POSLUMA®
flotufolastat F 18 injection

Blue Earth Diagnostics believes that accurate and appropriate billing and reimbursement processes and guidelines can help facilitate patient access to POSLUMA as prescribed.

Within this Reimbursement Resource Guide, we provide background information to support the benefits investigation, prior authorization, and claims submission processes.

This resource is provided to support patient access to POSLUMA as prescribed. This document contains factual information and is not intended to be legal or coding advice. Blue Earth Diagnostics does not guarantee coverage or reimbursement for POSLUMA. The information provided in this document is based upon current, general coding practices. The existence of billing codes does not guarantee coverage and payment. Payer policies vary and may change without notice. It is the providers' responsibility to determine and submit accurate information on claims. This includes submitting information such as proper codes, modifiers, charges, and invoices for the services that were rendered. The coding on claims should reflect medical necessity and be consistent with the documentation in the patient's medical record.

INDICATION

POSLUMA® (flotufolastat F 18) injection is 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

IMPORTANT SAFETY INFORMATION

- Image interpretation errors can occur with POSLUMA PET. 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 POSLUMA for imaging metastatic pelvic lymph nodes in patients prior to initial definitive therapy seems to be affected by serum PSA levels and risk grouping. The performance of POSLUMA for imaging patients with biochemical evidence of recurrence of prostate cancer seems to be affected by serum PSA levels. Flotufolastat F 18 uptake is not specific for prostate cancer and may occur in other types of cancer, in non-malignant processes, and in normal tissues. Clinical correlation, which may include histopathological evaluation, is recommended.
- Risk of Image Misinterpretation in Patients with Suspected Prostate Cancer Recurrence: The interpretation of POSLUMA PET may differ depending on imaging readers, particularly in the prostate/prostate bed region. Because of the associated risk of false positive interpretation, consider multidisciplinary consultation and histopathological confirmation when clinical decision-making hinges on flotufolastat F 18 uptake only in the prostate/prostate bed region or only on uptake interpreted as borderline.
- POSLUMA use contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer. Advise patients to hydrate before and after administration and to void frequently after administration. Ensure safe handling to minimize radiation exposure to the patient and health care providers.
- The adverse reactions reported in ≥0.4% of patients in clinical studies were diarrhea, blood pressure increase and injection site pain.
- 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 flotufolastat F 18 in prostate cancer. The effect of these therapies on performance of POSLUMA PET has not been established.

To report suspected adverse reactions to POSLUMA, call 1-844-POSLUMA (1-844-767-5862) or contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Full POSLUMA prescribing information is available at www.posluma.com/prescribing-information.pdf

BLUE EARTH DIAGNOSTICS
A Bracco Company

BEDPRC23-0072A 06/23

POSLUMA®
flotufolastat F 18 injection

In this guide you will find:

Your Blue Earth Diagnostics Field Reimbursement Manager is available to review information about local and national payer coverage requirements and to answer other reimbursement-related questions.

Thank you for your interest in Blue Earth Diagnostics and POSLUMA.

POSLUMA® (flotufolastat F 18) injection Coding Information Sheet

Information current as of May 30, 2023.

HCPCS code for POSLUMA®

In the absence of a product-specific code, a "Not Otherwise Classified (NOC)" HCPCS is required. Healthcare Providers should contact their Local Medicare Provider and Third-Party Payers for specific billing, coding, and payment guidelines.

HCPCS code	HCPCS descriptor
A9597	Positron Emission Tomography radiopharmaceutical, diagnostic, for tumor identification, not otherwise classified, 1 unit

For the A/B MAC to correctly reimburse NOC drugs and biologicals, providers must indicate the following in the 2400/SV101-7 data element, or Item 19 of the CMS 1500 form:

- The name of the drug,
- The total dosage (plus strength of dosage, if appropriate), and
- The method of administration

Important: List **one** unit of service in the 2400/SV1-04 data element or in item 24G of the CMS 1500 form. Do not quantity-bill NOC drugs and biologicals even if multiple units are provided. Medicare determines the proper payment of NOC drugs and biologicals by the narrative information, not the number of units billed. https://www.cms.gov/medicare-coveragedatabase/view/article.aspx?articleid=59073&ver=27&=

Most commonly used CPT Codes for POSLUMA PET Scans

The Current Procedural Terminology (CPT®) codes for PET imaging are 78811- 78816. Providers should choose the code that accurately describes the procedure performed and is supported by documentation in the medical record. Based on the POSLUMA's Prescribing Information, it is expected that the following 2 CPT codes will be commonly used for POSLUMA PET or PET/CT imaging of patients with prostate cancer prior to initial therapy or suspected recurrent prostate cancer based on elevated PSA levels:

CPT® code	CPT descriptor
78812	Positron emission tomography (PET) imaging; skull base to mid-thigh
78815	Positron emission tomography (PET) imaging with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; skull base to mid-thigh

Medicare Required Oncologic PET Billing Modifier

Medicare requires oncologic PET imaging be billed using either the PI or PS modifier.

