ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Pylclari 1 000 MBq/mL solution for injection
Pylclari 1 500 MBq/mL solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Pylclari 1 000 MBq/mL solution for injection

Each mL of solution contains 1 000 MBq of piflufolastat (^{18}F) at the date and time of calibration.

The total activity per vial ranges from 500 MBq to 10 000 MBq at the date and time of calibration.

Pylclari 1 500 MBq/mL solution for injection

Each mL of solution contains 1 500 MBq of piflufolastat (^{18}F) at the date and time of calibration.

The total activity per vial ranges from 750 MBq to 15 000 MBq at the date and time of calibration.

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

Excipients with known effect

Each mL of solution contains a maximum of 3.5 mg of sodium and 90 mg of ethanol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution with a pH ranging from 4.5 to 7.5.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Pylclari is indicated for the detection of prostate-specific membrane antigen (PSMA) positive lesions with positron emission tomography (PET) in adults with prostate cancer (PCa) in the following clinical settings:

- Primary staging of patients with high-risk PCa prior to initial curative therapy,
- To localize recurrence of PCa in patients with a suspected recurrence based on increasing serum prostate-specific antigen (PSA) levels after primary treatment with curative intent.

4.2 Posology and method of administration

This medicinal product is for use in designated nuclear medicine facilities only and should only be handled by authorised personnel.

Posology

The mean recommended activity of (^{18}F) piflufolastat is 4 MBq/kg of body weight and can vary from 3 to 5 MBq/kg of body weight depending on the PET equipment and acquisition mode used. The minimum activity should not fall below 190 MBq and the maximum activity should not exceed 360 MBq.

Renal impairment / Hepatic impairment
Piflufolastat (^{18}F) has only been studied in patients with mild renal impairment. Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in patients with severe impaired renal function.

Piflufolastat (^{18}F) has not been studied in patients with hepatic impairment.

Paediatric population
There is no relevant use of piflufolastat (^{18}F) in the paediatric population.

Method of administration

It is administered by a single intravenous injection.

Pylclari is presented in multidose vial. The minimal volume is 0.5 mL of solution per vial.
The volume of solution to be administered can range from 0.2 mL to 10 mL.

Precautions to be taken before handling or administering the medicinal product
For instruction before administration, see section 6.6.

For instructions on dilution of the medicinal product before administration, see section 12.

Image acquisition

It is recommended to position the patient supine with arms above the head. A non contrast-enhanced low-dose CT scan is performed from the vertex of the skull through mid-thigh for attenuation correction and anatomic correlation. The PET acquisition is performed from mid-thigh through the vertex of the skull, starting 90 to 120 minutes after tracer injection. It must include lower extremities if there is known or suspected disease. Image acquisition duration is 12 to 40 minutes depending on the type of PET cameras, number of bed positions (typically 6 to 8) and acquisition time per bed position (typically 2 minutes to 5 minutes). If the acquisition leads to indeterminate findings, and provided a sufficient activity remains for adequate counting statistics, late acquisitions can also be performed, thus reducing background activity.

For patient preparation, see section 4.4.

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

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 impairment

Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Paediatric population

For information on the use in paediatric population, see section 4.2.

Patient preparation

The patient should be well hydrated before the start of the examination and urged to void before the examination in order to reduce bladder activity and as often as possible during the first hours after the examination in order to reduce radiation exposure.

A diuretic expected to act within the uptake time period may be administered to improve interpretation of piflufolastat (^{18}F) PET/CT as it results in less activity depositions in ureters and the bladder.

After the procedure

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

Interpretation of piflufolastat (^{18}F) images

The recommended method for PET images interpretation with piflufolastat (^{18}F) PET/CT is the visual interpretation.

Lesions should be considered suspicious if uptake is greater than physiologic uptake in that tissue or greater than adjacent background if no physiologic uptake is expected.

Piflufolastat (^{18}F) accumulates in normal tissue where the density of PSMA is high including the lacrimal glands, salivary glands, liver, spleen, and kidneys. Normal organs demonstrate significant variability in the uptake of piflufolastat (^{18}F); however, the impact of tumor burden on normal uptake is minimal and unlikely to be clinically significant. The expression of PSMA can predominantly be found in prostate cancer, but can also be observed in other neoplasms (e.g. renal cell carcinoma, hepatocarcinoma, breast cancer, lung cancer and other malignancies) or non-malignant conditions (e.g hemangioma, ganglia, since they can mimic lymph nodes, benign bone disease as Paget's disease, or pulmonary sarcoidosis/granulomatosis).

Images should be interpreted only by readers trained in the interpretation of PET images with piflufolastat (^{18}F).

Clinical correlation, which may include histopathological evaluation of the suspected prostate cancer site, is recommended. A negative image does not rule out the presence of prostate cancer and a positive image does not confirm the presence of prostate cancer.

Piflufolastat (^{18}F) was not studied for detection of distant metastases in primary staging.

The performance of piflufolastat (^{18}F) for imaging of patients with biochemical evidence of recurrence of prostate cancer seems to be affected by serum PSA levels (see section 5.1). The performance of piflufolastat (^{18}F) for imaging of metastatic pelvic lymph nodes prior to initial definitive therapy seems to be affected by risk factors such as Gleason score.

Small lymph nodes metastases, or any lesion under spatial resolution of PET (= 5 mm) may be missed by piflufolastat (^{18}F) PET/CT.

To date no outcome data exist to support subsequent management of patients based on PSMA-PET in the primary staging. Therefore, treatment should not be changed based on piflufolastat (^{18}F) PET/CT findings only.

