SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Amyvid 800 MBq/mL solution for injection
Amyvid 1 900 MBq/mL solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Amyvid 800 MBq/mL solution for injection

Each mL of solution for injection contains 800 MBq of florbetapir (^{18}F) at the date and time of calibration (ToC).
The activity per vial ranges from 800 MBq to 12 000 MBq at the ToC.

Amyvid 1 900 MBq/mL solution for injection

Each mL of solution for injection contains 1 900 MBq of florbetapir (^{18}F) at the ToC.
The activity per vial ranges from 1 900 MBq to 28 500 MBq at the ToC.

Fluorine (^{18}F) decays to stable oxygen (^{18}O) with a half-life of approximately 110 minutes by emitting a positron radiation of 634 keV, followed by photonic annihilation radiation of 511 keV.

Excipients with known effect:

Each dose contains up to 790 mg of ethanol and 37 mg of sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Amyvid is a radiopharmaceutical indicated for use with Positron Emission Tomography (PET).

Diagnosis

Imaging of β-amyloid neuritic plaque density in the brains of adult patients with cognitive impairment who are being evaluated for Alzheimer's disease (AD) and other causes of cognitive impairment. Amyvid should be used in conjunction with a clinical evaluation.

A negative scan indicates sparse or no plaques, which is not consistent with a diagnosis of AD. For the limitations in the interpretation of a positive scan, see sections 4.4 and 5.1.

Monitoring

Imaging of β-amyloid neuritic plaque density in the brains of adult patients receiving amyloid-targeting therapy.

4.2 Posology and method of administration

A PET scan with florbetapir (^{18}F) should be requested by physicians skilled in the clinical management of neurodegenerative disorders.

Amyvid images should only be interpreted by readers trained in the interpretation of PET images with florbetapir (^{18}F). A recent co-registered computed tomography (CT) scan or magnetic resonance (MR) imaging of the patient to get a fused PET-CT or PET-MR image is recommended in cases of uncertainty about the location of grey matter and of the grey/white matter border in the PET scan (see section 4.4. Image interpretation).

Posology

The recommended activity for an adult weighing 70 kg is 370 MBq florbetapir (^{18}F). The volume of the injection should not be less than 1 mL and not exceed 10 mL.

Special populations

Elderly
No dose adjustment is recommended based on age.

Renal and hepatic impairment
Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients (see section 4.4).

Extensive dose-range and adjustment studies with the medicinal product in normal and special populations have not been performed. The pharmacokinetics of florbetapir (^{18}F) in patients with renal or hepatic impairment have not been characterised.

Paediatric population
There is no relevant use of Amyvid in the paediatric population.

Method of administration

Amyvid is for intravenous use and multidose use.

The activity of florbetapir (^{18}F) has to be measured with an activimeter (dose calibrator) immediately prior to injection.

The dose is administered by intravenous bolus injection, followed by a flush of sodium chloride 9 mg/mL (0.9%) solution for injection to ensure full delivery of the dose.

Injection of florbetapir (^{18}F) through a short intravenous catheter (approximately 4 cm or less) minimises the potential for adsorption of the active substance to the catheter.

The injection of florbetapir (^{18}F) must be intravenous in order to avoid irradiation as a result of local extravasation, as well as imaging artefacts.

Image acquisition
A 10 minute PET image should be acquired starting approximately 30 to 50 minutes after intravenous injection of Amyvid. Patients should be supine with the head positioned to centre the brain, including the cerebellum, in the PET scanner field of view. Reducing head movement with tape or other flexible head restraints may be employed. Reconstruction should include attenuation correction with resulting transaxial pixel sizes between 2.0 and 3.0 mm.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Limitations of use

A positive scan does not independently establish a diagnosis of AD or other cognitive disorder since neuritic plaque deposition in grey matter may be present in asymptomatic elderly and some neurodegenerative dementias (Alzheimer's disease, Lewy body dementia, Parkinson's disease dementia).

