KAISER PERMANENTE®

Kaiser Foundation Health Plan of Washington

Clinical Review Criteria
PSMA – PET SCAN

Criteria

For Medicare Members

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	None
Local Coverage Determinations (LCD)	None
Local Coverage Article (LCA)	Positron Emission Tomography Scans Coverage (A54668) ***Documents coverage indications for PET scans and radiopharmaceuticals including but not limited to:** *A9587* Gallium GA-68 Dotatate (neuroendocrine tumors) *A9515* Choline C-11, diagnostic (prostate cancer) *A9588* Fluciclovine F-18 (Axumin PET - prostate) *A9593, A9594, A9596, A9800* Gallium GA-68 PSMA-11 (PSMA PET – prostate) *A9595* Piflufolastat F-18 (PSMA PET – prostate) **For initial PSMA PET requests. There is currently no agreed up clinical role for repeat PSMA, in NCCN, and these are not covered.* ***Group 16 Paragraph (from LCA A54668 above)*** *The following diagnoses are applicable to Gallium ga-68 psma-11 (UCSF) and Gallium ga-68 psma-11 (UCLA) injections when billed with 78811, 78812, 78813, 78814, 78815 or 78816 with the PS modifier. Use A9593 for the UCSF OR A9594 for the UCLA formulation to bill for this service per CR 12142 effective 7/1/2021.* *When A9593 or A9594 is billed in the OPPS setting or in Part B outpatient setting, the diagnosis codes below will be paid, effective 07/01/2021.* ***NOTE**: Whenever a personal history diagnosis code (Z85.XXX) is on a claim, the claim must also contain a diagnosis code from the list of covered C, D, or R diagnosis codes.* ***Effective 09/10/2021**, the National Comprehensive Cancer Network (NCCN) Guidelines have been updated to allow PSMA-PET/CT or PSMA-PET/MRI with Ga-68 PSMA-11 to be considered effective for initial staging* of bone and soft tissues imaging with the use of the 'PI' modifier, or with suspected recurrence** based on elevated serum prostate-specific antigen (PSA) level, Providers must amend the KX modifier on the claim to attest that the use of the PI modifier is per NCCN Guidelines*

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	***Effective 05/10/2022**, PSMA-PET/ CT OR PSMA-PET/MRI with Ga-68 PSMA-11 may be used to screen patients for Pluvicto™ eligibility per NCCN Guidelines and Society of Nuclear Medicine and Molecular Imaging (SNMMI) Appropriate Use Criteria (AUC).* ** Per NCCN, only applies to "unfavorable intermediate, high, very high, risk patients on initial staging"* *** From NCCN, defining recurrence:* *After radical prostatectomy* *PSA persistence/recurrence after RP is defined as failure of PSA to fall to undetectable levels (PSA persistence) or undetectable PSA after RP with a subsequent detectable PSA that increases on 2 or more determinations (PSA recurrence) or that increases to PSA >0.1 ng/mL* *Recurrent after radiation (did not have radical prostatectomy)* *RTOG-ASTRO (Radiation Therapy Oncology Group - American Society for Therapeutic Radiology and Oncology) Phoenix Consensus: 1) PSA increase by 2 ng/mL or more above the nadir PSA is the standard definition for PSA recurrence after EBRT with or without HT; and 2) A recurrence evaluation should be considered when PSA has been confirmed to be increasing after radiation even if the increase above nadir is not yet 2 ng/mL, especially in candidates for salvage local therapy who are young and healthy. Retaining a strict version of the ASTRO definition allows comparison with a large existing body of literature. Rapid increase of PSA may warrant evaluation (prostate biopsy) prior to meeting the Phoenix definition, especially in younger or healthier patients.*

For Non-Medicare Members

PSMA (e.g., Pylarify, Gallium-68 and other FDA approved PSMA tracers) PET/CT Imaging Guidelines for Prostate Cancer

The criteria below apply to initial PSMA PET requests. There is currently no agreed up clinical role for repeat PSMA, and these are not covered.