Specific warnings

This medicinal product contains up to 3.5 mg sodium per mL equivalent to 0.2 % to the WHO recommended maximum daily intake of 2 g sodium for an adult.

This medicinal product contains up to 900 mg of alcohol (ethanol) in each administration which is equivalent to 90 mg per mL. The amount in 10 mL of this medicinal product is equivalent to less than 23 mL of beer or 11 mL of 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 interaction studies have been performed.

Androgen deprivation therapy (ADT) and other therapies targeting the androgen pathway, such as androgen receptor antagonists, may result in changes in uptake of piflufolastat (^{18}F) in prostate cancer. The effect of these therapies on performance of piflufolastat (^{18}F) PET has not been established.

Chronic treatment with diuretics does not seem to have any interference with piflufolastat (^{18}F) for interpretation of images.

4.6 Fertility, pregnancy and lactation

Pregnancy

Piflufolastat (^{18}F) is not intended for use in women.

Breast-feeding

Piflufolastat (^{18}F) is not intended for use in women.

Fertility

No studies on fertility have been performed.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of safety profile

The overall safety profile is based on data from its administration to 797 patients from three clinical studies and spontaneous reporting. In the clinical studies, each patient received a single administration with a median administered activity of 330 MBq.
Adverse reactions have been reported during clinical development and are listed below by MedDRA body system organ class.

Tabulated list of adverse reactions

The frequencies of adverse reactions are defined as follows: 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). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: Adverse reactions observed with piflufolastat (^{18}F)

MedDRA body system organ class	Adverse reactions	Frequency
Immune system disorders	Hypersensitivity	Uncommon
Metabolism and nutrition disorders	Dehydration	Uncommon
Psychiatric disorders	Disorientation	Uncommon
Nervous system disorders	Syncope	Not known*
	Dysgeusia	Common
	Headache	
	Dizziness	Uncommon
	Hyperaesthesia	
	Migraine	
Eye disorders	Visual field defect	Uncommon
Ear and labyrinth disorders	Vertigo	Uncommon
Gastrointestinal disorders	Nausea	Not known*
	Vomiting	
Skin and subcutaneous tissue disorders	Dry skin	Uncommon
	Rash	
Musculoskeletal and connective tissue disorders	Arthralgia	Uncommon
	Muscular weakness	
	Pain in extremity	
Renal and urinary disorders	Dysuria	Uncommon
General disorders and administration site conditions	Fatigue	Uncommon
	Chest discomfort	Uncommon
	Application site rash	
	Feeling abnormal	
	Injection site pain	

*Adverse reactions derived from spontaneous reporting with a not known frequency.

Description of selected adverse reactions

A total of 108 treatment emergent adverse events (TEAEs) were reported in 69 (8.6 %) patients, with headache (1.4 %), dysgeusia (1.0 %), and fatigue (0.5 %) being the most frequent. Three serious drug-related adverse events (hypersensitivity, headache, and paresthesia) were reported, all experienced by one patient and only hypersensitivity was assessed as drug-related in this patient who had a significant history of allergic reactions. All three serious drug-related adverse events were resolved.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects.

As the effective dose is 4.2 mSv when the maximal recommended activity of 360 MBq is administered in a 70 kg-weighted patient, these adverse reactions are expected to occur with a 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 national reporting system listed in Appendix V.

4.9 Overdose

The maximum amount of piflufolastat (^{18}F) injection that can be safely administered to humans has not been determined.

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 forced diuresis and frequent bladder voiding. It might be helpful to estimate the effective dose that was applied.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceuticals, other diagnostic radiopharmaceuticals for tumour detection, ATC code: V09IX16.

Mechanism of action

Prostate-Specific Membrane Antigen (PSMA), is a trans-membrane glycoprotein primarily expressed in normal human prostate epithelium at low levels, but may be overexpressed by malignant tissues, particularly by prostate cancer cells, including metastatic disease. Fluorine (^{18}F) is a β+ emitting radionuclide that enables positron emission tomography. Piflufolastat (^{18}F) is a selective second-generation fluorine-18-labeled small-molecule PSMA inhibitor. Based on the intensity of the signals, PET images obtained using piflufolastat (^{18}F) indicate the presence of PSMA expressing tissues.

Pharmacodynamic effects

At the chemical concentrations used for diagnostic examinations, this medicinal product does not appear to have any pharmacodynamic activity.

Clinical efficacy

The safety and efficacy of piflufolastat (^{18}F) were evaluated in three prospective, open-label, multi-center clinical studies in men with prostate cancer: OSPREY (NCT02981368), CONDOR (NCT03739684), and PYTHON (EudraCT number 2020-000121-37).

OSPREY cohort A enrolled a cohort of 268 men with high-risk biopsy-proven prostate cancer who were considered candidates for radical prostatectomy and pelvic lymph node dissection. Each patient received a single piflufolastat (^{18}F) PET/CT from mid-thigh to skull vertex. Three central independent readers blinded to all clinical information interpreted each PET scan for the presence of abnormal uptake in pelvic lymph nodes in multiple subregions, including the common iliac lymph nodes. Co-primary endpoints were specificity and sensitivity of piflufolastat (^{18}F) PET/CT against histopathology within the pelvic lymph nodes. Secondary endpoints were Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of piflufolastat (^{18}F) PET/CT to predict the presence or absence respectively of prostate cancer within the prostate gland and lymph nodes in Cohort A.

