide, the fractions remaining at selected intervals after calibration are shown in Table 3.

Table 2 Radiation Attenuation of 511 keV Photons by Lead Shielding

Shield Thickness (Pb) (mm)	Coefficient of Attenuation
0	0.00
4.1	0.50
8.3	0.25
13.2	0.10
26.4	0.01
52.8	0.001

Table 3 Physical Decay Chart for Fluorine-18

Minutes (Calibration time)	Fraction Remaining
0	1.00
15	0.909
30	0.826
60	0.683
110	0.500
220	0.250
440	0.060

INDICATIONS AND CLINICAL USE

FluGlucoScan Injection is indicated in Positron Emission Tomography (PET) for diagnostic use in patients for:

(1) the evaluation of pulmonary nodules to distinguish benign from malignant and the evaluation of non-small cell and small cell lung cancers for staging and restaging and;

(2) the evaluation of colorectal cancer for recurrence, restaging, and distant metastases.

For lung cancer evaluation, certain thoracic area non-cancerous lesions may show FluGlucoScan Injection uptake including acute and chronic infections (such as abscesses, tuberculosis and histoplasmosis), and inflammatory / granulomatous conditions (such as sarcoidosis, bronchiectasis, or post radiotherapy sites) that could mimic tumour accumulation. Absent or less intense relative uptake of FluGlucoScan Injection may be observed in specific lesions including bronchoalveolar, mucinous and lobular carcinoma as well as carcinoid and fibroadenoma sites.

For colorectal cancer evaluation, certain abdominal / pelvic area non-cancerous lesions may show FluGlucoScan Injection uptake including sites of post radiation or post surgical inflammatory response, lesion site flare following chemotherapy, colonic adenomas and bladder diverticula that could mimic tumour accumulation. Absent or less intense relative uptake of FluGlucoScan Injection may be observed in specific lesions including mucinous carcinoma.

Lesion size may also affect detectability based on relative ^{18}F-FDG accumulation and PET imaging system resolution, as it has been shown that ^{18}F-FDG PET imaging may have a lower sensitivity in evaluating lesion sizes of less than 1 cm.

CONTRAINDICATIONS

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing of ingredients, see the Dosage Forms, Composition and Packaging section of the product monograph.

WARNINGS AND PRECAUTIONS

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

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.
- FluGlucoScan Injection should not be administered to pregnant women unless it is considered that the benefits to be gained outweigh the potential hazards to the fetus.
- Where an assessment of the risk benefit ratio suggests the use of FluGlucoScan Injection in nursing women, formula feeding should be substituted for breast feeding for a period of 24 hours following the PET scan.

General

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 authorised 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 organisations.

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

FluGlucoScan Injection should be used within twelve hours from the time of calibration.

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 catheterisation should be taken following administration to incontinent patients to minimise the risk of radioactive contamination of clothing, bed linen and the patient's environment.

Special Populations

Diabetes Mellitus

Patients with diabetes may need stabilisation of blood glucose on the day preceding and on the day of the FluGlucoScan Injection PET scan.

Pregnant Women:

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, FluGlucoScan Injection should not be administered to pregnant women, unless it is considered that the benefits to be gained outweigh the potential hazards to the fetus.

Ideally examinations using FluGlucoScan Injection, especially those elective in nature of women of childbearing capacity should be performed during the first ten days following the onset of menses.

Nursing Women:

Where an assessment of the risk benefit ratio suggests the use of this product in nursing women, formula feeding should be substituted for breast feeding for a period of 24 hours following the PET scan.

Pediatrics (< 16 years of age):

The safety and efficacy of FluGlucoScan Injection in pediatric patients have not been established.

Geriatrics (> 75 years of age):

There are no known limitations on the clinical use of FluGlucoScan Injection in geriatric patients.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Reviews of the literature and the clinical trial data indicate that there are no known adverse drug reactions associated with the use of FluGlucoScan Injection.

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.

A single, multi-phase (Phase I/II, Phase III and Extended Phase III) clinical trial was conducted in a variety of cancer patients and a total of 575 patients were evaluated for safety. No FluGlucoScan Injection related adverse reactions have been observed. FluGlucoScan Injection has also been used in approximately 1300 additional patients encompassing various cancer types. No FluGlucoScan Injection related adverse reactions have been observed.

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

There are no known clinical trial adverse drug reactions (< 1%) associated with FluGlucoScan Injection.

Abnormal Hematologic and Clinical Chemistry Findings

Evaluation of 21 patients in the Phase I/II stage of the clinical trial indicated that no clinically significant changes in laboratory measurements were associated with FluGlucoScan Injection.

Post-Market Adverse Drug Reactions

There are no known post-market adverse drug reactions associated with FluGlucoScan Injection.

DRUG INTERACTIONS

Drug-Drug Interactions

Interactions with other drugs have not been established.

Drug-Food Interactions

Patients can not eat or drink (except water) for four hours prior to the administration of FluGlucoScan Injection in order to diminish insulin-induced glucose utilisation.

Drug-Herb Interactions

Interactions with herbal products have not been established.

Drug-Laboratory Interactions

Interactions with laboratory tests have not been established.

DOSAGE AND ADMINISTRATION

Dosing Considerations

Although, the dose required for the imaging study is determined by the patient's weight and the acquisition parameters of each particular PET camera, a minimum dosage of 100 MBq is used as a guideline to ensure that the PET scan is of diagnostic quality. A maximum dosage of 740 MBq is defined as the upper dosing limit, as any amount of drug exceeding that dose would not improve the diagnostic quality of the PET scan while unnecessarily increasing the absorbed radiation dose to the patient.

