PYLARIFY®
Piflufolastat F 18 Injection

Clinical Guidelines Summary

Evaluation of appropriate use of PSMA PET imaging in prostate cancer (NCCN, SNMMI, AUA/SUO)

INDICATION

PYLARIFY (piflufolastat F 18) Injection is a radioactive diagnostic agent indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer:

- with suspected metastasis who are candidates for initial definitive therapy.
- with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level

SELECTED IMPORTANT SAFETY INFORMATION

Radiation Risks

Diagnostic radiopharmaceuticals, including PYLARIFY, expose patients to radiation. Radiation exposure is associated with a dose-dependent increased risk of cancer. Ensure safe handling and preparation procedures to protect patients and health care workers from unintentional radiation exposure. Advise patients to hydrate before and after administration and to void frequently after administration.

For important risk and use information, please see Indications and Important Safety Information on page 6 and Full Prescribing Information, also available at www.PYLARIFY.com, or call Customer Service at 1-800-964-0446.

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

The NCCN Guidelines® state that because of the increased sensitivity and specificity of PSMA-PET tracers for detecting micrometastatic disease compared to CT, MRI, and bone scan at both initial staging and BCR [biochemical recurrence], PSMA-PET/CT or PSMA-PET/MRI can serve as a more effective frontline imaging tool for these patients.[1]

- Initial staging
- Detection of BCR
- Workup for progression of disease in bone and soft tissues

> ***"Although the FDA has approved Ga-68 PSMA-11 for use with Lu-177-PSMA-617, the panel believes that F-18 piflufolastat PSMA and F-18 flotufolastat PSMA can also be used in the same space due to multiple reports describing the equivalency of these imaging agents."***
>
> –NCCN Guidelines for Prostate Cancer, V.1.2025[1]

Initial risk stratification and staging workup for clinically localized disease[1]

Risk Group	Clinical/Pathologic Features			Additional Evaluation
Intermediate	Has all of the following: • No high-risk group features • No very-high-risk group features • Has one or more intermediate risk factors (IRFs): -cT2b-cT2c -Grade Group 2 or 3 -PSA 10-20 ng/mL	Favorable intermediate	Has all of the following: • 1 IRF • Grade Group 1 or 2 • <50% biopsy cores positive (eg, <6 of 12 cores)	• Confirmatory testing can be used to assess the appropriateness of active surveillance
		Unfavorable intermediate	Has one or more of the following: • 2 or 3 IRFs • Grade Group 3 • ≥50% biopsy cores positive (eg, ≥6 of 12 cores)	• Soft tissue imaging and consider bone imaging
High	Has one or more high-risk features, but does not meet criteria for very high risk: • cT3-cT4 • Grade Group 4 or Grade Group 5 • PSA >20 ng/mL			Bone and soft tissue imaging
Very High	Has at least two of the following: • cT3-cT4 • Grade Group 4 or 5 • PSA >40 ng/mL			Bone and soft tissue imaging

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SNMMI Appropriate Use Criteria

Clinical scenarios for PSMA PET[2]

Scenario No.	Description	Pathologic	Score
1	Patients with suspected prostate cancer (eg, high/rising PSA levels, abnormal digital rectal examination results) evaluated for targeted biopsy and detection of intraprostatic tumor	Rarely appropriate	3
2	Patients with very low, low, and favorable intermediate-risk prostate cancer	Rarely appropriate	2
3	Newly diagnosed unfavorable intermediate, high-risk, or very-high-risk prostate cancer	Appropriate	8
4	Newly diagnosed unfavorable intermediate, high-risk, or very-high-risk prostate cancer with negative/equivocal or oligometastatic disease on conventional imaging	Appropriate	8
5	Newly diagnosed prostate cancer with widespread metastatic disease on conventional imaging	May be appropriate	4
6	PSA persistence or PSA rise from undetectable level after radical prostatectomy	Appropriate	9
7	PSA rise above nadir after definitive radiotherapy	Appropriate	9
8	PSA rise after focal therapy of the primary tumor	May be appropriate	5
9	nmCRPC (M0) on conventional imaging	Appropriate	7
10	Posttreatment PSA rise in the mCRPC setting in a patient not being considered for PSMA-targeted radioligand therapy	May be appropriate	6
11	Evaluation of eligibility for patients being considered for PSMA-targeted radioligand therapy	Appropriate	9
12	Evaluation of response to therapy	May be appropriate	5

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AUA/SUO Guidelines for Advanced Prostate Cancer[3]