A total of 252 patients (94 %) underwent prostatectomy and pelvic lymph node dissection and had sufficient histopathology data for evaluation of the pelvic lymph nodes. Surgical specimens were separated into three regions: left hemipelvis, right hemipelvis, and other. For each patient, piflufolastat (^{18}F) PET/CT results and histopathology results obtained from dissected pelvic lymph nodes were compared by surgical region. PET/CT results in locations that were not dissected were excluded from analysis. For the 252 evaluable patients, the mean age was 64 years (range 46 to 84 years). The median serum PSA was 9.3 ng/mL. The total Gleason score was 7 for 19 %, 8 for 46 %, and 9 for 34 % of the patients, with the remainder of the patients having Gleason scores of 6 or 10.

The pre-defined thresholds for the co-primary endpoints were 40 % for sensitivity and 80 % for specificity. Sensitivity did not reach statistical significance for at least 2 of the 3 independent imaging reviewers, therefore, it was considered a failed study.

Table 2 shows piflufolastat (^{18}F) PET/CT performance by reader using pelvic lymph node histopathology as standard of truth, at the patient-level with region matching (one true positive region defines a true positive patient). Approximately 24% of the evaluable patients had pelvic lymph node metastases based on histopathology (95% confidence interval: 19 %, 29 %).

Table 2: Performance evaluation of piflufolastat (^{18}F) PET/CT for pelvic lymph node metastasis detection in OSPREY cohort A (n=252) using Patient-Level and Region-Matched analysis.

	Reader 1	**Reader 2**	**Reader 3**
True positive	23	17	23
False Positive	7	4	9
False Negative	36	43	37
True Negative	186	188	183
Sensitivity, % (95% CI)	39 (27;51)	28 (17;40)	38 (26;51)
Specificity, % (95% CI)	96 (94;99)	98 (95;99)	95 (92;98)
PPV, % (95% CI)	77 (62;92)	81 (59;93)	72 (56;87)
NPV, % (95% CI)	84 (79;89)	81 (76;86)	83 (78;88)

Abbreviations: CI = confidence interval, PPV = positive predictive value, NPV = negative predictive value

For primary staging (OSPREY Cohort A), high level reader agreement for pelvic lymph nodes metastases (92.5 %) was achieved with Fleiss' kappa statistic of 0.78 (95 %CI: 0.71; 0.85).

In exploratory analyses, there were numerical trends towards more true positive results among patients with total Gleason score of 8 or higher and among patients with tumor stage of T2c or higher relative to those patients with lower Gleason score or tumor stage.

A comparison on diagnostic performance of piflufolastat (^{18}F) PET/CT with baseline conventional imaging (CI) in patients with high risk prostate cancer from Osprey Cohort A was performed as a post-

hoc study. Piflufolastat (^{18}F) PET/CT demonstrated a 3-fold higher PPV than conventional imaging (median 86.7 % vs. 28.3 %, respectively) despite similar sensitivity (median 40.3 % for piflufolastat (^{18}F) PET/CT and 42.6 % for conventional imaging). Mean specificiy of piflufolastat (^{18}F) PET/CT was 97.9 % and 65.1 % for CI and mean NPV 83.2 % vs. 78.8 % respectively.

CONDOR enrolled 208 patients with biochemical evidence of suspected recurrent prostate cancer after initial treatment (radical prostatectomy in 85 % of the patients). The median serum PSA was 0.82 ng/mL. All enrolled patients had negative or equivocal for prostate cancer conventional imaging evaluation (for most patients, CT or MRI) within 60 days prior to receiving piflufolastat (^{18}F). All patients received a single PET/CT from mid-thigh to skull vertex with optional imaging of the lower extremities. Three independent central readers, blinded to all clinical information, evaluated each PET/CT scan for the presence and location of positive lesions. Location of each lesion was categorized into 5 regions (prostate/prostate bed, pelvic lymph nodes, other lymph nodes, soft tissue, bone). The primary endpoint was the correct localisation rate (CLR) at the patient level, defined as the percentage of patients for whom there was a one-to-one correspondence between localisation of at least one lesion identified on piflufolastat (^{18}F) PET/CT imaging and the composite truth standard. If the lower bound of the 95 % CI was >0.2 (CLR of 20 %) for at least 2 of the 3 independent imaging reviewers, then the primary endpoint analysis was considered a success. The secondary endpoint was the impact on patient management (IMP) defined as the percentage of patients with a change in intended prostate cancer treatment plans due to piflufolastat (^{18}F) PET/CT as measured by comparison of intended management questionnaires completed pre- and post- piflufolastat (^{18}F) PET/CT imaging results.

Depending on the reader, a total of 123 to 137 patients (59 % to 66 %) had at least one lesion that was identified as piflufolastat (^{18}F) PET-positive (Table 3). The region most commonly observed to have a PET-positive finding was pelvic lymph nodes (40 % to 42 % of all PET-positive regions) and the least common region was soft tissue (6 % to 7 %).

Depending on the reader, 99 to 104 patients with a piflufolastat (^{18}F) PET-positive region had location-matched composite reference standard information that consisted of histopathology, imaging (CT, MRI, ultrasound, fluciclovine (^{18}F) PET, choline PET, or bone scan) obtained within 60 days of the PET/CT scan, or response of serum PSA level to targeted radiotherapy. Table 3 shows patient-level performance results of piflufolastat (^{18}F) PET/CT by reader, including location-matched positive predictive value, also known as Correct Localization Rate (CLR). A patient was considered true positive if they had at least one matching location positive on both piflufolastat (^{18}F) PET/CT and the composite reference standard.