I. Initial Staging evaluation and assessment for metastatic disease:

- NCCN high or very high-risk disease (T3a or higher primary, Gleason 8-10, or PSA > 20)*:
  - Conventional imaging should be completed first for metastatic assessment within the last 2 months (i.e., bone scan and CT scan).
  - PSMA PET/CT can be considered for all patients in this category if conventional imaging is negative and concern remains for possible metastatic disease.
  - Axumin PET/CT not recommended/indicated.

- NCCN unfavorable intermediate risk disease (cT2b-T2c, Gleason 7, PSA 10-20, or ≥ 50% core biopsies positive)*:
  - Conventional imaging should be completed first for metastatic assessment within the last 2 months (i.e., bone scan and CT scan).
  - PSMA PET/CT can be considered for equivocal/indeterminate results on conventional imaging.
  - Axumin PET/CT not recommended/indicated.

- NCCN favorable intermediate and lower risk disease (Not fitting above criteria)*:
  - Not covered.

II. Biochemical recurrence and subsequent treatment strategy:

- Serologic relapse after surgery (PSA ≥ 0.5 ng/ml):

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  - Conventional imaging with CT and/or bone scan should be performed first if not already done so within the last 2 months.
  - PSMA PET/CT can be considered for patients in whom local salvage EBRT is planned/considered. If widespread systemic disease is present, patient is not a candidate for PSMA.

- Serologic relapse after EBRT or brachytherapy (patient did not have surgery) PSA rise of 2ng/ml or more above nadir on two separate occasions (Phoenix criteria*):
  - Conventional imaging with CT and/or bone scan should be performed first if not already done so within the last 2 months.
  - PSMA PET/CT can be considered for patients in whom salvage surgery or localized therapy is planned/considered. If widespread systemic disease is present, patient is not a candidate for PSMA.

- Known or suspected oligometastatic disease with plan/consideration for focal radiation therapy:
  - PSA ≥ 0.5ng/ml and PSA doubling time ≥ to 3 months (Note: a more rapid doubling time increases the risk of systemic disease and may render focal treatment non-indicated. PSADT*** is most accurate for PSA values over 1ng/ml).
  - Conventional imaging with CT and/or bone scan should be performed first if not already done so, within the last 2 months.
  - PSMA PET/CT imaging can be considered if:
    - Radiation oncology would recommend, and the patient would agree to consider treatment of oligometastatic disease (generally ≤ to 5 lesions) if confirmed

- Non-metastatic castration resistant prostate cancer (CRPC)**:
  - PSA ≥ 0.5ng/ml and PSA doubling time ≥ to 3 months (Note: a more rapid doubling time increases the risk of systemic disease and may render focal treatment non-indicated. PSADT*** is most accurate for PSA values over 1ng/ml).
  - Conventional imaging with CT and/or bone scan must be performed first within the prior 2 months, and results are negative for metastatic disease.
  - PSMA PET/CT can be considered if conventional imaging negative, and PSA ≥ 0.5ng/ml, and PSADT*** ≤ to 10 months

- Known diffuse/non-oligometastatic metastatic prostate cancer (CRPC*):
  - PSMA PET/CT can be considered if patient is a definite candidate for PSMA Lutetium for CRPC. Click HERE for Radiopharmaceuticals—Pluvicto criteria
  - Pending further research neither PSMA nor Axumin PET/CT should be used to monitor disease.

*Per NCCN Guidelines Version 1.2023 Prostate Cancer

Initial Risk Stratification and Staging Workup for Clinically Localized Disease	
Risk Group	**Clinical/Pathologic Features**
Very Low	Has all of the following: • cT1c • Grade Group 1 • PSA <10 ng/ml • Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core • PSA density <0.15 ng/mL/g
Low	Has all of the following but does not qualify for very low risk: • cT1-cT2a • Grade Group 1 • PSA <10 ng/mL

