Mass General Brigham
Health Plan

Medical Policy
Prostate-Specific Membrane Antigen Imaging for Patients with Prostate Cancer

Policy Number: 049

	Commercial and Qualified Health Plans	Mass General Brigham ACO	Medicare Advantage	OneCare	Senior Care Options (SCO)
Authorization required	X (78812, 78813, 78814, 78815, 78816)		X (78812, 78813, 78814, 78815, 78816)		
No notification or authorization	X (A9593, A9594, A9595, A9596, A9608, A9800)	X	X (A9593, A9594, A9595, A9596, A9608, A9800)	X	X
Not payable		X (A9608)			

Overview
Pylarify (piflufolastat F18), Posluma (flotufolastat F18), and Gallium Ga-68 PSMA-11 (gallium Ga 68 gozetotide) are radioactive diagnostic agents 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, or with suspected recurrence.

Criteria
Mass General Brigham Health Plan may authorize coverage of Positron Emission Tomography (PET) using a PSMA-11 radiotracer, with or without computed tomography (CT), for adult male members with prostate cancer when **one** of the following criteria is met:

I. Initial work up of prostate cancer with one the following:

A. Unfavorable intermediate-risk disease; or

B. High risk disease; or

C. Very high-risk disease; or

D. Inconclusive bone findings on both CT/MRI and bone scan; or

E. Conventional imaging studies (CT and bone scan) suggest minimal or low volume metastatic disease that needs further evaluation.

II. Restaging/Recurrence of non-metastatic prostate cancer, when **all** of the following are met:

A. Previously treated with prostatectomy or radiation therapy; and

B. Any of the following:
- PSA persistence, which is defined as detectable PSA (0.1 ng/mL or greater) at 3 months post-operatively; or

- Rising PSA on two or more occasions; or
- PSA rises to at least 0.1 ng/mL if PSA was previously undetectable; and

C. The member is a candidate for salvage local therapy.

III. Workup of suspected progression in previously treated metastatic prostate cancer, when **both** of the following are met:

A. Previously treated with a novel hormone therapy (abiraterone, enzalutamide, darolutamide, or apalutamide); and

B. Previously treated with docetaxel.

Additional information

1. Dosing and Administration
   - Pylarify: A multiple-dose vial containing 37 MBq/mL to 2,960 MBq/mL (1 mCi/mL to 80 mCi/mL) of Pylarify (Piflufolastat F 18) at calibration date and time.
   - Posluma: A multiple-dose vial containing 296 MBq/mL to 5,846 MBq/mL (8 mCi/mL to 158 mCi/mL) as flotufolastat F 18 gallium in approximately 25 mL at end of synthesis supplied as a clear, colorless solution.
   - Gallium Ga-68 PSMA-11: A multiple-dose vial containing 30 mL 18.5 MBq/mL to 185 MBq/mL (0.5 mCi/mL to 5 mCi/mL) at calibration time.
2. Duration of Therapy
   - Single bolus intravenous injection
3. Monitoring
   - Monitor patients for hypersensitivity reactions, particularly patients with a history of allergy to other drugs and foods

Exclusions

- A PET/CT has been performed within the past 3 months.

Medicare Variation

Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for medical necessity determinations for its Medicare Advantage plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for medical necessity determinations. **At the time of Mass General Brigham Health Plan's most recent policy review, CMS did not have any NCDs/LCDs for PSMA-11 imaging for prostate cancer.**

MassHealth Variation

Mass General Brigham Health Plan uses guidance from MassHealth for medical necessity determinations for its Mass General Brigham ACO members. When there is no guidance from MassHealth for the requested service, Mass General Brigham Health Plan's medical policies are used for medical necessity determinations. **As of Mass General Brigham Health Plan's most recent policy review, MassHealth did not have medical necessity guidance for piflufolastat F18 or Gallium Ga-68 PSMA-11 (gallium Ga 68 gozetotide), and flotufolastat is considered not payable.**

OneCare and SCO Variation

Mass General Brigham Health Plan uses guidance from CMS for medical necessity determinations for its OneCare and SCO plan members. NCDs, LCDs, LCAs, and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan uses medical necessity guidelines from MassHealth. When there is no guidance from CMS or from MassHealth, Mass General Brigham Health Plan's medical policies are used for medical necessity determinations.