BCR without metastatic disease after exhaustion of local treatment options

- In patients with PSA recurrence after failure of local therapy who are at higher risk for the development of metastases (eg, PSADT <12 months), clinicians should perform periodic staging evaluations consisting of cross-sectional imaging (CT, MRI) and technetium bone scan and/or preferably PSMA PET imaging
- Clinicians should utilize PSMA PET imaging preferentially, where available, in patients with PSA recurrence after failure of local therapy as an alternative to conventional imaging due to its greater sensitivity or in the setting of negative conventional imaging

Metastatic hormone-sensitive prostate cancer (mHSPC)

- Clinicians should assess the extent of metastatic disease (lymph node, bone, and visceral metastases) in newly diagnosed mHSPC patients
- Patients diagnosed with aggressive cancer defined by D'Amico risk factors (cT3a or greater, Grade Group 4/5, or PSA >20 ng/mL) should undergo routine bone scan and cross-sectional imaging (CT or MRI) or PET imaging at the time of diagnosis. PSMA PET availability is increasing in the US and detects metastatic disease at low PSA values
- Both ^{68}Ga-PSMA-11 and ^{18}F-DCFPyL are indicated for patients with suspected prostate cancer metastasis considering local therapy, as well as for patients with suspected prostate cancer recurrence based on elevated serum PSA levels. Utilization of PSMA PET may lead to the diagnosis of metastatic disease not previously detected with conventional imaging

Nonmetastatic castration-resistant prostate cancer (nmCRPC)

- Clinicians should assess patients with nmCRPC for development of metastatic disease using conventional or PSMA PET imaging at intervals of 6 to 12 months

Metastatic castration-resistant prostate cancer (mCRPC)

- In patients with mCRPC without PSA progression or new symptoms, clinicians should perform imaging at least annually
- In patients with mCRPC with disease progression (PSA or radiographic progression or new disease-related symptoms) having previously received docetaxel and androgen pathway inhibitor who are considering ^{177}Lu-PSMA-617, clinicians should order PSMA PET imaging

AUA=American Urological Association; BCR=biochemically recurrent/biochemical recurrence; CRPC=castration-resistant prostate cancer; CT=computed tomography; FDA=US Food and Drug Administration; IRF=intermediate risk factor; mCRPC=metastatic CRPC; mHSPC=metastatic hormone-sensitive prostate cancer; MRI=magnetic resonance imaging; NCCN=National Comprehensive Cancer Network; nmCRPC=nonmetastatic CRPC; PET=positron emission tomography; PSA=prostate-specific antigen; PSADT=PSA doubling time; PSMA=prostate-specific membrane antigen; SNMMI=Society of Nuclear Medicine and Molecular Imaging; SUO=Society of Urologic Oncology.

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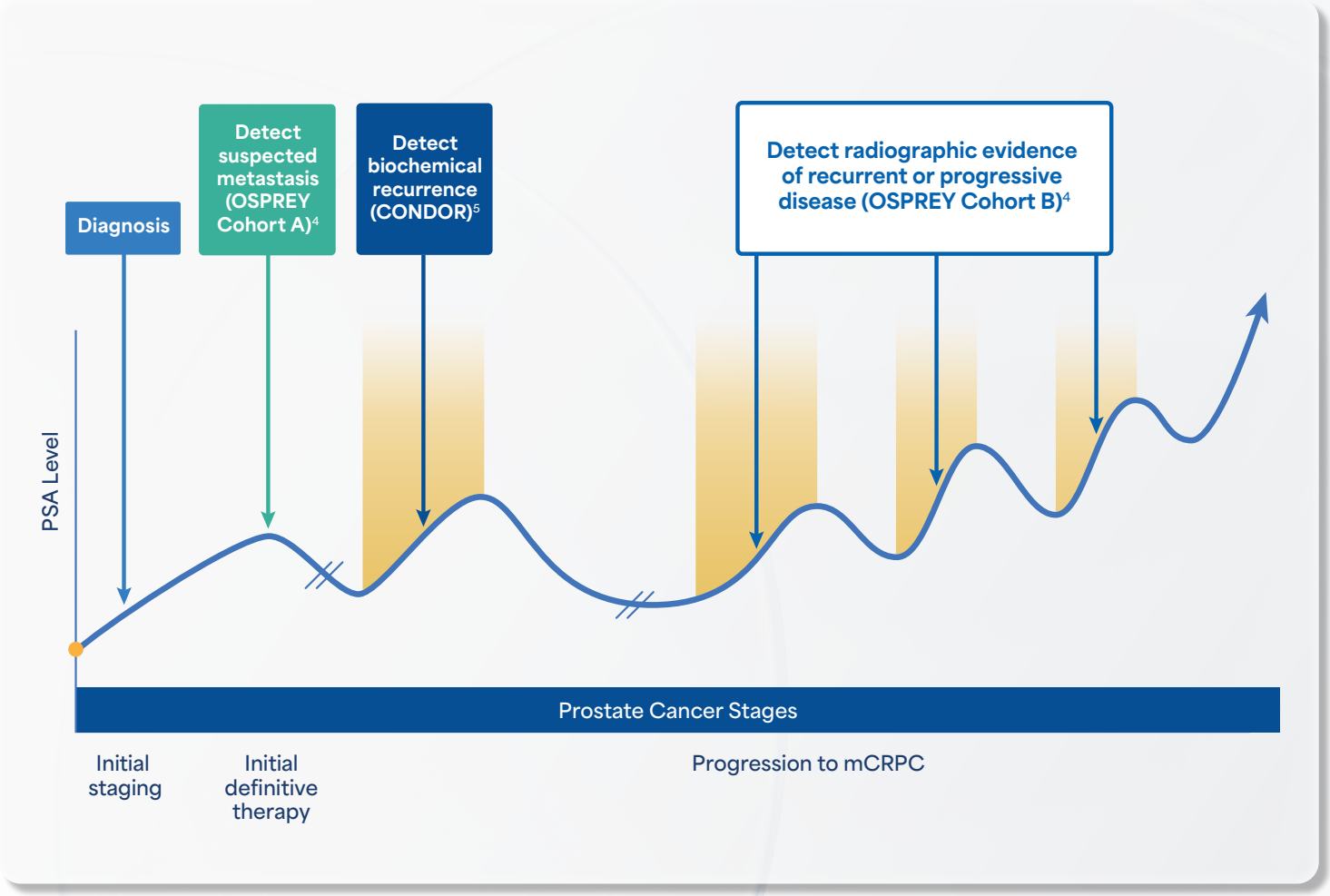
PYLARIFY can help provide clarity