Table 3. Patient-Level Performance of piflufolastat (^{18}F) PET/CT in CONDOR (n=208)

	Reader 1	**Reader 2**	**Reader 3**
PET-negative	71	84	85
PET-positive	137	124	123
True positive	89	87	84
False positive	15	13	15
Unevaluable (PET-positive Without Reference Standard)	33	24	24
CLR % (95% CI)	86 (79,92)	87 (80,94)	85 (78,92)

Abbreviations: CLR = location-matched positive predictive value, CI = confidence interval

Table 4 shows patient-level piflufolastat (^{18}F) PET/CT results from the majority read stratified by serum PSA level. Percent PET positivity was calculated as the proportion of patients with a positive PET/CT out of all patients scanned. The likelihood of a patient having at least one piflufolastat (^{18}F) PET-positive lesion generally increased with higher serum PSA level.

Table 4: Patient-Level piflufolastat (^{18}F) PET results and percent PET positivity* stratified by serum PSA level in the CONDOR study using majority result among three readers (n=199)**

PSA (ng/mL)	PET positive patients				PET negative patients	Percent PET positivity (95% CI) *
	Total	TP	FP	Unevaluable (Without reference standard)		
< 0.5	24	11	4	9	45	35 (24;46)
≥0.5 and <1	18	12	3	3	18	50 (34;66)
≥1 and <2	21	15	3	3	10	68 (51;84)
≥2	57	50	3	4	6	90 (83;98)
Total	120	88	13	19	79	60 (54;67)

* Percent PET positivity = PET positive patients/total patients scanned. PET positive patients include true positive and false positive patients as well as those who did not have reference standard information.

** Six patients were excluded from this table due to lack of baseline PSA level, and three patients were excluded from this table due to lack of majority result among three readers.

Abbreviations: TP = true positive, FP = false positive, CI = confidence interval

For the 207 patients with medical management questionnaires completed by treating physicians at pre- and post-PSMA imaging, 64 % (131/207) of patients had a change in intended management after piflufolastat (^{18}F) PET/CT. Of the patients with changed clinical plans, 79 % (103/131) were due to positive PSMA PET/CT findings, and 21 % (28/131) were due to negative scans. The most frequent changes were from salvage local therapy to systemic therapy (58 patients), from observation to initiating any therapy (49 patients), from noncurative systemic therapy to salvage local therapy (43 patients), and from planned treatment to observation (no treatment) (9 patients).

PYTHON was a randomised, open-label, two-treatment cross-over study. It enrolled 217 male patients with first biochemical recurrence of prostate cancer, who underwent definitive therapy (radical prostatectomy (RP) ± extented lymph node dissection (eLND) in 73.2 % patients, EBRT or brachytherapy in 26.8 % patients). The primary endpoint was detection rate (DR) defined as number of patients defined as positive at patient level by the independent readers among the total number of patients assessed (for piflufolastat (^{18}F) PET/CT and fluorocholine (^{18}F) PET/CT). A significant difference of 12 % detection rate in favour of piflufolastat (^{18}F) against Fluorocholine (^{18}F) was pre-defined. Secondary endpoints were sensitivity (ratio between the number of patients defined as positive for a given region by the independent readers and the total number of patients assessed as positive for a given region by the truth panel), concordance (ratio between the number of regions defined as positive by both piflufolastat (^{18}F) PET/CT and Fluorocholine (^{18}F) PET/CT + the number of regions defined as negative by both piflufolastat (^{18}F) PET/CT and Fluorocholine (^{18}F) PET/CT and the total number of assessed regions) and impact on patient management.

Two-hundred one patients performed one piflufolastat (^{18}F) PET/CT and one fluorocholine (^{18}F) PET/CT from mid-thigh to skull vertex in a randomised order. Three independent central readers, blinded to all clinical information, evaluated each piflufolastat (^{18}F) and each fluorocholine (^{18}F) PET/CT for the presence and location of positive lesions. Location of each lesion was categorized into 5 regions (prostate/prostate bed, pelvic lymph nodes, other lymph nodes, bone, soft tissue). Recurrence was detected by the blind read experts in 119 (60.4%) and 82 (41.0%) of the patients with piflufolastat (^{18}F) and fluorocholine (^{18}F) PET/CT, respectively. Details of overall independent reader's interpretation by PSA level is given in Table 5.

Table 5: Per-patient detection rate of PET/CT by PSA level in PYTHON study (N=201)

PSA (ng/mL) level at first injection	piflufolastat (^{18}F)	fluorocholine (^{18}F)
PSA < 0.2 (n=6)	2 (33.3%)	1 (16.7%)
PSA [0.2 - 0.5] (N=68)	24 (35.3%)	21 (30.9%))
PSA [0.51 - 1] (N=31)	17 (54.8%)	10 (32.3%)
PSA [1.01 - 2] (N=19)	13 (68.4%)	6 (31.6%)
PSA >2 (N=57)	50 (87.7%)	39 (68.4%)

Per-patient sensitivity was assessed for 37 patients with a standard of truth and is reported in Table 6. Per-patient sensitivity of (^{18}F)-piflufolastat was significantly higher than that of (^{18}F)-fluorocholine ($p<0.0001$).

Table 6: Per-patient sensitivity (n=37)

PET/CT	piflufolastat (^{18}F)	fluorocholine (^{18}F)
Sensitivity (95% CI)	58.3% (95% CI 51.5;64.9)	40.6% (95% CI 34.1;47.5)

The concordance rate between (^{18}F)-piflufolastat PET/CT and (^{18}F)-fluorocholine PET/CT according to central blind readers, per-region was remarkably high for all regions of interest, namely prostate bed: 87.3 % (81.9; 91.3), pelvic lymph nodes: 73.9 % (67.3; 79.5), extrapelvic lymph nodes: 86.5% (81.0; 90.6), bones: 86.9 % (81.5;91.0), and other organs: 92.0 % (87.3; 95.1).