Codes

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

Authorized Codes	Code Description
78812	PET IMAGING SKULL BASE TO MID-THIGH
78813	PET IMAGING WHOLE BODY
78814	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; limited area (eg, chest, head/neck)
78815	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; skull base to mid-thigh
78816	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; whole body
A9593	Gallium ga-68 psma-11, diagnostic, (ucsf), 1 millicurie
A9594	Gallium ga-68 psma-11, diagnostic, (ucsf), 1 millicurie
A9595	Piflufolastat f-18, diagnostic, 1 millicurie
A9596	Gallium Ga-68 gozetotide, diagnostic (Illuccix), 1 mCi
A9608	Flotufolastat f18, diagnostic, 1 millicurie
A9800	Gallium Ga-68 gozetotide, diagnostic (Locametz), 1mCi

Summary of Evidence

Three PSMA targeted PET imaging agents have been FDA approved since December 2020. A short review of these agents, Posluma, Gozetotide, and Pylarify summarizes key findings for the pivotal studies that support the use of each agent for prostate cancer staging and biochemical recurrence detection (BCR). PSMA agents are used to detect pelvic nodal and distant metastases particularly for individuals with high and very high-risk prostate cancer and offer greater sensitivity and specificity for detection in bone and soft tissue than conventional imaging or F-18 Fluciclovine scanning.

Flotufolastat F18 (brand name: Posluma) approval was based on prospective studies. (Lighthouse studies by Hope et al. JAMA Oncology in 2021; package insert accessed March 2025). The first study enrolled 356 patients with unfavorable intermediate or higher-risk prostate cancer (Gleason score 7 and above) undergoing initial staging before radical prostatectomy and pelvic lymph node dissection. Flotufolastat F18 was compared to

conventional imaging (as interpreted by 3 expert readers) with histopathologic findings from prostatectomy as the reference standard. Flotufolastat F18 demonstrated 23-30% sensitivity and 93-97% specificity in detecting pelvic lymph node metastases, significantly outperforming standard imaging for pre-surgical staging.

The second study evaluated 391 patients with biochemical recurrence (BCR) after primary treatment including radical prostatectomy (79%). For this study, recurrence was suspected by an increase in in PSA level above 0.2 ng/ml, or at least 2 ng/ml following nadir after treatment, and confirmed by pathology or conventional imaging. The study found that Flotufolastat F18 detected recurrent lesions in 75% of cases, even at low PSA levels. Detection rates were 64% for PSA <0.5 ng/mL, 76% for PSA 0.5–1.0 ng/mL, and 93% for PSA 1.0–2.0 ng/mL.

Ga-68 PSMA-11 (Gozetotide) is a PSMA-targeted PET imaging agent approved based on the pivotal VIA study, which included two significant components: one for initial staging and the other for biochemical recurrence detection (Fendler et al. 2020). The VIA study was a prospective, multicenter clinical trial that evaluated the diagnostic accuracy of Ga-68 PSMA-11 PET/CT in 325 patients with high-risk prostate cancer (Gleason score 7 or greater) undergoing initial staging before definitive treatment. The study compared Ga-68 PSMA-11 PET/CT with conventional imaging (CT, MRI, bone scans) and used histopathology from prostatectomy as the reference standard. The results among 6 expert readers showed that Ga-68 PSMA-11 PET/CT had a range from 36- 60% sensitivity and 83-96 % specificity for detecting pelvic lymph node metastases, outperforming conventional imaging in terms of diagnostic accuracy.