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<table>
<tr><td rowspan="2">Intermediate</td><td rowspan="2">Has all of the following:
No high-risk group features
No very-high-risk features
Has one or more intermediate risk factors (IRFs):
cT2b-cT2c
Grade Group 2 or 3
PSA 10-20 ng/mL</td><td>Favorable intermediate</td><td>Has all of the following:
1IRF
Grade Group 1 or 2
<50% biopsy cores positive (e.g., <6 of 12 cores)</td></tr>
<tr><td>Unfavorable intermediate</td><td>Has one ore more of the following:
2 or 3 IRFs
Grade Group 3
≥50% biopsy cores positive (e.g., ≥ 6 of 12 cores)</td></tr>
<tr><td>High</td><td colspan="3">Has no very-high-risk features and has exactly one high-risk feature:
cT3a OR
Grade Group 4 or Grade Group 5 OR
PSA >20 ng/mL</td></tr>
<tr><td>Very High</td><td colspan="3">Has at least one of the following:
cT3b-cT4
Primary Gleason pattern 5
2 or 3 high-risk features
>4 cores with Grade Group 4 or 5</td></tr>
</table>

** Castration Resistant Prostate Cancer (CRPC):
Castration resistance is defined as evidence of disease progression (via PSA level or evidence of metastasis on imaging) despite castrate level of testosterone (less than 50)

***Prostate-Specific Antigen Doubling Time (PSADT): The number of months it would take for PSA to increase two-fold

For covered criteria:

If requesting this service (*or these services*), please send the following documentation to support medical necessity:

- Last 6 months of clinical notes from requesting provider &/or specialist

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Background

Prostate cancer is the second most frequently diagnosed cancer across the globe (Wolff et al., 2015). A 2008-2010 data estimated that 15% of men in the United States will be diagnosed with prostate cancer at some point in their lives (Wolff et al., 2015). However, the mortality rate is low because it is a slow growing cancer.

Treatment is based on a number of factors including tumor stage, prostate specific antigen (PSA) value, Gleason score (GS), patient's age, concomitant diseases, life expectancy and patient's preference (Warmuth, Johansson, & Mad, 2010). A wide range of options are available for prostate cancer and these include active surveillance, watchful waiting, radical prostatectomy, hormone therapy, radiotherapy, external beam radiotherapy (EBRT), brachytherapy and chemotherapy (Wolff et al., 2015).

Iimportant proportion (20 to 50%) of men treated for prostate cancer will experience recurrence (Bruce, Lang, McNeel, & Liu, 2012; Roehl, Han, Ramos, Antenor, & Catalona, 2004; Simmons, Stephenson, & Klein, 2007). Of those with recurrent prostate cancer, a high proportion (25%) will develop metastatic disease with morbidity and mortality (Boorjian et al., 2011; James et al., 2015). Given the impact of recurrence, and for better treatment, it is

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crucial to determine the sites of the recurrence. Diagnostic tests include MRI, bone scintigraphy, CT. However, the accuracy of these standard imaging tests is low (diagnostic yield of 11%) (Choueiri, Dreicer, Paciorek, Carroll, & Konety, 2008). Therefore, tests with better diagnostic yield are necessary. Positron emission tomography (PET) with fluciclovine radiotracer has been the center of attention.

PET is a molecular imaging technique using tumor biology to improve detection of prostate cancer (Parent & Schuster, 2018). PET with tracers visualize receptor profile of tumor cells. Axumin or fluciclovine or Anti-1-amino-3-18F-flurocyclobutane-1-carboxylic acid (18F-fluciclovine) is an amino acid PET radiotracer. The characteristics of the tumor-imaging of this radiotracer is similar to the increased amino acid transport found in prostate cancer (Parent & Schuster, 2018). It visualizes the increased amino acid transport associated with tumor cells compared to normal tissues.

One of the benefits of Axumin PET/CT is helping to select optimal treatment strategy (i.e., salvage surgery vs. XRT vs. systemic therapy, depending on site(s)/extent of disease involvement). This can help with resource utilization and patient morbidity: e.g., bypassing futile surgery or local XRT if PET (which is generally more sensitive) identifies more extensive and/or distant disease than CT/MR identify; alternatively, using focal XRT or SABR and avoiding systemic therapy if only isolated or oligometastatic disease.