Dosage

The recommended dose of FluGlucoScan Injection for an adult is dependent upon patient body weight and the requirements of the PET scanner used for a particular type of study, but falls within the range of 100 – 740 MBq (2.7 - 20.0 mCi) by intravenous injection. For example, a typical PET scanner may require the administration of 5 MBq/kg of patient body weight for a whole body scan so that for a patient weighing 70 kg, the required dose would be 350 MBq (70 kg x 5 MBq/kg).

The final patient dose should be calculated using proper decay factors from the time of calibration and measured by a suitable radioactivity calibration system before administration. Patients should receive a single dose per day of FluGlucoScan Injection, with sufficient time between doses to allow for substantial decay (both physical and biological) of previous administration(s).

Administration

Patients can not eat or drink (except water) four hours prior to the administration of FluGlucoScan Injection in order to stabilize blood glucose levels. Patients with diabetes should not eat or drink (except water) for four hours prior to the administration of FluGlucoScan Injection. Patients with diabetes should also avoid taking insulin two hours prior to receiving FluGlucoScan Injection. To ensure a stable glycemic state (blood glucose ≤ 10 mmol / L), the patient's blood glucose level should be checked prior to receiving FluGlucoScan Injection. Patients must be able to lie still for approximately one to two hours (sedation may be required) and, for certain scan types, may be required to raise their arms over their head. Proper hydration, a urinary catheter and / or a diuretic may be required to eliminate confusing urinary tract activity that may confound PET scan interpretation of the abdomen and /or pelvis. The patient should void prior to being positioned on the scanner table. Proper hydration and frequent urination is recommended following a PET examination to minimise radiation exposure to the bladder.

Using appropriate shielding and aseptic technique, the appropriate amount of FluGlucoScan Injection should be drawn into an appropriately sized syringe and needle. The patient dose should be measured by a suitable radioactivity calibration system prior to administration.

FluGlucoScan Injection, like other parenteral drug products, should be inspected visually for particulate matter and discolouration before administration whenever solution and container permit. Preparations containing particulate matter or discolouration should not be administered to the patient; rather they should be disposed of in a safe manner that is compliant with applicable regulations.

Image Acquisition, Reconstruction and Interpretation

The acquisition parameters for imaging with FluGlucoScan Injection will vary depending upon the type of PET scanner and images required. For limited field tomographic imaging using a dedicated PET camera, careful patient positioning will allow for the clear delineation of metabolic activity in lesions previously identified through physical or other imaging examinations.

Emission imaging should begin approximately 30 to 60 minutes following administration of FluGlucoScan Injection. Emission image acquisition typically ranges from six to fifteen minutes,

collecting between five to fifteen million total counts depending upon the number of body positions required. Whole body imaging can be obtained with correction for photon attenuation, which requires acquisition of transmission images. Elimination of image artifacts requires the exact repositioning at each level of the patient during the acquisitions of both the transmissions and emission whole body images.

For the determination of tumour metabolic rates, dynamic imaging using a dedicated PET system is recommended. Following the transmission image, a sequence of serial images is initiated at the time of use of FluGlucoScan Injection and continues for approximately 60 to 90 minutes.

Standard transaxial images are reconstructed in the form of transaxial 128 x 128 pixel images or a pixel size of 4 to 5 mm. Image sets can be re-oriented into coronal and / or sagittal slices. The contiguous transaxial and / or coronal or sagittal slices can then be examined by visual inspection and interpreted relative to the normal physiological uptake of FluGlucoScan Injection in the brain, myocardium, liver, spleen, stomach, intestines, kidneys or urine. Increased or abnormal FluGlucoScan Injection uptake can signify neoplasms. Healing surgical wounds, infections, granulomatous tissue, or other inflammatory tissue responses may also show areas of increased FluGlucoScan Injection uptake. Practitioners should be appropriately trained in the interpretation of FluGlucoScan Injection PET images.

Tumour metabolism can also be estimated using semi-quantitative or quantitative methods. The semi-quantitative estimate of tumour metabolism (i.e. standard uptake values [SUV]) is based on relative lesion radioactivity normalised to the injected dose and patient body weight. It requires a static emission image acquired following the plateau of FluGlucoScan Injection concentration levels (approximately 30 minutes), the total administered dose of FluGlucoScan Injection, and the patient's height and weight for measurement of lean body mass or of body surface area. Additional data which may be required include the measurement of arterial input function and the determination of the plasma FluGlucoScan Injection levels and glucose concentrations. A calibration factor will be required between scanner events in terms of (counts / pixel / sec) and in vitro measured activity concentrations in (counts / ml / sec). This can be accomplished by imaging a cylindrical phantom with a known concentration of positron emitter and by measuring the activity of an aliquot of the cylinder solution in a well counter. This measurement can be corrected for blood glucose concentration.

Estimates of metabolic tumour rates, either using quantitative or semi-quantitative methods, are obtained by assigning regions of interest (ROI) to the tumour and the blood pool on the dynamically acquired images. The resulting time activity curves are then fitted with a tracer compartment model or submitted to graphical analysis in order to derive the phosphorylation of ^{18}F-2-deoxyglucose.

Instructions for Preparation and Use

The components of the vial are isotonic, 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 is performed on the product prior to release.