From initial staging and throughout the prostate cancer journey



Piflufolastat F 18 Injection (PYLARIFY®) is National Comprehensive Cancer Network® (NCCN®) Recommended (Category 2A*)[1]

*Category 2A recommendations are made when, based upon lower-level evidence, there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.[1]

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IMPORTANT SAFETY INFORMATION

Contraindications
None.

Warnings and Precautions

Risk of Image Misinterpretation
Imaging interpretation errors can occur with PYLARIFY imaging. A negative image does not rule out the presence of prostate cancer and a positive image does not confirm the presence of prostate cancer. The performance of PYLARIFY for imaging of patients with biochemical evidence of recurrence of prostate cancer seems to be affected by serum PSA levels. The performance of PYLARIFY for imaging of metastatic pelvic lymph nodes prior to initial definitive therapy seems to be affected by risk factors such as Gleason score and tumor stage. PYLARIFY uptake is not specific for prostate cancer and may occur with other types of cancer as well as non-malignant processes and in normal tissues. Clinical correlation, which may include histopathological evaluation of the suspected prostate cancer site, is recommended.

Hypersensitivity Reactions
Monitor patients for hypersensitivity reactions, particularly patients with a history of allergy to other drugs and foods. Reactions may be delayed. Always have trained staff and resuscitation equipment available.

Radiation Risks
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Adverse Reactions
The most frequently reported adverse reactions were headaches, dysgeusia and fatigue, occurring at rate of ≤2% during clinical studies with PYLARIFY. In addition, a delayed hypersensitivity reaction was reported in one patient (0.2%) with a history of allergic reactions.

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

To report suspected adverse reactions for PYLARIFY, call 1-800-362-2668 or contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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References:
1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer. V.1.2025. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed December 11, 2024. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **2.** Appropriate use criteria for prostate-specific membrane antigen (PSMA) PET imaging. Society of Nuclear Medicine & Molecular Imaging. Updated March 2022. Accessed August 8, 2024. https://snmmi.org/Web/Clinical-Practice/Appropriate-Use-Criteria/Articles/Appropriate-Use-Criteria-for-Prostate-Specific-Membrane-Antigen--PSMA--PET-Imaging **3.** Lowrance W, Dreicer R, Jarrard DF, et al. Updates to advanced prostate cancer: AUA/SUO guideline (2023). *J Urol*. 2024;209(6):1082-1090. **4.** Pienta KJ, Gorin MA, Rowe SP, et al. A phase 2/3 prospective multicenter study of the diagnostic accuracy of prostate specific membrane antigen PET/CT with ^{18}F-DCFPyL in prostate cancer patients (OSPREY). *J Urol*. 2021;206(1):52-61. **5.** Morris MJ, Rowe SP, Gorin MA, et al. Diagnostic performance of ^{18}F-DCFPyL-PET/CT in men with biochemically recurrent prostate cancer: results from the CONDOR phase III, multicenter study. *Clin Cancer Res*. 2021;27(13):3674-3682.

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