Medical Technology Assessment Committee (MTAC)

Prostate-Specific Membrane Antigen Radioligand Therapy for the Treatment of Metastatic Castration-Resistant

MTAT Review: September 2022

Evidence Conclusion: The Medical Technology Assessment Team (MTAT) reviewed the evidence on prostate-specific membrane antigen (PSMA) targeted radioligand therapy (PRLT) for the treatment of metastatic castration-resistant prostate cancer (mCRPC) on July 14, 2022. There is moderate- to low-certainty evidence from 100 studies (5 randomized controlled trial (RCTs), 3 retrospective comparative, 22 prospective non-comparative, 70 retrospective non-comparative) with 6,183 patients regarding the efficacy and safety of 177-Lu PRLT for the treatment of mCRPC.

PROSTATE-SPECIFIC MEMBRANE ANTIGEN (PSMA) RADIOTRACERS FOR IMAGING (PET OR PET/CT) IN PATIENTS WITH RECURRENT PROSTATE CANCER

INTC Review: June 28, 2021

There is insufficient evidence regarding prostate-specific membrane antigen (PSMA) radiotracers for imaging (PET or PET/CT) compared to alternative tests for improving health outcomes in men with suspected or confirmed recurrent prostate cancer.

Although the available published evidence supports the clinical validity of PSMA radiotracers for PET or PET/CT imaging, and that testing with these agents can change management by more frequently detecting or better characterizing early metastatic lesions, analyses that show this intervention improves health outcomes compared to alternative strategies is currently of insufficient quantity and quality. The quality of the body of evidence across key comparisons and outcomes of interest was found to be low-quality. Monitoring for developments in the evidence on and utilization of PSMA imaging and emerging therapeutics (e.g. 177Lu-PSMA-617) for prostate cancer may be needed.

References

Abramaowitz, M., Li, T., Buyyounouski, M., Ross, E, Uzzo, R., Pollack, A. & Horwitz, E. (2007). The Phoenix definition of biochemical failure predicts for overall survival in patients with prostate cancer. *American Cancer Society, 112*(1), 55-60. Retrieved from Pubmed Database.

Comprehensive Cancer Network (NCCN). 2022. *Prostate Cancer (Version 1.2023)*. Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf

Hofman MS, Emmett L, Violet J, Y Zhang A, Lawrence NJ, Stockler M, Francis RJ, Iravani A, Williams S, Azad A, Martin A, McJannett M; ANZUP TheraP team; Davis ID. TheraP: a randomized phase 2 trial of ^{177}Lu-PSMA-617 theranostic treatment vs cabazitaxel in progressive metastatic castration-resistant prostate cancer (Clinical Trial Protocol ANZUP 1603). BJU Int. 2019 Nov;124 Suppl 1:5-13. doi: 10.1111/bju.14876. Epub 2019 Oct 22. PMID: 31638341.

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Applicable Codes

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:
PSMA - PET

CPT® Codes	Description
78811	Positron emission tomography (PET) imaging; limited area (eg, chest, head/neck)
78812	Positron emission tomography (PET) imaging; skull base to mid-thigh
78813	Positron emission tomography (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
HCPCS Codes	**Description**
A9593	Gallium Ga-68 PSMA-11, diagnostic, (UCSF), 1 mCi
A9594	Gallium Ga-68 PSMA-11, diagnostic, (UCLA), 1 mCi
A9595	Piflufolastat f-18, diagnostic, 1 mCi
A9596	Gallium Ga-68 gozetotide, diagnostic, (Illuccix), 1 mCi
A9800	Gallium Ga-**68** gozetotide, diagnostic, (Locametz), 1 mCi

Non-Medicare Members:
Axumin – PET is no longer recommended

HCPCS Codes	Description
A9588	Fluciclovine F-18, diagnostic, 1 mCi

***Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

****To verify authorization requirements for a specific code by plan type, please use the **Pre-authorization Code Check**.

Date Created	Date Reviewed	Date Last Revised
01/09/2023	01/10/2023[MPC]	03/03/2023

[MPC] Medical Policy Committee

Revision History	Description
01/09/2023	MPC approved coverage criteria for PSMA (e.g., Pylarify, Gallium-68 and other FDA approved PSMA tracers) PET/CT Imaging Guidelines for Prostate Cancer, with Axumin PET no longer recommended. Requires 60-day notice; effective June 01, 2023.
03/03/2023	Updated applicable new codes from 10/01/2023 to include A9800. Updated References to include TheraP and Vision Trials.

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