RADIATION DOSIMETRY

Estimated Absorbed Doses (mGy/MBq) from Intravenous Administration of ^{18}F-FDG[2]

Organ	Absorbed dose per Unit Activity Administered (mGy/mBq)
	Adult
Adrenals	0.012
Bladder	0.160
Bone Surfaces	0.011
Brain	0.028
Breast	0.009
Gall Bladder	0.012
Stomach	0.011
Small Intestine	0.013
Colon	0.013
Upper Large Intestine	0.012
Lower Large Intestine	0.015
Heart	0.062
Kidney	0.021
Liver	0.011
Lungs	0.010
Muscles	0.011
Esophagus	0.011
Ovaries	0.015
Pancreas	0.012
Red Marrow	0.011
Skin	0.008
Spleen	0.011
Testes	0.012
Thymus	0.011
Thyroid	0.010
Uterus	0.021
Remaining Organs	0.011

[2] The International Commission on Radiological Protection (ICRP) 80. Radiation dose to patients from radiopharmaceuticals. Addendum 2 to ICRP publication 53. Ann ICRP 1998; 28:1,47,49.

Effective Dose for ^{18}F-FDG[2]

Parameter	Age Group Adult
Effective Dose (mSv/MBq)	0.019

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

^{18}F-FDG is actively transported from blood to tissue in a manner similar to glucose, 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, the ^{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 PET scanner takes advantage of the positron decay of ^{18}F to identify those tissues that have an abnormal accumulation of the radioisotope.

Pharmacodynamics

^{18}F-FDG, as a glucose analogue, concentrates in cells that rely upon glucose as a primary energy source, or in cells whose dependence on glucose increases under pathophysiologic conditions. ^{18}F-FDG 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 the cell as it is not a suitable substrate for dephosphorylation by glucose-6-phosphate. Therefore, within a given tissue or pathophysiological process, the retention and clearance of ^{18}F-FDG reflect a balance involving glucose transporter proteins, hexokinase and glucose-6-phosphatase activities. When allowance is made for the kinetic differences between glucose and ^{18}F-FDG transport and phosphorylation, ^{18}F-FDG can be used to assess glucose metabolism.

In comparison to background activity of the specific organ or tissue type, regions of decreased or absent uptake of ^{18}F-FDG reflect the decrease or absence of glucose metabolism. Regions of increased uptake (relative to background) of ^{18}F-FDG reflect greater than normal rates of glucose metabolism.

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.

Pharmacokinetics

Absorption:

FluGlucoScan Injection is intended for intravenous administration only.

Distribution:

^{18}F-FDG accumulates throughout the body in proportion to glucose metabolism. Due to their high glycolytic rates, the brain and heart generally exhibit the highest accumulations post-prandially, therefore a fasting state is desirable to minimise uptake in these organs. Other tissues that exhibit the potential for moderate glucose metabolic rates and therefore ^{18}F-FDG uptake are the liver, spleen, thyroid, gut and bone marrow. As active skeletal muscle will accumulate ^{18}F-FDG, a relaxed state, especially during the initial uptake phase, is important to minimise uptake in these organs. ^{18}F-FDG has been shown to accumulate in primary and metastatic tumours throughout the body, possibly related to the concentration of glucose transporters in the cell membrane , the tumour proliferation rate, the degree of tumour differentiation, and the number of viable cancer cells present in the tumour.

Metabolism:

^{18}F-FDG is phosphorylated to ^{18}F-FDG-6-phosphate by hexokinase, with no significant further metabolism taking place within the duration of the PET scan.

Excretion:

^{18}F-FDG is excreted unchanged in the urine (approximately 20 % of the administered activity is excreted within the first 2 hours), therefore the urinary tract can show intense accumulation of ^{18}F-FDG. Seventy-five (75) % of the administered activity of ^{18}F-FDG is retained with an effective half-life of 1.83 hours; 19% has an effective half-life of 0.26 hours and the remaining 6 % has an effective half-life of 1.53 hours.

The time to peak concentration is approximately 30 minutes in highly metabolic tissues such as the brain. Since the time to peak concentration depends on the glucose metabolic rate and whole body clearance of ^{18}F-FDG, less metabolically active tissues such as many tumours may not reach peak concentrations until nearly 2 hours. The time also depends on the balance between the uptake of ^{18}F-FDG, the clearance of ^{18}F-FDG from the blood and radioactive decay.

Special Populations and Conditions

No data available.

OVERDOSAGE

Overdoses of FluGlucoScan Injection have not been reported. In case of overdose, the patient should be monitored for adverse drug reactions and managed as clinically indicated.

STORAGE AND STABILITY

The multi-dose vial containing FluGlucoScan Injection should be stored upright at room temperature in a shielded area until administration, within twelve hours from time of calibration. All regulations regarding the handling of radioactive material should be followed.