For the limitations of use in patients with mild cognitive impairment (MCI), see section 5.1.

The efficacy of Amyvid for predicting development of AD has not been established (see section 5.1).

Some scans may be difficult to interpret due to image noise, atrophy with a thinned cortical ribbon, or image blur, which could lead to interpretation errors. For cases in which there is uncertainty about the location of grey matter and of the grey/white matter border on the PET scan, and a co-registered recent CT or MR image is available, the interpreter should examine the fused PET-CT or PET-MR image to clarify the relationship of the PET radioactivity and the grey matter anatomy.

Increased uptake has been identified in extracerebral structures such as salivary glands, skin, muscles and bone in some cases (see section 5.2). Examination of sagittal images and co-registered CT or MR images could help to distinguish occipital bone from occipital grey matter.

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 impairment and hepatic impairment

Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible. Florbetapir (^{18}F) is excreted primarily through the hepatobiliary system and patients with hepatic impairment have the potential of increased radiation exposure (see section 4.2).

Paediatric population

For information on the use in the paediatric population, see sections 4.2 or 5.1.

Interpretation of Amyvid images

Amyvid images should only be interpreted by readers trained in the interpretation of PET images with florbetapir (^{18}F). A negative scan indicates sparse or no density of cortical β-amyloid plaques. A positive scan indicates moderate to frequent density. Image interpretation errors in the estimation of brain β-amyloid neuritic plaque density, including false negatives, have been observed.

Review of images should be primarily in the transaxial orientation with access as needed to the sagittal and coronal planes. It is recommended that review of images

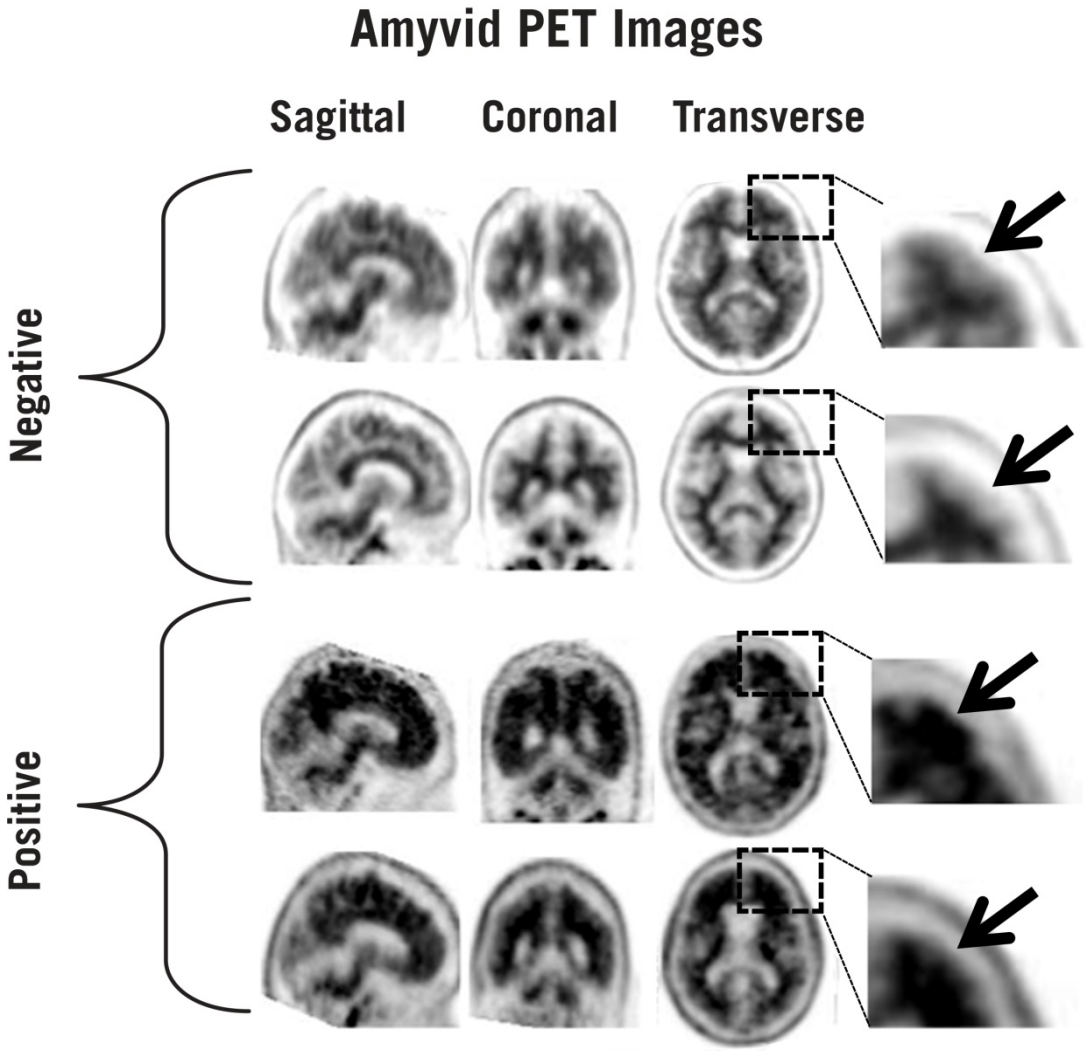
include all transaxial slices of the brain using a black-white scale with the maximum intensity of the scale set to the maximum intensity of all brain pixels.