Regarding the localization of recurrence, the central readers achieved an agreement of 84.2% with a Fleiss' kappa statistic of 0.58 (95 % CI: 0.47; 0.70) for all biopsy images in OSPREY Cohort B. In CONDOR, the central readers exhibited 76% agreement in interpreting positive or negative piflufolastat (^{18}F) PET/CT scans with a Fleiss' kappa statistic of 0.65 (95 % CI: 0.58; 0.73), while the concordance between each central reader and the local reader ranged from 83% to 84%. In PYTHON, the inter-reader agreement percentage was 67.8 %, and the corresponding Fleiss' kappa was 0.55 (95 % CI: 0.47; 0.63).

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Pylclari in all subsets of the paediatric population in diagnosis of prostate cancer (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Distribution

Blood levels decline in a biphasic fashion. The distribution half-life is 0.17 ± 0.04 hours and the elimination half-life is 3.47 ± 0.49 hours.

Organ uptake

Physiologic accumulation of piflufolastat (^{18}F) is observed in the kidneys (16.5% of administered activity), liver (9.3 %), and lung (2.9 %), within 60 minutes of intravenous administration. Most of the remaining 70 % of activity at 60 minutes is with the rest of the body background region.

Elimination

The only radioactive component detected in plasma samples by high-performance liquid chromatography (HPLC) up to 173 minutes post-injection was unchanged piflufolastat (^{18}F). Elimination is by urinary excretion. In the first 8 hours post-injection, approximately 50% of administered radioactivity is excreted in the urine.

Half-life

The biological and effective half-life of piflufolastat (^{18}F) are 3.47 ± 0.49 hours and approximately 70 minutes, respectively.

Renal/Hepatic impairment

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

5.3 Preclinical safety data

An extended single dose toxicity study was conducted in rats with the non-radioactive pharmaceutical. No adverse reactions were observed in any of the animals, and no deaths occurred at the highest tested dose of 0.5 mg/kg. This dose is over 875-fold higher than the maximum clinical dose of 40 µg/patient (or 0.5714 µg/kg for a reference body weight of 70 kg); on a body surface area basis, this dose is approximately 142-fold higher, suggesting adequate safety margin.

No other studies were conducted.

This medicinal product is not intended for regular or continuous administration. At the chemical concentrations and the activities used for diagnostic examinations, additional studies does not appear to be necessary.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol
Sodium chloride 9 mg/mL (0.9 %) solution for injection
Sodium ascorbate

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 12.

6.3 Shelf life

10 hours from calibration time.
Date and time of expiry are indicated on the labels.

After the first withdrawal, this medicinal product does not require any special storage conditions.

After dilution, store for up to 4 hours without exceeding the expiry time.

6.4 Special precautions for storage

Store in the original lead shielding.

This medicinal product does not require any special storage conditions.

For storage conditions after first withdrawal of the medicinal product, see section 6.3.

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

6.5 Nature and contents of container

15 mL Type I glass vial, closed with a chlorobutyl stopper and an aluminium seal.

Pack size: one multidose vial contains 0.5 mL to 10 mL of solution, corresponding to:
- 500 to 10 000 MBq at calibration time of Pylclari 1 000 MBq/mL
- 750 to 15 000 MBq at calibration time of Pylclari 1 500 MBq/mL

6.6 Special precautions for disposal and other handling

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.

Precautions to be taken before handling or administering the medicinal product

This product is administered via an intravenous flexible catheter. The administration must be strictly intravenous in order to avoid irradiation as a result of local extravasation, as well as imaging artefacts. The bolus administration will be followed by a flush of 5-10 mL sodium chloride 9 mg/mL (0.9 %) solution for injection, to ensure full delivery of the dose.

For instructions on dilution of the medicinal product before administration, see section 12.

If at any time in the preparation of this medicinal product 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 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 medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

CURIUM PET FRANCE
3 rue Marie Curie, Biopole Clermont-Limagne
63 360 Saint-Beauzire - France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1746/001
EU/1/23/1746/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24 July 2023

10. DATE OF REVISION OF THE TEXT

11. DOSIMETRY

Data listed below are from sponsored clinical studies.

Assumptions:
Fluorine (^{18}F) decays to stable oxygen (^{18}O) with a half-life of 110 minutes by emitting a positronic radiation of maximum energy of 634 keV, followed by photonic annihilation radiations of 511 keV. Piflufolastat (^{18}F) exhibits bi-exponential behaviour in blood, with a distribution half-life of 0.17 ± 0.044 hours and an elimination half-life of 3.47 ± 0.49 hours. It distributes to the kidneys (16.5 % of administered activity), liver (9.3 %), and lung (2.9 %), within minutes of intravenous administration.

Methodology:
The time-integrated activity in source tissue was obtained from longitudinal imaging data. Contours or volumes of interest (VOIs) were typically drawn around different activity-containing organs that were identified on each image at each time-point. The S-value was obtained by Monte Carlo simulation. The absorbed doses calculation was performed on OLINDA/EXM software (2005). The resulting effective dose was calculated according to ICRP 60.

ORGAN	ABSORBED DOSE PER UNIT ACTIVITY ADMINISTERED (mGy/MBq)
Adrenals	0.0131
Bone surfaces	0.0099
Brain	0.0021
Breast	0.0058
Gallbladder wall	0.0141
Gastrointestinal tract	
Stomach wall	0.0092
Small Intestine wall	0.0089
Upper large intestine wall	0.0091
Lower Large Intestine wall	0.0073
Heart wall	0.0171
Kidneys	0.123
Liver	0.037
Lungs	0.0102
Muscles	0.0069
Pancreas	0.0124
Red marrow	0.0071
Skin	0.0052
Spleen	0.0271
Testes	0.0059
Thymus	0.007
Thyroid	0.0062
Urinary bladder wall	0.0072
Effective dose (mSv/MBq)	**0.0116**

The effective dose resulting from the administration of a maximal recommended activity of 360 MBq for an adult weighing 70 kg is about 4.2 mSv.