SPECIAL HANDLING INSTRUCTIONS

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

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

FluGlucoScan Injection is supplied in a 20 mL, multi-dose, sterile, non-pyrogenic glass vial containing at least 0.5 GBq of no carrier added ^{18}F-fluorodeoxyglucose in approximately 16 mL of citrate buffer and / or saline.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

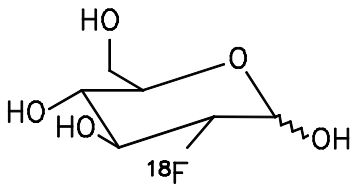
Drug Substance

Proper name: ^{18}F-fluorodeoxyglucose, ^{18}F-FDG

Chemical name: 2-deoxy-^{18}F-fluoro-D-glucose

Molecular formula and molecular mass: $C_6H_{11}{}^{18}F\ O_5$, MW = 181.1

Structural formula:



Product Characteristics

FluGlucoScan Injection is a clear, colourless solution supplied in a multi-dose (20 mL), sterile, nonpyrogenic glass vial containing at least 0.5 GBq of no carrier added ^{18}F-fluorodeoxyglucose in approximately 16 mL of citrate buffer and / or saline. Sodium citrate, saline and Sterile Water for Injection are used as formulation excipients. Product is prepared on a daily basis with expiry time of 12 hours from the calibration time noted on the label.

The radionuclide present in the drug product is fluorine-18 (^{18}F), which decays by positron (β+) emission and has a half-life of 109.7 minutes. 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 4).

Table 4 Principal Emission Data for Fluorine 18

Radiation / Emission	Percent per Disintegration	Mean Energy
Positron (β+)	96.9	249.8 keV
Gamma (±)*	193.8	511.0 keV

*Produced by positron annihilation

The specific gamma ray constant for fluorine-18 is 0.3 Gy/hr/kBq (6.0 R/hr/mCi) at 1 cm. The lead shielding half value layer (HVL) for the 511 keV photons is 4.1 mm. A range of values for the attenuation of radiation results from the interposition of various thicknesses of lead shielding. The range of attenuation coefficients for this radionuclide is shown in Table 5. For example, the interposition of an 8.3 mm thickness of lead shielding, with a coefficient of attenuation of 0.25, will decrease the external radiation by 75%.

Table 5 Radiation Attenuation of 511 keV Photons by Lead Shielding

Lead Shield Thickness (mm)	Coefficient of Attenuation
0	0.00
4.1	0.50
8.3	0.25
13.2	0.10
26.4	0.01
52.8	0.001

For use in correcting for physical decay of this radionuclide, the fractions remaining at selected intervals after calibration are shown in Table 6.

Table 6 Physical Decay Chart for Fluorine-18

Minutes	Fraction Remaining
0*	1.00
15	0.909
30	0.826
60	0.683
110	0.500
220	0.250
440	0.060

*Calibration Time

The specific activity of no carrier added ^{18}F-FDG has been calculated to be approximately 63.3 GBq / nmol or 348 MBq / ng (1.7 Ci / nmol or 9.4 mCi / ng) with a total calculated amount of ^{18}F-FDG present as approximately 1.58 nmol (or 287 ng) per vial at a concentration of approximately 17.9 ng / mL (or 98.8 pmol /mL). Citrate buffer (approximately 8.4 mg/mL) and / or sodium chloride (7.0-9.4 mg/mL) are also present in the solution prepared using Sterile Water for Injection.

CLINICAL TRIALS

Study demographics and trial design

Study Title: A Phase I/II, Phase III and Extended Phase III Study of ^{18}F-Fluorodeoxyglucose (FluGlucoScan™ Injection) in Patients with Cancer or Suspected Cancer (DX-FDG-001)

The trial design was a combined continuous Phase I/II, Phase III, Extended Phase III, diagnostic imaging, controlled, open label, multi-centre, clinical trial in a broad cross-section of patients with oncologic disease. These included carcinoma of the brain, breast, colorectal, head & neck, lung, thyroid, esophageal, and lymphoma, melanoma, PRUNK and neuroendocrine tumours (Table 7). Approximately 1893 patients had been enrolled up to the cut-off date of September 29, 2005 and, of these, 575 were evaluated for safety and 331 were evaluated for efficacy. Demographic data for the patients evaluated for efficacy are presented in Table 8

Table 7 Demographic Data for Patients in Phase I/II, Phase III and Extended Phase III Studies included in NDS

Parameter	Phase I / II	Phase III	Extended Phase III
Total patient numbers	21	351	224*
Gender	Female: 13 Male: 8	Female: 185 Male: 166	Female: 111 Male: 113
Age (years)	Mean: 63.5 Median: 65.2 Range: 30.8 – 79.2	Mean: 57.9 Median: 58.9 Range: 17.4 – 89.0	Mean: 63.8 Median: 64.6 Range: 22.2 – 88.8
Indications and Distributions	Brain: 1 Breast: 6 Lung: 7 Primary Unknown: 1 Thyroid: 1 Esophageal: 2 Lymphoma: 3	Brain: 7 Breast: 65 Colorectal: 34 Esophageal: 10 Head & Neck: 15 Lymphoma: 22 Lung: 140 Melanoma: 9 Neuroendocrine: 11 Primary Unknown: 12 Thyroid: 26	Colorectal: 147 Lung: 77

* sequential evaluable lung and colorectal cancer patients
† dose is calculated individually for each patient dependent upon patient weight, PET scanner type

Table 8 Demographic Data for Efficacy Patients from Phase III / Extended Phase III Study

Disease Category	Parameter	Value
Lung Cancer (SPN)	Total Patient Numbers	125
	Gender	
	Total Patients	Female: 64 Male: 61
	Phase III Patients	Female: 28 Male: 36
	Extended Phase III Patient	Female: 36 Male: 25
	Age (years)	Mean: 64.8 Median: 66.6 Range: (37.0 – 84.1)
Recurrent Colorectal Cancer	Total Patient Numbers	148
	Gender	
	Total Patients	Female: 65 Male: 83
	Phase III Patients	Female: 13 Male: 17
	Extended Phase III Patient	Female: 52 Male: 66
	Age (years)	Mean: 63.0 Median: 64.3 Range: (30.3 – 88.0)

Study results

Safety results:

Table 9 summarises the results of the safety analysis for FluGlucoScan Injection.