Interpretation of the image as negative or positive is made by visually comparing the activity in cortical grey matter with activity in adjacent white matter (see Figure 1).

Negative scans have more activity in white matter than in grey matter, creating clear grey-white contrast. Positive scans will have either:

a) Two or more brain areas (each larger than a single cortical gyrus) in which there is reduced or absent grey-white contrast. This is the most common appearance of a positive scan; or
b) One or more areas in which grey matter activity is intense and clearly exceeds activity in adjacent white matter.

Figure 1: Amyvid PET cases showing examples of negative scans (top two rows) and positive scans (bottom two rows). Left to right panels show sagittal, coronal, and transverse PET image slices. Final panel to right shows enlarged picture of the brain area in the box. The top two arrows are pointing to normal preserved grey-white contrast with the cortical activity less than the adjacent white matter. The bottom two arrows indicate areas of decreased grey-white contrast with increased cortical activity that is comparable to the activity in the adjacent white matter.



Adjunctive use of quantitative information for image interpretation:
Adjunctive use of amyloid PET quantitative information should only be used by readers trained in the application of quantitative information to aid visual image interpretation, including recommendations for selection of appropriate software to support the methods. Incorporation of quantitative information generated by CE-marked image quantitation software as an adjunct to the visual interpretation method may improve readers' accuracy. Readers should visually interpret the scan, then perform quantitation according to manufacturer's instructions, including quality checks of the quantitative process, and compare quantitation of scan with typical ranges for negative and positive scans. If the quantitation result is inconsistent with the initial visual interpretation:

1. The spatial normalisation and fit of the scan to the template should be re-checked to confirm the accuracy of the placement of the regions of interest (ROIs), search for CSF or bone within the ROI, and evaluate the potential impact of atrophy or ventriculomegaly on quantitation.
2. The basis for making a visual positive or negative determination should be reviewed:
   a. In the case of an amyloid positive initial visual read and negative quantitation, the physician should consider whether the positive visual interpretation might be based on tracer retention in regions outside the ROIs that contribute to the cortical average standardised uptake value ratio (SUVR).
   b. In the case of an amyloid negative initial visual read and an amyloid positive quantitation, the regions corresponding to the ROIs with elevated SUVR should be examined to determine whether there is a loss of grey/white contrast in these areas.
3. The cerebellum region should be examined to confirm the fit of the ROI and the level of grey/white contrast, which provides a standard for visual comparison to cortex. Possible structural anomalies that could influence quantitation of the cerebellar region should be considered.
4. A final interpretation of the scan should be made based on the final visual read after conducting resolution steps 1-3 above.

