

Fludeoxyglucose (18F)

Core Safety Profile

4.3 Contraindications

Hypersensitivity to the active substance(s), to any of the excipients listed in section 6.1

4.4. Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions

If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification

For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required diagnostic information.

Renal and hepatic impairment

Due to the major renal excretion of fludeoxyglucose (^{18}F), in patients with reduced kidney function, careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible. Activity should be adjusted if necessary.

Paediatric population

For information on the use in paediatric population, see sections 4.2 or 5.1. Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11).

Patient preparation

{(Invented) name} should be given to sufficiently hydrated patients fasting for a minimum of 4 hours, in order to obtain a maximum target activity, since glucose uptake in the cells is limited ("saturation kinetics"). The amount of liquid should not be limited (beverages containing glucose must be avoided). In order to obtain images of best quality and to reduce the radiation exposure of the bladder, patients should be encouraged to drink sufficient amounts and to empty their bladder prior to and after the PET

examination.

- Oncology and neurology and infectious diseases

In order to avoid hyperfixation of the tracer in muscle, it is advisable for patients to avoid all strenuous physical activity prior to the examination and to remain at rest between the injection and examination and during acquisition of images (patients should be comfortably lying down without reading or speaking).

The cerebral glucose metabolism depends on the brain activity. Thus, neurological examinations should be performed after a relaxation period in a darkened room and with low background noise.

A blood glucose test should be performed prior to administration since hyperglycaemia may result in a reduced sensitivity of {(Invented) name}, especially when glycaemia is greater than 8 mmol/L. Similarly, PET with fludeoxyglucose (^{18}F) should be avoided in subjects presenting uncontrolled diabetes.

- Cardiology

Since glucose uptake in the myocardium is insulin-dependent, for a myocardial examination a glucose loading of 50 g approximately 1 hour prior to the administration of {(Invented) name} is recommended. Alternatively, especially for patients with diabetes mellitus, the blood sugar level can be adjusted by a combined infusion of insulin and glucose (insulin-glucose-clamp) if needed.

Interpretation of the PET with fludeoxyglucose (^{18}F) images

In the exploration of inflammatory bowel diseases, diagnostic performance of fludeoxyglucose (^{18}F) has not been directly compared with that of scintigraphy using labelled white blood cells which may be indicated prior to fludeoxyglucose (^{18}F) PET or after fludeoxyglucose (^{18}F) PET when inconclusive.

Infectious and/or inflammatory diseases as well as regenerative processes after surgery can result in a significant uptake of fludeoxyglucose (^{18}F) and therefore lead to false positive results, when search for infectious or inflammatory lesions is not the aim of the fludeoxyglucose (^{18}F) PET. In cases where fludeoxyglucose (^{18}F) accumulation can be caused by either cancer, infection or inflammation, additional diagnostic techniques for the determination of the causative pathologic alteration may be required to supplement the information obtained by PET with fludeoxyglucose (^{18}F). In some settings e.g. staging of myeloma, both malignant and infectious foci are searched for and may be distinguished with a good accuracy on topographic criteria e.g. uptake at extramedullary sites and/or bone and joint lesions would be atypical for multiple myeloma lesions and identified cases associated with infection. There are currently no other criteria to distinguish infection and inflammation by means of fludeoxyglucose (^{18}F) imaging.

Because of the high physiologic uptake of fludeoxyglucose (^{18}F) within brain,

heart and kidneys, PET/CT with fludeoxyglucose (^{18}F) has not been evaluated for the detection of septic metastatic foci in these organs when the patient has been referred due to bacteraemia or endocarditis.

False positive or false negative PET with fludeoxyglucose (^{18}F) results cannot be excluded after radiotherapy within the first 2-4 months. If the clinical indication is demanding an earlier diagnosis by PET with fludeoxyglucose (^{18}F), the reason for earlier PET with fludeoxyglucose (^{18}F) examination must be reasonably documented.

A delay of at least 4-6 weeks after the last administration of chemotherapy is optimal, in particular to avoid false negative results. If the clinical indication is demanding an earlier diagnosis by PET with fludeoxyglucose (^{18}F), the reason for earlier PET with fludeoxyglucose (^{18}F) examination must be reasonably documented. In case of chemotherapy regimen with cycles shorter than 4 weeks, the PET with fludeoxyglucose (^{18}F) examination should be done just before re-starting a new cycle.

In low-grade lymphoma, lower oesophagus cancer and suspicion of recurrent ovarian cancer, only positive predictive values have to be considered because of a limited sensitivity of PET with fludeoxyglucose (^{18}F). Fludeoxyglucose (^{18}F) is not effective in detecting brain metastases.

The accuracy of fludeoxyglucose (^{18}F) PET imaging is better using PET/CT than PET cameras alone.

When a hybrid PET-CT scanner is used with or without administration CT contrast media, some artefacts may occur on the attenuation-corrected PET images.

After the procedure

Close contact with infants and pregnant women should be restricted during the initial 12 hours following the injection.

Specific warnings

[If applicable taking into account the dilution with sodium chloride]:

Depending on the time when you administer the injection, the content of sodium given to the patient may in some cases be greater than 1 mmol (23 mg). This should be taken into account in patient on low sodium diet. Precautions with respect to environmental hazard see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

All medicinal products that modify blood glucose levels can affect the sensitivity of the examination (e.g. corticosteroids, valproate, carbamazepine, phenytoin, phenobarbital and catecholamines).

Under administration of colony-stimulating factors (CSFs), there is an increased uptake of fludeoxyglucose (^{18}F) in the bone marrow and the spleen for several days. This must be taken into account for the interpretation of PET imaging. Separating CSF therapy from PET imaging by an interval of at least 5 days may diminish this interference.

The administration of glucose and insulin influences the influx of

fludeoxyglucose (^{18}F) into the cells. In the case of high blood glucose levels as well as low plasma insulin levels, the influx of fludeoxyglucose (^{18}F) into organs and tumours is reduced.

No formal studies on the interaction between fludeoxyglucose (^{18}F) and any contrast for computed tomography have been performed.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman

has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy

Radionuclide procedures carried out on pregnant women also involve radiation dose to the foetus. Only essential investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and foetus.

Breast-feeding

Before administering radiopharmaceuticals to a mother who is breastfeeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding, and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breastfeeding should be interrupted for 12 hours and the expressed feeds discarded.

Close contact with infants should be restricted during the initial 12 hours following injection.

Fertility

No studies on fertility have been performed.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 7.6 mSv when the

maximal recommended activity of 400 MBq is administered these adverse reactions are expected to occur with a low probability.

4.9 Overdose

In the event of administration of a radiation overdose with fludeoxyglucose (^{18}F) the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by forced diuresis and frequent bladder voiding. It might be helpful to estimate the effective dose that was applied.