Table 9 Summary of Safety Results from Clinical Trials

Study # (Name)	Primary Safety Endpoints	Results
Phase I/II	Evaluation of safety by assessment of adverse events, vital signs, haematology and blood chemistry.	Twenty-one (21) patients were analysed for safety. No adverse reactions observed or reported and no significant changes observed in patient vital signs, haematology or blood chemistry due to administration of FluGlucoScan Injection.
Phase III/Extended Phase III	Evaluation of safety by assessment of adverse events and vital signs.	Five hundred and seventy-five (575) patients were analysed for safety. No adverse reactions were observed or reported and no significant changes observed in patient vital signs due to administration of FluGlucoScan Injection.

A study of over 80,000 ^{18}F-FDG injections (1) and the USP DI Product Monograph for Fludeoxyglucose F 18 Systemic (2) confirm that there are no known side/adverse effects associated with the use of ^{18}F-FDG establishing its safety profile.

Efficacy Results:

Final efficacy was determined from Phase III and Extended Phase III of the clinical trial as described inTable 10.

Table 10 Final Efficacy Analysis Summary

Patient Source:	Patient Demographics (Tumour Type, Gender and Number)	Primary Efficacy Endpoints
Phase III	Sixty-four (64) patients (28 females and 36 males) with pulmonary nodules and thirty (30) patients (13 females and 17 males) with recurrent colorectal cancer were included in the efficacy analysis.	Evaluation of efficacy by assessment of sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of FluGlucoScan Injection for detection of solitary pulmonary nodules (SPN) and recurrent colorectal cancer compared to appropriate matched literature values.
Extended Phase III	Sixty-one (61) patients (36 females and 25 males) with pulmonary nodules and one hundred eighteen (118) (52 females and 66 males) with recurrent colorectal cancer were included in the efficacy analysis.	

Diagnostic outcomes on a per patient basis were determined using FluGlucoScan Injection scan outcome values and all applicable clinical information. Sensitivity (ratio of true positive target lesions to total positive target lesions), specificity (ratio of true negative target lesions to total negative target lesions), accuracy (ratio of total correct studies to the total number of target lesions), PPV (ratio of true positive target lesions to total number of positive lesions) and NPV (ratio of true negative target lesions to total number of negative lesions) of FluGlucoScan Injection PET scans obtained were determined. Confidence intervals (95% CI) for sensitivity, specificity, accuracy, PPV and NPV were derived using the exact binomial calculations. Statistical comparison to the indication matched literature values (obtained from appropriate meta-analyses) was conducted using an exact binomial test.

Table 11 and Table 12 shows the overall sensitivity, specificity, accuracy, PPV and NPV of FluGlucoScan Injection PET imaging for the final efficacy analysis population compared to corresponding literature values for patients with solitary pulmonary nodules (SPNs) or recurrent colorectal cancer, respectively.

Table 11 Clinical Diagnostic Parameter Efficacy Results for Patients with SPNs

Source	Indication	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	PPV (95% CI)	NPV (95% CI)
Supporting Clinical Literature	Diagnosis (Pulmonary	95.2 (93.9–96.3) n = 1360	75.2 (70.9-79.0) n = 467	90.0 (88.6-91.4) n = 1827	91.8 (90.2-93.2) n = 1411	84.4 (80.5-87.7) n = 416
Clinical Trial Data	Diagnosis (Pulmonary	96.9 (89.3-99.6) n = 65	80.0 (67.7-89.2) n = 60	88.8 (81.9-93.7) n = 125	84.0 (73.7-91.4) n = 75	96.0 (86.3-99.5) n = 50
p-value		0.2829	0.1991	0.6819	0.9868	0.0065*

* Significantly different $p < 0.05$
n = number of patients evaluated; p-value = one-sided mid p - value

Table 12 Clinical Diagnostic Parameter Efficacy Results for Patients with Recurrent Colorectal Cancer

Source	Indication	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	PPV (95% CI)	NPV (95% CI)
Supporting Clinical Literature	Recurrent	96.1 (93.9-97.6) n = 508	93.5 (91.3-95.4) n = 620	94.7 (93.2-95.9) n = 1128	92.4 (89.8-94.5) n = 528	96.7 (94.9-97.9) n = 600
ACB Clinical Trial Data		94.1 (87.6-97.8) n = 102	84.8 (71.1–93.7) n = 46	91.2 (85.4-95.2) n = 148	93.2 (86.5-97.2) n = 103	86.7 (73.2-94.9) n = 45
p-value		0.8438	0.9815	0.9611	0.3991	0.9979

n = number of patients evaluated; p-value = one-sided mid p - value

Lung Cancer

Lung cancer is the leading cause of cancer related mortality in the western world, with approximately 170,000 new cases diagnosed each year in the U.S.A. In Canada, 29% of all cancer related deaths in males and 25% in females are attributable to cancer of the lung. Pulmonary nodules are typically encountered in patients with lung cancer, with many nodules incidentally discovered during work-up for unrelated signs or symptoms. Although suspicious nodules can frequently be addressed through percutaneous biopsy or thoracoscopic surgery; less definitive lesions often require serial imaging with conventional radiography (i.e. chest x-rays) or CT over a period of several months. Fortunately, the preferential uptake of FluGlucoScan Injection in metabolically active lung cancers can quickly differentiate malignant nodules from those of a benign nature thus minimising the amount of time required for diagnosis, reducing the number of invasive diagnostic procedures in the event of FluGlucoScan Injection negative lesions and permitting a timely implementation of patient therapy.