The second part of the VIA study evaluated 635 patients with biochemical recurrence (BCR) after prior definitive treatment (surgery or radiation) who had negative or equivocal conventional imaging results. Ga-68 PSMA-11 PET/CT was used to detect recurrent disease in these patients. A subset of 210—including 64% with prostatectomy and 73% with radiotherapy—had at least one reference baseline value for one or more: pathology, baseline conventional imaging or a previous gozetotide PET (within 12 months) or serial serum PSA. The study demonstrated that Ga-68 PSMA-11 PET/CT was able to detect recurrent disease in 74% of cases, with detection rates improving as PSA levels increased: 36% for PSA <0.5 ng/mL, 56% for PSA 0.5–1.0 ng/mL, and 83% for PSA 1.0–2.0 ng/mL.

Piflufolastat F-18 (brand name: Pylarify) was FDA-approved in May 2021 as the first F-18–labeled PSMA-targeted PET imaging agent for prostate cancer staging and biochemical recurrence (BCR) detection. Its approval was based on two pivotal prospective clinical trials: OSPREY and CONDOR, both led by Morris et al. and published in The Journal of Urology and Clinical Cancer Research in 2021.

The OSPREY trial enrolled 268 patients with high-risk prostate cancer undergoing initial staging for prostate cancer (Gleason score 7 or greater) before surgery. Piflufolastat F-18 PET/CT was compared to surgical pathology as the reference standard. The study demonstrated sensitivity of 28-39 % and specificity of 95-98)% in detecting pelvic lymph node metastases, with high specificity ensuring low false-positive rates. These findings supported the diagnostic utility of Pylarify for pre-surgical staging, particularly in identifying metastatic disease beyond conventional imaging (Morris et al., J Urol, 2021).

The CONDOR trial evaluated 208 patients with biochemical recurrence (BCR) of prostate cancer after prior definitive therapy (surgery or radiation) who had negative or equivocal conventional imaging results. Entry required PSA at least 0.2 ng/ml after prostatectomy or an increase PSA of at least 2 ng/ml above nadir after therapy. Piflufolastat F-18 PET/CT detected PSMA-positive lesions in 85% of patients, even at low PSA levels. Detection rates were 36% for PSA <0.5 ng/mL, 63% for PSA 0.5–1.0 ng/mL, and 87% for PSA 1.0–2.0 ng/mL.

The studies above have established PSMA-targeted PET as an important tool in assessing and reassessing extent of disease in patients with prostate cancer. The medical necessity criteria above are based primarily on current guidelines from NCCN (2025) and EANM (Fendler et al. 2023) that establish criteria for appropriate use.

Effective
January 2026: Off-cycle review. Updated prior authorization table and added variation for OneCare and SCO members.
July 2025: Off-cycle review. Updated criteria based on latest NCCN guidelines. References updated. Code disclaimer updated.
June 2025: Off-cycle review. Updated prior authorization table at top of policy: took radiotracers off PA. Updated MassHealth variation.
April 2025: Off-cycle review. Summary of evidence added. References updated.
March 2025: Annual review. Changed name of policy. Added MassHealth variation. Updated table to reflect that PET scans do not require PA for MassHealth. Code list updated.
January 2025: Off-cycle review. Updated Restaging/Recurrent eligibility criteria per NCCN guidelines. Clarified language in Medicare Variation. Code disclaimer added. Code list updated. Added code for Posluma. Added criteria for Posluma. References updated. Updated PA table at top of policy to reflect that MassHealth does not cover Posluma.
March 2024: Annual review.
January 2024: Off-cycle review. MassHealth coverage added to table.
October 2023: Annual review. Medicare Advantage added to table. Initial Work-up criteria edited for clarity. Medicare Variation language added. References updated.
November 2022: Off-cycle review. Added generic name to Gallium G-68 PSMA-11. Added codes for Illuccix and Locametz.
July 2022: Effective Date. Added criteria for Gallium Ga-68 PSMA-11.

Reference
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