<u>After the procedure</u>

Close contact with infants and pregnant women should be restricted during the initial 24 hours following the injection.

<u>Sodium</u>

This medicinal product contains up to 37 mg sodium per dose, equivalent to 1.85 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

<u>Ethanol</u>

This medicinal product contains 790 mg of alcohol (ethanol) in each 10 mL dose, which is equivalent to 11.3 mg/kg (administered to an adult with 70 kg). The amount in 10 mL of this medicinal product is equivalent to less than 20 mL beer or 8 mL wine.
The small amount of alcohol in this medicinal product will not have any noticeable effects.

4.5 Interaction with other medicinal products and other forms of interaction

No *in vivo* interaction studies have been performed.

In vitro binding studies have not shown interference of florbetapir (^{18}F) binding to β-amyloid plaques in the presence of other common medicinal products taken by AD patients.

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.
No studies have been conducted in pregnant women. No animal studies have been conducted to investigate the reproductive effects of florbetapir (^{18}F) (see section 5.3).

Breast-feeding

It is not known whether florbetapir (^{18}F) is excreted in human milk during breast-feeding. Before administering radiopharmaceuticals to a mother who is breast-feeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breast-feeding, 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, breast-feeding should be interrupted for 24 hours and the expressed feeds discarded.

Close contact with infants should be restricted during the initial 24 hours following injection.

Fertility

No studies on fertility have been performed.

4.7 Effects on ability to drive and use machines

Amyvid has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety profile of Amyvid is based on its administrations to 5 847 subjects in clinical trials.

Tabulated list of adverse reactions

Frequencies are defined as very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1/10 000); not known (cannot be estimated from the available data). While they may in reality occur at lower frequencies than indicated below, the size of the source database did not allow for the assignment of frequency categories lower than the category "uncommon" (≥1/1 000 to <1/100).

System organ class	Common	Uncommon
Nervous system disorders	Headache	Dysgeusia
Vascular disorders		Flushing
Gastrointestinal disorders		Nausea
Skin and subcutaneous tissue disorders		Pruritus Urticaria
General disorders and administration site conditions		Injection site reaction[a] Infusion site rash

[a]Injection site reaction includes injection site haemorrhage, injection site irritation, and injection site pain

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 7 mSv when the recommended activity of 370 MBq of florbetapir (^{18}F) is administered, these adverse reactions are expected to occur with low probability.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Due to the small quantity of florbetapir (^{18}F) in each dose, overdose is not expected to result in pharmacological effects. In the event of administration of a radiation overdose, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by frequent micturition and defaecation. It might be helpful to estimate the effective dose that was applied.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic radiopharmaceutical, central nervous system, ATC code: V09AX05

Mechanism of action

Florbetapir (^{18}F) binds to β-amyloid neuritic plaques. Binding studies using traditional neuropathological staining methods in post-mortem AD brains demonstrated statistically significant ($p < 0.0001$) correlations between *in vitro* florbetapir (^{18}F) binding and β-amyloid aggregate deposition. *In vivo*, correlation was assessed in end-of-life patients between florbetapir (^{18}F) uptake in cortical grey matter and the total β-amyloid burden using 4G8 anti-amyloid antibody that stains β-amyloid found in both neuritic and diffuse plaques. The *in vivo* binding of florbetapir (^{18}F) to other β-amyloid structures or other brain structures or receptors remains unknown.

Pharmacodynamic effects

At the low chemical concentrations present in Amyvid, florbetapir (^{18}F) does not have any detectable pharmacological activity.

In completed clinical trials, uptake of florbetapir (^{18}F) in 6 predefined cortical areas of the brain (precuneus, frontal, anterior cingulate, posterior cingulate, parietal and temporal) was measured quantitatively using standardised uptake values (SUV). Cortical average SUV ratios (SUVRs, relative to cerebellum)

are higher in AD patients compared with those of healthy volunteer subjects. The average cortical to cerebellar SUVR values in AD patients show continual substantial increases from time zero through 30 minutes post-administration, with only small changes thereafter up to 90 minutes post-injection. No differences in SUVR results were noted in subjects taking common AD treatments relative to those not taking AD treatments.