When compared to the cumulative literature diagnostic parameter values (Table 11), FluGlucoScan Injection diagnostic parameter values for patients with pulmonary nodules demonstrate an absolute difference of not greater than 7% (except for the NPV - where the difference between FluGlucoScan Injection NPV and that of the cumulative literature is statistically significant and is greater by an absolute difference of 11.6%), indicating that FluGlucoScan Injection is indeed comparable to other marketed ^{18}F-FDG products for the diagnostic evaluation of pulmonary nodules.

Staging and Restaging of Lung Cancer

Once diagnosed with a primary lung cancer, patients undergo a series of staging procedures to determine the extent of their disease in accordance to the Tumour-Nodes-Metastases (TNM) classificatory scheme and to plan their optimal treatment strategy. Although CT is employed ubiquitously for the staging of primary lung cancer, it is limited by the inability to delineate tumour tissue from obstructive or inflammatory changes, differentiate benign accumulations of pleural fluid from those of a more malignant nature, and accurately characterize mediastinal and hilar lymph nodes. In contrast, the metabolic imaging capabilities of ^{18}F-FDG PET can accurately discriminate active tumour from atelectasis or pneumonia, verify the presence of malignant pleural effusions, and delineate the nodal spread of disease. Indeed the negative predictive values for the ^{18}F-FDG PET evaluation of mediastinal nodes are reported to be greater than 90.0%, suggesting that patients identified as ^{18}F -FDG PET-negative for metastases can proceed to surgery with confidence that their disease is localized (Table 13).

For patients with recurrent disease, ^{18}F-FDG PET also proves useful in the identification of local intrathoracic recurrence and metastatic disease (Table 13). ^{18}F-FDG PET can accurately characterize new pulmonary nodules or masses in the ipsilateral or contralateral lung, identify distant metastatic disease sites and delineate post-therapeutic tissue changes from malignancies. In contrast, the proper evaluation of distant metastases with conventional imaging techniques requires numerous scans, including CT, MRI and skeletal scintigraphy. Serial CT studies are also required to document any post-therapeutic tissue changes, resulting in the delayed implementation of

appropriate patient therapy.

Table 13 Summary of Supporting Clinical Literature Diagnostic Parameter Values for ^{18}F-FDG PET Staging and Restaging of Lung Cancer

Source	Indication	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	PPV (95% CI)	NPV (95% CI)
Supporting Clinical Literature	Staging	84.6 (82.0 - 87.0) n = 845	87.9 (86.2 - 89.4) n = 1623	86.8 (85.4 - 88.1) n = 2468	78.4 (75.6 – 81.0) n = 913	91.6 (90.2 – 93.0) n = 1555
Supporting Clinical Literature	Restaging	96.4 (93.2 – 98.3) n = 249	86.0 (81.4 – 89.9) n = 279	90.9 (88.1 – 93.2) n = 528	86.0 (81.4 – 89.9) n = 279	96.4 (93.2 – 98.3) n = 249

The established comparability of FluGlucoScan Injection with literature ^{18}F-FDG in SPN evaluation (Table 11), the established literature benefit of ^{18}F-FDG in staging and restaging of lung cancer (Table 13) and the similar biochemical patterns in these tumour types supports the application of FluGlucoScan Injection in these indications. Thus the combination of clinical trial data and literature analysis establishes the use of FluGlucoScan Injection in all claimed indications for lung cancer.

Recurrent Colorectal Cancer

It is estimated that 25 - 40% of patients treated surgically for a primary colorectal cancer will experience disease recurrence. In 20% of these cases, the recurrence is localized and therefore amenable to curative resection. Unfortunately the use of standard techniques, such as carcinoembryonic antigen (CEA) assays, CT and MRI, for the detection of disease recurrence is often hindered by poor accuracy. Scarring, fibrosis and other post-therapeutic tissue changes are often difficult to differentiate from malignancy using CT and MRI, requiring patients to undergo serial examinations over a period of several months before receiving the correct diagnosis. In contrast, ^{18}F-FDG PET can quickly and accurately discriminate malignancy from metabolically inactive tissue changes and identify hepatic, extrahepatic and distant metastases, facilitating patient diagnosis and treatment planning (Table 12). ^{18}F -FDG PET has a further advantage in that only a single study is required to make these determinations unlike other conventional imaging techniques.

When compared to the cumulative literature diagnostic parameter values (Table 12), FluGlucoScan Injection diagnostic parameter values demonstrate a difference of not greater than 10%, indicating that FluGlucoScan Injection is indeed comparable to other marketed ^{18}F-FDG products for the diagnostic evaluation colorectal cancer recurrence and the restaging of disease.

DETAILED PHARMACOLOGY

The hydroxyl group on 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 to the point in the glycolytic pathway where its anomalous structure prevents the final conversion of the 2-deoxyglucose-6-phosphate by phosphohexose-isomerase 1 (3).

Gallagher *et al*. (4, 5) have studied the tissue distribution of ^{18}F-FDG in animals. 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 two hours and, to a lesser extent, in the brain where it decreases slowly from one to two hours. 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 to 25% of injected dose at 90 minutes.