For an administered activity of 360 MBq, the typical radiation doses to the critical organs (kidneys, liver and spleen) are 44.3 mGy, 13.3 mGy and 9.8 mGy respectively.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Method of preparation

This ready-to-use medicinal product can be diluted with sodium chloride 9 mg/mL (0.9%) solution for injection.

Withdrawals of the appropriate volume should be performed under aseptic conditions. The vial must not be opened. After 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 and qualified application system.

If the integrity of this vial is compromised, the medicinal product should not be used.

This medicinal product should only be used when the injection volume is greater than 0.2 mL. If the injection volume is between 0.2 and 1 mL, only syringes of an appropriate size (1 mL) should be used.

Quality control

The packaging must be checked before use and the activity of the solution must be measured using an activimeter.

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

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

CURIUM PET FRANCE
10 AVENUE CHARLES PEGUY
95200 SARCELLES - FRANCE

CURIUM PET FRANCE
CHU XAVIER ARNOZAN
AVENUE DU HAUT LEVEQUE
33604 PESSAC - FRANCE

CURIUM PET FRANCE
136 IMPASSE DES QUATRE MOLLARDS
38280 JANNEYRIAS – FRANCE

CURIUM PET FRANCE
1-3 RUE GERMAINE RICHIER
37100 TOURS – FRANCE

CURIUM ITALY S.R.L.
VIA GIUSEPPE RIPAMONTI, 435, MILANO,
20141 – ITALY

CURIUM ITALY S.R.L.
TOR VERGATA, VIALE OXFORD, 81, ROME
00133 – ITALY

ISTITUTO DI FISIOLOGIA CLINICA DEL CNR
VIA GIUSEPPE MORUZZI, 1, PISA
56124 – ITALY

CURIUM AUSTRIA GMBH
SEILERSTÄTTE 4
LINZ, 4020 - AUSTRIA

CURIUM FINLAND OY
SAUKONPAADENRANTA 2
HELSINKI, 00180 - FINLAND

CURIUM PHARMA SPAIN, S.A.
C/ MANUEL BARTOLOMÉ COSSIO, 10
E-28040 MADRID - SPAIN

CURIUM PHARMA SPAIN, S.A.
THOMAS ALVA EDISON, 7
41092 SEVILLA – SPAIN

CURIUM PHARMA SPAIN, S.A.
POL. IND. CONPISA, C/VEGUILLAS, 2 NAVE 16
28864 AJALVIR – SPAIN

SYN INNOVATION LABORATORIES
SOUSAKI SITE AG. THEODOROI,
KORINTHIA PREFECTURE 20003 - GREECE

CURIUM PET FRANCE
3 RUE MARIE CURIE, BIOPOLE CLERMONT-LIMAGNE
63 360 SAINT-BEAUZIRE - FRANCE

CURIUM PET FRANCE
TECHNOPOLE DE CHATEAU GOMBERT
RUE LOUIS LEPRINCE RINGUET
13013 MARSEILLE - FRANCE

CURIUM PET FRANCE
CHU DE BRABOIS
4 RUE DU MORVAN
54500 VANDŒUVRE-LES-NANCY CEDEX - FRANCE

CYCLOTRON VU
VAN DER BOECHORSTSTRAAT 6A
AMSTERDAM, 1081 BT - NETHERLANDS

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

Prior to launch of piflufolastat (^{18}F) in each Member State, the Marketing Authorisation Holder (MAH) must agree about the content and format of the educational programme, including communication media, distribution modalities, and any other aspects of the programme, with the National Competent Authority (NCA).
The educational programme is aimed to reduce the risk of PET imaging interpretation errors.

The MAH shall ensure that, in each Member State where piflufolastat (^{18}F) is marketed, medical practitioners qualified to interpret PET scans in their country who are expected to use piflufolastat (^{18}F) have access to the self-training educational material.

Provision of a self-training program containing the following information:
- Physiological distribution of piflufolastat (^{18}F).
- Image interpretation guidelines.
- Examples of incidental findings on PET-CT with piflufolastat (^{18}F).
- Examples of positive and negative findings on PET-CT with piflufolastat (^{18}F)
- Demonstration cases with image interpretation.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

SHIELD LABEL

1. NAME OF THE MEDICINAL PRODUCT

Pylclari 1 000 MBq/mL solution for injection
piflufolastat (^{18}F)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each mL of solution contains 1 000 MBq of piflufolastat (^{18}F) at date and time of calibration (ToC).

3. LIST OF EXCIPIENTS

Excipients: Ethanol, sodium chloride 9 mg/mL (0.9 %) solution for injection, sodium ascorbate.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 multidose vial

Volume : {xx.x} mL

Activity (Act.) : 1 000 MBq/mL at ToC. : DDMMYYYY ({hh:mm} {Time Zone}). Or Activity : MBq/vial at ToC. : DDMMYYYY ({hh:mm} {Time Zone}).