Clinical efficacy

A pivotal study in 59 end-of-life patients was aimed at establishing the diagnostic performance of Amyvid to detect the cortical neuritic plaque density (no or sparse vs. moderate or frequent). The PET results were compared with the maximal neuritic plaque density measured on sections of frontal, temporal or parietal cortex at the patient's autopsy within 24 months of PET scan. The cognitive status of the subjects could not be reliably measured. In all 59 subjects, a blinded PET reading by 5 nuclear medicine physicians resulted in a majority read sensitivity of 92% (95% CI: 78-98%) and specificity of 100% (95% CI: 80-100%). In a study of 47 young (<40 years) healthy volunteers, presumed to be free of β-amyloid, all Amyvid PET scans were negative.

Sensitivity and specificity to detect the cortical neuritic plaque density of Amyvid was further investigated in two additional studies, in which different sets of readers interpreted images from some subjects followed to autopsy in the pivotal study. Their results closely paralleled the results obtained in the pivotal trial. Inter-rater agreement using Fleiss' kappa values ranged from 0.75 to 0.85.

In a longitudinal study, 142 subjects (clinically diagnosed as MCI, AD or cognitively normal) underwent baseline florbetapir (^{18}F) PET scans, and were followed for 3 years to evaluate the relationship between Amyvid imaging and changes in diagnostic status.

Diagnostic performance values of florbetapir (^{18}F) PET are tabulated below:

	Agreement with baseline diagnosis of MCI N=51	*Agreement with baseline diagnosis of clinical AD* N=31
Sensitivity	19/51 = 37.3% (95% CI: 24.1-51.9%)	21/31 = 67.7% (95% CI: 51.3-84.2%)
Specificity	*Using non-MCI cases (cognitively normal & clinical AD)* 69/100 = 69.0% (95% CI: 59.9-78.1%)	*Using non-AD cases (cognitively normal & MCI)* 91/120 = 75.8% (95% CI: 68.2-83.5%)
Positive likelihood ratio	1.20 (95% CI: 0.76-1.91)	2.80 (95% CI: 1.88-4.18)

Of the patients who had been clinically diagnosed with MCI at study entry, 9 (19%) converted to clinical AD 36 months later. Of the 17 MCI patients who

had a positive PET scan, 6 (35%) were diagnosed with clinical probable AD 36 months later compared to 3 (10%) of 30 who had a negative scan. Sensitivity of Amyvid scan to show the MCI conversion rate to AD in 9 converters was 66.7% (95% CI: 35-88%), specificity in 38 non-converters was 71.0% (95% CI: 55-83%) and positive likelihood ratio was 2.31 (95% CI: 1.2-4.5). The design of this study does not allow estimating the risk of MCI progression to clinical AD.

Adjunctive use of quantitative information for image interpretation
The feasibility and reliability of using CE-marked quantitative software as an adjunct to clinical qualitative interpretation was investigated in two studies using three different commercially available quantitative software packages. Participating readers first evaluated a set of 96 PET scans, including 46 scans with autopsy standard of truth, using the visual qualitative read method to establish a baseline and were subsequently asked to re-evaluate the same set of scans with or without access to quantitative software information. Across all participating readers who had access to quantitative information, average reader accuracy on the scans with autopsy standard of truth improved from 90.1% at baseline to 93.1% (p-value <0.0001), with no observed decrease in either sensitivity or specificity.

Monitoring response to anti-amyloid therapy
Florbetapir PET imaging has been utilised to confirm eligibility and monitor brain amyloid plaque levels (for example, Centiloids) in AD drug development studies.

Paediatric population

The licensing authority has waived the obligation to submit the results of studies with Amyvid in all subsets of the paediatric population as there is no intended use in the paediatric population.