Kearfott *et al.* (6) studied groups of mice (CD-1 strain) and rats (Sprague-Dawley strain) injected intravenous (IV) with tracer amounts of ^{18}F-FDG and sacrificed at 1, 5, 30, 60, and 120 minutes for tissue biodistribution analysis. They also studied two mongrel dogs with imaging at 40 to 80 minutes post IV injection of tracer doses for tissue biodistribution analysis with arterial blood sampling at 0 to 10, 15, 20, 30, 40, 45, 60, and 90 minutes. The dogs were sacrificed at 60 and 120 minutes. Tissue biodistribution (percent of injected dose per gram - %ID/gram) for blood, brain, liver, spleen, lung, heart, kidney, bone, muscle and bladder over the time periods indicated for mice and rats was reported. Tissue biodistribution (percent of injected dose per one percent of body weight - %ID/gram/1%body weight) for blood, brain (left and right hemisphere, cerebellum), liver,

spleen, lung, heart (left and right atria and ventricle), kidney, bone, muscle, and bladder wall for the dogs was determined. Tissue pharmacokinetic parameters in heart and brain were estimated.

TOXICOLOGY

Fluorodeoxyglucose (FDG)

Bessell *et al*. (7) studied the toxicology of FDG injected intraperitoneally in mice and rats and reported the LD50 in mice as 600 mg/kg.

Reivich *et al*. (8) studied the toxicology of FDG in mice and dogs. Mice were injected intraperitoneally with FDG (3 weekly doses of 14.3 mg/kg – 3000 times the human dose). No effect was noted on animal weight, no gross or microscopic abnormalities were noted and no immediate or long term effects were noted. Dogs were injected intravenously with three doses of 0.72 mg/kg and showed no clinical signs or symptoms of adverse effects. No significant abnormalities were detected in the blood, urine or cerebrospinal fluid. No significant gross or microscopic abnormalities were noted in internal organs.

Som *et al*.(9) studied the toxicology of FDG in mice and dogs. Mice were injected intraperitoneally with FDG (3 weekly doses of 14.3 mg/kg – 3000 times the human dose). No effect was noted on animal weight and no gross or microscopic abnormalities were noted. Dogs were injected intravenously with three doses of 0.72 mg/kg and no significant abnormalities were detected in the blood, urine or cerebrospinal fluid. No significant gross or microscopic abnormalities were noted in internal organs. No abnormalities of body temperature, blood pressure, pulse or breathing were observed in the dogs.

Acetonitrile, Ethanol, Acetone and Kryptofix 222

Potential impurities that have been observed in very small amounts in FluGlucoScan Injection are acetonitrile, acetone and Kryptofix 222 (Kryptofix) and therefore, the potential impact of their presence on product safety was assessed.

The acetonitrile limit for FluGlucoScan Injection follows the ICH Q3C(R3) specification for this residual solvent and thus provides a large safety factor for exposure of the patient to this potentially toxic chemical.

The ethanol limit for FluGlucoScan Injection follows the ICH Q3C(R3) specification for this residual solvent and thus provides a large safety factor for exposure of the patient to this low toxicity chemical.

The acetone limit for FluGlucoScan Injection follows the ICH Q3C(R3) specification for this residual solvent and thus provides a large safety factor for exposure of the patient to this low toxicity chemical.

The acute toxicity of Kryptofix has been evaluated in rats and mice (10). The LD_{50} of an intravenous dose in mice was 35 mg/kg and of an intraperitoneal dose was 110 mg/kg. The LD_{50} of an intravenous dose in rats was 32 mg/kg and of an intraperitoneal dose was 153 mg/kg. Doses of

up to 188.25 mg/kg (route not specified) in rats demonstrated transient elevations in liver enzymes but no other histopathological changes were evident (11). The Kryptofix limit (≤ 50 µg/mL) for FluGlucoScan Injection follows the USP 30 specification and is more than two orders of magnitude below the lethal dose in rodents, delivered intravenously. Thus a more than reasonable safety margin is realised for the (worst case) Kryptofix content in FluGlucoScan Injection based on these assessments.

