NEW DRUG APPROVAL

Brand Name	Pylarify®
Generic Name	piflufolastat F 18
Drug Manufacturer	Progenics Pharmaceuticals, Inc.

New Drug Approval

FDA Approval Date: May 26, 2021

Review designation: Priority

Type of review: Type 1 - New Molecular Entity; New Drug Application NDA: 214793

Dispensing restrictions: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

The prostate is a walnut-sized gland that is involved in the production of semen. It is located below a man's bladder, in front of the rectum. Prostate cancer is the abnormal growth of cells in the prostate gland.

Worldwide, there are an estimated 1,400,000 new cases of prostate cancer annually, making it the second most commonly diagnosed cancer in men. Among men in the United States, it is the leading cause of cancer, accounting for 26 percent of cancer diagnoses. For an American male, there is a 12 percent lifetime risk of being diagnosed with prostate cancer. Surveillance, Epidemiology, and End Results (SEER) data indicate that between 2010 and 2015, the overall incidence of prostate cancer in the United States decreased, particularly for low-risk disease, while the incidence of metastatic disease (per 100,000) increased from 6.2 to 7.1 in men aged 50 to 74 and from 16.8 to 22.6 in men ≥75 years. The declining incidence rate for low-risk disease was temporally associated with decreased prostate cancer screening following the 2012 US Preventive Services Task Force (USPSTF) recommendation against prostate cancer screening. Data from 2016 onward show that the declining rate of low-risk disease has stabilized for men ≥75 years, but rates of regional-stage (annual percent change of 11.1) and distant-stage (annual percent change of 5.0) disease continue to significantly increase for men aged >50 years.

Prostate cancer mortality rates have declined in the United States between 1992 and 2017, decreasing from 39 to 19 per 100,000 persons. Simulation models suggest that prostate-specific antigen (PSA) screening could account for 45 to 70 percent of the decline, mainly by decreasing the incidence of distant-stage disease. Other factors that may explain the decline in mortality rates include advances in treatments for men with localized prostate cancer as well as for those with distant-stage disease. For example, the use of androgen deprivation therapy or other chemotherapies could allow men with advanced-stage disease to live long enough to die from a concomitant condition, rather than from prostate cancer.

Efficacy

The studies were evaluated in two prospective, open-label, multi-center clinical studies in men with prostate cancer: OSPREY (NCT02981368) and CONDOR (NCT03739684).

Pylarify® PET performance by reader through comparison to pelvic lymph node histopathology at the patient-level with region matching, such that at least 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 5: Patient-Level, Region-Matched Performance of PYLARIFY PET for Detection of Pelvic Lymph Node Metastasis in OSPREY (n=252)

	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

Table below shows patient-level performance results of Pylarify® PET by reader, including location -matched positive predictive value [true positive / (true positive + false positive)], also known as Correct Localization Rate (CLR). For these results, a patient was considered true positive if they had at least one matching location positive on both Pylarify® PET and the composite reference standard. In addition to calculating location-matched positive predictive value in the Evaluable Set (CLR), an exploratory analysis of positive predictive value in all scanned patients (Imputed CLR) was performed in which Pylarify® PET-positive patients who lacked reference standard information were imputed using an estimated likelihood that at least one PET-positive lesion was reference standard positive, based on patient-specific factors.

Table 6: Patient-Level Performance of PYLARIFY PET in CONDOR (n=208)

	Reader 1	Reader 2	Reader 3
True Positive (TP)	89	87	84
False Positive (FP)	15	13	15
PET-Positive Without Reference Standard	33	24	24
PET-Negative	71	84	85
CLR % (95% CI)	86 (79, 92)	87 (80, 94)	85 (78, 92)
Imputed CLR % (95% CI)	78 (71, 85)	81 (74, 88)	79 (72, 86)

Abbreviations: TP = true positive, FP = false positive, CLR = location-matched positive predictive value in the Evaluable Set [TP/(TP + FP)], Imputed CLR = location-matched positive predictive value in all scanned patients using an imputation approach based on patient-specific factors for PET-Positive Without Reference Standard, CI = confidence interval

Safety

ADVERSE EVENTS

The safety of Pylarify® was evaluated in 593 patients, each receiving one dose of Pylarify®. The average injected activity was 340 ± 26 MBq (9.2 ± 0.7 mCi). The adverse reactions reported in >0.5% of patients within the studies are shown in Table below. In addition, a hypersensitivity reaction was reported in one patient (0.2%) with a history of allergic reaction.

Table. Adverse Reactions with a Frequency >0.5% in Patients Who Received Pylarify® (n = 593)

Adverse Reaction	n (%)
Headache	13 (2%)
Dysgeusia	10 (2%)
Fatigue	7 (1%)

WARNINGS & PRECAUTIONS

- Risk of Image Misinterpretation: Pylarify® uptake can be seen in a variety of tumor types as well as in non-malignant processes and normal tissues. Image interpretation errors can occur with Pylarify® imaging.
- Hypersensitivity Reactions: Monitor patients for hypersensitivity reactions, particularly patients with a history of allergy to other drugs and foods.
- Radiation Risk: Ensure safe drug handling to protect patients and health care workers from unintentional radiation exposure.

CONTRAINDICATIONS

None.

Clinical Pharmacology

MECHANISMS OF ACTION

Piflufolastat F 18 binds to cells that express PSMA, including malignant prostate cancer cells, which usually overexpress PSMA. Fluorine-18 (F 18) is a β+ emitting radionuclide that enables positron emission tomography.

Dose & Administration

ADULTS

The recommended amount of radioactivity to be administered for PET imaging is 333 MBq (9 mCi) with an acceptable range of 296 MBq to 370 MBq (8 mCi to 10 mCi) administered as a single bolus intravenous injection.

PEDIATRICS

The safety and effectiveness of Pylarify® in pediatric patients have not been established.

GERIATRICS

Refer to adult dose.

RENAL IMPAIRMENT

N/A

HEPATIC IMPAIRMENT

N/A

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Injection: clear, colorless solution in a multiple-dose vial containing 37 MBq/mL to 2,960 MBq/mL (1 mCi/mL to 80 mCi/mL) of piflufolastat F18 at calibration date and time.