5.2 Pharmacokinetic properties

Distribution

Florbetapir (^{18}F) is distributed throughout the body within several minutes of injection, and then is rapidly metabolised.

Organ uptake

Maximal brain uptake of florbetapir (^{18}F) occurs within several minutes of injection, followed by rapid brain clearance during the first 30 minutes following injection. The organs of greatest exposure are organs of elimination, mainly the gallbladder, liver, and intestines.

Healthy controls show relatively low levels of florbetapir (^{18}F) retention in cortex and cerebellum. Regional analyses show slightly higher levels of retention in the caudate, putamen and hippocampus. The highest level of uptake is in regions mainly composed of white matter (pons and centrum

semiovale). In AD subjects, cortical regions and putamen show significantly greater uptake compared to controls. In AD subjects, as in controls, there is low retention in cerebellum and hippocampus and high retention in pons and centrum semiovale.

The biophysical basis of the white matter retention of florbetapir (^{18}F) in the living human brain cannot be definitively explained. It is hypothesised that slower clearance of the radiopharmaceutical may contribute to white matter retention since regional cerebral blood flow in white matter is less than half of that of cortex. Uptake has also been identified in some cases in extracerebral structures such as scalp, salivary glands, muscles and cranial bone. The reason for this uptake is unknown, but may be due to accumulation of florbetapir (^{18}F) or to any of its radioactive metabolites or to blood radioactivity.

Elimination

Elimination occurs primarily by clearance through the liver and excretion into the gallbladder and the intestines. Some accumulation/excretion is also observed in the urinary bladder. Radioactivity in urine is present as polar metabolites of florbetapir (^{18}F).

Half-life

Florbetapir (^{18}F) is very rapidly cleared from circulation post-intravenous injection. Less than 5% of the injected ^{18}F radioactivity remains in blood 20 minutes following administration, and less than 2% is present 45 minutes after administration. The residual ^{18}F in circulation during the 30-90 minute imaging window is principally in the form of polar ^{18}F species. The radioactive half-life of ^{18}F is 110 minutes.

Renal/hepatic impairment

The pharmacokinetics in patients with renal or hepatic impairment have not been characterised.

5.3 Preclinical safety data

Animal toxicology and safety pharmacology

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology and single and repeated dose toxicity, in which florbetapir [the non-radioactive form of florbetapir (^{18}F)] was used. An acute dose study was conducted in rats, and the NOAEL (no observable adverse effect level) was determined to be at least 100 times maximum human dose. The potential toxicity of 28 days of repeated intravenous injections of florbetapir was tested in rats and dogs, and the NOAEL was found to be at least 25 times the maximum human dose.

In an *in vitro* bacterial reverse mutation assay (Ames test), increases in the number of revertant colonies were observed in 2 of the 5 strains exposed to florbetapir. In a chromosomal aberration *in vitro* study with cultured human peripheral lymphocyte cells, florbetapir did not increase the percent of cells with structural aberrations with 3 hour exposure with or without activation; however, 22 hour exposure produced an increase in structural aberrations at all tested concentrations. Potential *in vivo* genotoxicity of florbetapir was evaluated in a rat micronucleus study. In this assay, florbetapir did not increase the number of micronucleated polychromatic erythrocytes at the highest achievable dose level, 372 µg/kg/day, when given twice daily for 3 consecutive days. This dose is approximately 500 times the maximum human dose, and showed no evidence of mutagenicity.

No studies have been conducted in animals to investigate the potential long term carcinogenicity, fertility, or reproductive effects of florbetapir (^{18}F).

No animal toxicology and safety pharmacology studies have been performed with florbetapir (^{18}F).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol, anhydrous
Sodium ascorbate
Sodium chloride
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Amyvid 800 MBq/mL solution for injection

7.5 hours from the ToC.

Amyvid 1 900 MBq/mL solution for injection

10 hours from the ToC.

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions.

Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

6.5 Nature and contents of container

Amyvid is supplied in 10 mL or 15 mL clear Type I borosilicate glass vials with FluroTec-coated chlorobutyl elastomeric stoppers and aluminium seals.

Amyvid 800 MBq/mL solution for injection

One multidose vial of 10 mL capacity contains 1 to 10 mL of solution, corresponding to 800 to 8 000 MBq at ToC.
One multidose vial of 15 mL capacity contains 1 to 15 mL of solution, corresponding to 800 to 12 000 MBq at ToC.

Amyvid 1 900 MBq/mL solution for injection

One multidose vial of 10 mL capacity contains 1 to 10 mL of solution, corresponding to 1 900 to 19 000 MBq at ToC.
One multidose vial of 15 mL capacity contains 1 to 15 mL of solution, corresponding to 1 900 to 28 500 MBq at ToC.

As a result of differences in the manufacturing process, it is possible that vials of some product batches are distributed with punctured rubber stoppers.

Each vial is enclosed in a shielded container of appropriate thickness to minimise external radiation exposure.

Pack size: 1 vial.

6.6 Special precautions for disposal

General warning

Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.

Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

If the integrity of the vial is compromised it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The administration of radiopharmaceuticals creates risks for other persons (including pregnant healthcare professionals) from external radiation or contamination from spill of urine, vomiting etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.,
Papendorpseweg 83,
3528 BJ Utrecht,
The Netherlands

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 14895/0233

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/01/2021

10 DATE OF REVISION OF THE TEXT

27/11/2024

11. DOSIMETRY

The estimated absorbed radiation doses to organs and tissues of an average adult patient (70 kg) per 370 MBq of florbetapir (^{18}F) using standard methods for dosimetry calculations (ICRP Volume 30) is tabulated below. No assumptions were made regarding urinary bladder voiding.

	Dose absorbed per activity administered (µGy/MBq)
Organ/tissue	Average
Adrenal	13.6
Brain	10.0
Breasts	6.2
Gallbladder wall	143.0
Lower large intestine wall	27.8
Small intestine	65.5
Stomach wall	11.7
Upper large intestine wall	74.4
Heart wall	12.7
Kidneys	13.0
Liver	64.4
Lungs	8.5
Muscle	8.6
Ovaries	17.6
Pancreas	14.4
Red marrow	14.3
Osteogenic cells	27.6
Skin	5.9
Spleen	8.9
Testes	6.8
Thymus	7.3
Thyroid	6.8
Urinary bladder wall	27.1
Uterus	15.6
Total body	11.6
Effective Dose *[µSv/MBq]*[a]	18.6

[a] Assumed quality factor (Q) of 1 for conversion of absorbed dose to effective dose for ^{18}F.

The effective dose resulting from the administration of a 370 MBq dose for an adult weighing 70 kg is about 7 mSv. If a CT scan is simultaneously performed as part of the PET procedure, exposure to ionising radiation will increase in an amount dependent on the settings used in the CT acquisition. For an administered activity of 370 MBq the typical radiation dose to the target organ (brain) is 3.7 mGy.

For an administered activity of 370 MBq the typical radiation doses delivered to the critical organs, gallbladder, upper large intestine wall, lower large intestine wall, small intestine and liver are 53 mGy, 27.5 mGy, 10.3 mGy, 24.2 mGy and 23.8 mGy, respectively.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Method of preparation

The package must be checked before use and the activity measured using an activimeter.

Withdrawals should be performed under aseptic conditions. The vials must not be opened before disinfecting the stopper, the solution should be withdrawn via the stopper using a single dose syringe fitted with suitable protective shielding and a disposable sterile needle or using an authorised automated application system. Only polypropylene/HDPE syringes should be used. If the integrity of the vial is compromised, the product should not be used.

Amyvid may be diluted aseptically with sodium chloride 9 mg/mL (0.9%) solution for injection to a maximum dilution of 1:5. Diluted product must be used within 4 hours of dilution.

Quality control

The solution should be inspected visually prior to use. Only clear solutions, free of visible particles should be used.