REFERENCES

1. Silberstein EB. Positron-Emitting Radiopharmaceuticals: How Safe Are They? Cancer Biother Radiopharm 2001 Feb; 16(1):13-5.
2. The United States Pharmacopeia Convention, Inc. USPDI – Drug Advice for the Health Care Professional. Vol. 1. [monograph on the Internet]. Greenwood Village: Thomson Micromedex; 2003. [cited 2007 Feb 22]. Available from: http://uspdi.micromedex.com/view_file.html?file=fludeoxyglucose.pdf&dir=v1/excluded
3. Pauwels EKJ, Sturm EJC, Bombardieri E, Cleton FJ, Stokkel MPM. Positron-emission tomography with [^{18}F]fluorodeoxyglucose: Part I. Biochemical uptake mechanism and its implication for clinical studies. J Cancer Res Clin Oncol 2000 Oct; 126(10):549-59.
4. Gallagher BM, Fowler JS, Gutterson NI, MacGregor RR, Wan C-N, Wolf AP. Metabolic Trapping as a Principle of Radiopharmaceutical Design: Some Factors Responsible for the Biodistribution of [^{18}F] 2-Deoxy-2-Fluoro-D-Glucose. J Nucl Med 1978 Oct; 19(10):1154-61.
5. Gallagher BM, Ansari A, Atkins H, Casella V, Christman DR, Fowler JS, et al. Radiopharmaceuticals XXVII. ^{18}F-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 Oct; 18(10):990-6.
6. Kearfott KJ, Elmaleh DR, Goodman M, Correira JA, Alpert NM, Ackerman RH, et al. Comparison of 2- and 3-18F-Fluoro-deoxy-D-glucose for Studies of Tissue Metabolism. Int J Nucl Med Biol 1984;11(1):15-22.
7. Bessell EM, Courtenay VD, Foster AB, Jones M, Westwood JH. Some *In Vivo* and *In Vitro* Antitumour Effects of the Deoxyfluoro-D-Glucopyranoses. Eur J Cancer 1973 Jul; 9(7):463-70.
8. Reivich M, Kuhl D, Wolf A, Greenberg J, Phelps M, Ido T, et al. The [^{18}F]fluorodeoxyglucose method for the measurement of local cerebral glucose utilization in man. Cir Res 1979 Jan; 44(1):127-37.
9. Som P, Atkins HL, Bandoypadhyay D, Fowler JS, MacGregor RR, Matsui K, et al. A Fluorinated Glucose Analog, 2-fluoro-2-deoxy-D-glucose (F-18): Nontoxic Tracer for Rapid Tumor Detection. J Nucl Med 1980 Jul; 21(7):670-5.
10. Baudot P, Jacque M, Robin M. Effect of a Diaza-Polyoxa-Macrobicylic Complexing Agent on the Urinary Elimination of Lead in Lead-Poisoned Rats. Toxicol Appl Pharmacol 1977 Jul; 41(1):113-8.
11. Bauman M, Schäffer E, Greim H. Short-term Studies with the Cryptating Agent Hexaoxa-diaza-bicyclo-hexacosane in Rats. Arch Toxicol Suppl 1984; Suppl 7:427-9.

PART III: CONSUMER INFORMATION

FluGlucoScan™ Injection

^{18}F - Fluorodeoxyglucose, ^{18}F-FDG

This leaflet is part III of a three-part "Product Monograph" published when FluGlucoScan 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 FluGlucoScan Injection. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
FluGlucoScan Injection is a radioactive drug which is used in conjunction with a diagnostic Positron Emission Tomography (PET) scan to help your physician evaluate your cancer.

What it does:
FluGlucoScan Injection is a radioactive form of sugar with the radioisotope, Fluorine-18, attached to it. When it is injected into a vein, it is distributed throughout your body. Cancer cells require more sugar to function and, therefore, FluGlucoScan Injection will concentrate in them. A diagnostic scanning test, called a PET scan, uses the radioisotope in FluGlucoScan Injection to make whole-body images. These images can help your physician detect the presence and the location of cancer cells within your body.

When it should not be used:
The FluGlucoScan Injection should not be used if you:

- are pregnant or nursing
- are allergic to any components of FluGlucoScan Injection
- are diabetic with uncontrolled blood sugar levels

What the medicinal ingredient is:
F-18 Fluorodeoxyglucose (a radioactive form of sugar)

What the important nonmedicinal ingredients are:
Citrate buffer, Sodium Chloride (salt) and Water

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- **Because FluGlucoScan Injection is a radio-pharmaceutical, it should be used only by those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans.**
- **FluGlucoScan Injection should not be administered to pregnant women unless it is considered that the benefits to be gained outweigh the potential hazards to the fetus.**
- **FluGlucoScan Injection can be passed through breast milk to your nursing infant. To avoid unnecessary exposure of your infant to radiation, breast-feeding should be substituted with formula feeding for a period of 24 hours following the PET scan**

BEFORE you receive FluGlucoScan Injection talk to your doctor or pharmacist if:

- you have any allergies to the FluGlucoScan Injection or its ingredients
- you have diabetes, as your blood sugar levels may have to be assessed prior having your PET scan with FluGlucoScan Injection
- you think you may be or are pregnant
- you are breast feeding your baby

INTERACTIONS WITH THIS MEDICATION

Interactions between FluGlucoScan Injection and other drugs, herbal remedies, and food or food products have not been established.

PROPER USE OF THIS MEDICATION

This product (FluGlucoScan Injection) 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 FluGlucoScan Injection.

You may be asked to eat nothing and drink only water for four hours before your scheduled PET scan with FluGlucoScan Injection.

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

No side effects have been associated with the use of FluGlucoScan Injection in clinical trials.

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

There are no known serious side effects associated with FluGlucoScan Injection. If you experience any unusual symptoms or allergic reactions (such as itching, rash, hives, elevated heart rate, nausea or vomiting), contact your physician or pharmacist.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs. If you suspect you have a serious or unexpected reaction to this drug you may notify Health Canada by:

Toll-free telephone 866 – 234 – 2345
Toll-free tax 866 – 678 -6789
By email: cadrmp@hc-sc.gc.ca

By regular mail:
National AR Centre
Marketed Health Products Safety and Effectiveness
Information Division
Marketed Health Products Directorate
Tunney's Pasture, ALO 0701C
Ottawa ON K1A 0K9

Note: Before contacting Health Canada, you should contact your physician or pharmacist.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

http://www.hc-sc.gc.ca/dhp-mps/brgtherap/index_e.html

or

http://www.fluglucoscan.ca

or by contacting the sponsor, Alberta Cancer Board, at 1–780–432-8771.

This leaflet was prepared by the Alberta Cancer Board.

Last revised October 2, 2007