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {DDMMYYYY} {hh:mm} {Time Zone}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose according to local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

CURIUM PET FRANCE
3 rue Marie Curie, Biopole Clermont-Limagne
63 360 Saint-Beauzire - France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1746/001

13. BATCH NUMBER

Batch {vial number}

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Pylclari 1 000 MBq/mL solution for injection

piflufolastat (^{18}F)
Intravenous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP: ToC + 10h

4. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Batch {vial number}

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Act. : ≤ 1 000 MBq/mL at ToC (see shield label)
Volume : {xx.x} mL

6. OTHER

Manufacturer : **CURIUM PET France**-Sarcelles – France
Or
Manufacturer : **CURIUM PET France-**Janneyrias – France
Or
Manufacturer : **CURIUM PET France-**Pessac - France
Or
Manufacturer : **CURIUM PHARMA SPAIN** Sevilla - Spain
Or
Manufacturer : **CURIUM PHARMA SPAIN** Madrid - Spain
Or
Manufacturer : **CURIUM PHARMA SPAIN** Ajalvir - Spain
Or
Manufacturer : **CURIUM ITALY S.R.L** Milano - Italy
Or
Manufacturer : **CURIUM ITALY S.R.L** Rome - Italy
Or
Manufacturer : **ISTITUTO DI FISIOLOGIA CLINICA DEL CNR** Pisa - Italy
Or
Manufacturer : **SYN INNOVATION LABORATORIES** - Greece

Or
Manufacturer : **CURIUM AUSTRIA GMBH** - Austria
Or
Manufacturer : **CURIUM FINLAND OY** - Finland
Or
Manufacturer: **CURIUM PET France-**Marseille - France
Or
Manufacturer: **CURIUM PET France**-Nancy – France
Or
Manufacturer: **CURIUM PET France-**Tours – France
Or
Manufacturer: **CYCLOTRON VU** - Netherlands

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

SHIELD LABEL

1. NAME OF THE MEDICINAL PRODUCT

Pylclari 1 500 MBq/mL solution for injection
piflufolastat (^{18}F)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each mL of solution contains 1 500 MBq of piflufolastat (^{18}F) at date and time of calibration (ToC).

3. LIST OF EXCIPIENTS

Excipients: Ethanol, sodium chloride 9 mg/mL (0.9 %) solution for injection, sodium ascorbate.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 multidose vial

Volume : {xx.x} mL

Activity (Act.): 1 500 MBq/mL at ToC. : DDMMYYYY ({hh:mm} {Time Zone}). Or Activity : MBq/vial at ToC. : DDMMYYYY ({hh:mm} {Time Zone}).

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {DDMMYYYY} {hh:mm} {Time Zone}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose according to local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

CURIUM PET FRANCE
3 rue Marie Curie, Biopole Clermont-Limagne
63 360 Saint-Beauzire - France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1746/002

13. BATCH NUMBER

Batch {vial number}

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Pylclari 1 500 MBq/mL solution for injection

piflufolastat (^{18}F)
Intravenous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP: ToC + 10h

4. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Batch {vial number}

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Act. : ≤ 1 500 MBq/mL at ToC (see shield label)
Volume : {xx.x} mL

6. OTHER

Manufacturer: **CURIUM PET France**-Sarcelles - France
Or
Manufacturer: **CURIUM PET France-**Janneyrias - France
Or
Manufacturer: **CURIUM PET France-**Pessac - France
Or
Manufacturer: **CURIUM PHARMA SPAIN** Sevilla - Spain
Or
Manufacturer: **CURIUM PHARMA SPAIN** Madrid - Spain
Or
Manufacturer: **CURIUM PHARMA SPAIN** Ajalvir - Spain
Or
Manufacturer: **CURIUM ITALY S.R.L** Milano – Italy
Or
Manufacturer : **CURIUM ITALY S.R.L** Rome - Italy
Or
Manufacturer : **ISTITUTO DI FISIOLOGIA CLINICA DEL CNR** Pisa - Italy
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Or
Manufacturer: **CURIUM PET France**-Nancy - France
Or
Manufacturer: **CURIUM PET France**-Tours - France
Or
Manufacturer: **CYCLOTRON VU** - Netherlands

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Pylclari 1 000 MBq/mL solution for injection
Pylclari 1 500 MBq/mL solution for injection
piflufolastat (^{18}F)

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects

Read all of this leaflet carefully before you are given this medicine because it contains important information for you
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Pylclari is and what it is used for

This medicine is a radiopharmaceutical product for diagnostic use only.

Pylclari contains the active substance piflufolastat (^{18}F), which contains radioactive fluorine (^{18}F). It is given so that doctors can perform a special type of scan called a positron emission tomography (PET) scan to detect specific types of cancer cells with a protein called prostate-specific membrane antigen (PSMA). This medicine is used in patients:
- with prostate cancer who are at high risk of the disease spreading to other parts of the body and who is suitable for treatment which can cure the cancer
- have received previous treatment for prostate cancer and in whom the cancer is suspected to have returned based on the results from other tests (e.g., prostate specific antigen, PSA).

Pylclari PET scan can can help your doctor find the locations of the disease.
You should discuss the results of the test with the doctor that requested the scan.

The use of Pylclari does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the radiopharmaceutical outweighs the risk due to radiation.

2. What you need to know before Pylclari is given to you

Pylclari must not be used
If you are allergic to piflufolastat (^{18}F) or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Take special care with Pylclari
- if you have kidney problems
- if you are on a low sodium diet (see section 2 "Pylclari contains sodium").

Before administration of Pylclari you should
Drink plenty of water before the start of the examination in order to urinate as often as possible during the first hours after the scan.

Children and adolescents
This medicine is not intended for use in children and adolescents.

Other medicines and Pylclari
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines, such as hormonotherapy to treat your prostate cancer, since they may interfere with the interpretation of the images.

Pregnancy and breast-feeding
This medicine is not intended for use in women.

Driving and using machines
It is considered unlikely that this medicine will affect your ability to drive or to use machines.

Pylclari contains alcohol (ethanol)
This medicine contains up to 900 mg alcohol per administration equivalent to less than 23 mL of beer or 11 mL of wine. The small amount of alcohol in this medicine will not have any noticeable effect.

Pylclari contains sodium
This medicine contains up to 35 mg of sodium (main component of cooking/table salt) in each dose. This is equivalent to 2 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How Pylclari is given

There are strict laws on the use, handling and disposal of radiopharmaceutical products. Pylclari will only be used in specially controlled areas. This product will only be handled and given to you by people who are trained and qualified to use it safely. These persons will take special care for the safe use of this medicine and will keep you informed of their actions.

Recommended dose
The nuclear medicine doctor supervising the procedure will decide on the quantity of this medicine to be used in your case. It will be the smallest quantity necessary to get the desired information. The mean recommended amount is 4 MBq/kg of body weight ; it is about 280 megabecquerel for an adult of 70 kg (MBq, the unit used to express radioactivity).

Administration of Pylclari and conduct of the procedure
- This medicine will be given as a single injection into a vein in your arm.
- One injection is sufficient to conduct the test that your doctor needs.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure.
The scan will usually start between 90 and 120 minutes after Pylclari injection is given.

After administration of Pylclari you should:
- avoid any close contact with young children and pregnant women for the 12 hours following the injection

- drink plenty of water in order to urinate (pass water) frequently, to eliminate the product from your body.

The nuclear medicine doctor will inform you if you need to take any other special precautions after receiving this medicine. Contact your nuclear medicine doctor if you have any questions.

If you have been given more Pylclari than you should
An overdose is unlikely because you will only receive a single dose of Pylclari precisely controlled by the nuclear medicine doctor supervising the procedure.

However, in case of an overdose, you will receive the appropriate treatment. The nuclear medicine doctor in charge of the procedure may provide ways to increase the passing of urine in order to facilitate the removal of the medicine from your body.

Should you have any further question on the use of Pylclari, please ask your nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Common (may affect up to 1 in 10 people):
- dysgeusia (altered taste in the mouth),
- headache.

Uncommon (may affect up to 1 in 100 people):
- hypersensitivity (allergic reactions),
- dehydration (when the body loses too much water and other fluids that it needs to work normally),
- confusion about time and place,
- tiredness,
- dizziness,
- increased sensitivity or heightened pain response to stimuli such as light touch or sound,
- migraine,
- vertigo (a spinning sensation),
- muscular weakness,
- visual field defect,
- dry skin,
- rash,
- arthralgia (joint pain),
- pain in extremity,
- dysuria (urination trouble),
- chest discomfort,
- rash at the site of administration,
- feeling abnormal,
- pain at the site of administration.

Not known (frequency cannot be estimated from the available data):
- fainting
- nausea (feeling sick)
- vomiting

This radiopharmaceutical will deliver low amounts of ionising radiation associated with the least risk of cancer and hereditary abnormalities.

Reporting of side effects
If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V By reporting side effects, you can help provide more information on the safety of this medicine.

5. How Pylclari is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

The following information is intended for the specialist only.
Pylclari must not be used after the expiry date which is stated on the shield label after 'EXP'.

6. Contents of the pack and other information

What Pylclari contains
- The active substance is piflufolastat (^{18}F). Each mL of solution contains 1 000 MBq or 1 500 MBq of Pylclari at the date and time of calibration.
- The other ingredients are ethanol, sodium chloride 9 mg/ml (0.9 %) solution for injection and sodium ascorbate.

Please see section 2 "Pylclari contains sodium and ethanol".

What Pylclari looks like and contents of the pack
Pylclari is a clear, colourless solution presented in a glass vial.
Each multidose vial contains 0.5 to 10 mL of solution, corresponding to 500 to 15 000 MBq at the date and time of calibration.

Marketing Authorisation Holder
CURIUM PET FRANCE
3 rue Marie Curie, Biopole Clermont-Limagne
63 360 Saint-Beauzire -France

Manufacturers

CURIUM PET FRANCE
10 AVENUE CHARLES PEGUY
95200 SARCELLES - FRANCE

CURIUM PET FRANCE
CHU XAVIER ARNOZAN
AVENUE DU HAUT LEVEQUE
33604 PESSAC - FRANCE

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LINZ, 4020 - AUSTRIA

CURIUM PET FRANCE
3 RUE MARIE CURIE, BIOPOLE CLERMONT-LIMAGNE
63 360 SAINT-BEAUZIRE - FRANCE

CURIUM PET FRANCE
TECHNOPOLE DE CHATEAU GOMBERT
RUE LOUIS LEPRINCE RINGUET
13013 MARSEILLE - FRANCE

CURIUM PET FRANCE
CHU DE BRABOIS
4 RUE DU MORVAN
54500 VANDŒUVRE-LES-NANCY CEDEX - FRANCE

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CURIUM PET FRANCE
1-3 RUE GERMAINE RICHIER
37100 TOURS – FRANCE

ISTITUTO DI FISIOLOGIA CLINICA DEL CNR
VIA GIUSEPPE MORUZZI, 1, PISA
56124 – ITALY

CURIUM ITALY S.R.L.
TOR VERGATA, VIALE OXFORD, 81, ROME
00133 – ITALY

CURIUM PHARMA SPAIN, S.A.
POL. IND. CONPISA, C/VEGUILLAS, 2 NAVE 16
28864 AJALVIR – SPAIN

This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

The complete SmPC of Pylclari is provided as a separate document in the product package, with the objective to provide healthcare professionals with other additional scientific and practical information about the administration and use of this radiopharmaceutical.

Please refer to the SmPC.