Modifier	ICD-10 descriptor
PI	Positron Emission Tomography (PET) or PET/Computed Tomography (CT) to inform the initial treatment strategy of tumors that are biopsy proven or strongly suspected of being cancerous based on other diagnostic testing. Short descriptor: PET tumor init tx strat
PS	Positron Emission Tomography (PET) or PET/Computed Tomography (CT) to inform the subsequent treatment strategy of cancerous tumors when the beneficiary's treating physician determines that the PET study is needed to inform subsequent antitumor strategy. Short descriptor: PET tumor subsq tx strategy

https://www.cms.gov/Regulations-and Guidance/Guidance/Transmittals/downloads/R1833CP.pdf

National Drug Code (NDC) Codes for POSLUMA

NDC Code for POSLUMA® (flotufolastat F 18) injection	NDC Code Descriptor
69932-002-01	10-digit NDC Code for a single dose of POSLUMA
69932-0002-01	11-digit NDC Code for a single dose of POSLUMA

This is the published code associated with the Wholesale Acquisition Cost (WAC) submitted by Blue Earth Diagnostics.

It is recommended to follow payer coding and billing guidelines regarding which NDC number is appropriate.

ICD-10-CM Codes most commonly used for POSLUMA PET Scans

ICD-10-CM Codes	Descriptor
C61	Malignant neoplasm of the prostate
R97.20	Elevated prostate specific antigen (PSA)
R97.21	Rising PSA following treatment for malignant neoplasm of the prostate
Z85.46	Personal history of malignant neoplasm of prostate
Z19.1	Hormone Sensitive malignancy status
Z19.2	Hormone resistant malignancy status

The above codes are representative. Providers should choose the code(s) that most accurately describes the patient's diagnoses.

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" codes.

https://www.cms.gov/medicare/coverage/determinationprocess/downloads/petforsolidtumorsoncologicdxcodesattachment_NCD220_6_17.pdf

Your Blue Earth Diagnostics Field Reimbursement Manager is available to review information about local and national payer coverage requirements and to answer other reimbursement-related questions.

Prior Authorization Helpful Tips

Information current as of May 30, 2023.

Prior authorizations

A process used to determine if a patient's procedure, service, or medication will be covered. This process does not guarantee payment. A prior authorization is not predetermined by a health plan.

- **Electronic submission can reduce complexity of manual submissions**
- **May be conducted via the telephone for certain payers**
- **Collect all pertinent information**
  - ☐ Patient demographics, including name, insurance policy # and date of birth
  - ☐ Place of Service: IDTF, Physician Office, Outpatient Hospital
  - ☐ Physician Information including name and Tax ID number
  - ☐ All other items required by the health plan
- **Performing provider's information**
  - ☐ Physician/Facility Name
  - ☐ Tax ID number & NPI number
  - ☐ Address, Phone and Fax number
  - ☐ Email (if available)
  - ☐ Contact name
- **Provider must have appropriate documentation readily available**
  - ☐ Letter of medical necessity
  - ☐ Patient records detailing relevant diagnosis
  - ☐ Supporting documentation for diagnostic procedure (CPT/HCPCS codes, diagnosis codes)
  - ☐ Document any authorization number (e.g., may request in writing from payer)
  - ☐ Be sure to follow all criteria set forth by the payer

*For initial staging authorizations, provide documentation to support how the patient meets Unfavorable Intermediate, High, or Very High Risk for metastatic disease

NOTE: *Verify benefits, eligibility, coverage, and requirements for prior authorization with payer.*

Predetermination

Determination of the reimbursement amount from a third party before a healthcare service is performed. It does not guarantee payment.

- **Collect all pertinent information**
- **Electronic submission can reduce complexity of manual submissions**
- **Insight may be gained on reimbursement (payment) for POSLUMA and PET scan**
- **May be able to gain insight into contract limitations with payer**

NOTE: *Many of the steps above would be used with a predetermination.*

Prior Authorization Helpful Tips

Denial: POSLUMA or PET or both

APPEAL PROCESS

PAPER/ELECTRONIC

- **Be sure to use proper form**
- **Follow exact criteria of payer**
- **Include physician notes**
- **Physician notes should document the use of product/scan**
- **May use "Template Appeal Letter" or "Letter of Medical Necessity" provided by Blue Earth Diagnostics as a guide**
- **Submit in a timely manner and through proper channels provided by payer**

PEER TO PEER

- **Contact payer to schedule a peer to peer**
- **Request an individual well-versed in radiopharmaceuticals or a physician of the same specialty**
- **Request notification of assigned payer individual a week prior to scheduled appointment**
- **Be sure to have all documentation ready**
  - ☐ Reference number for existing claim denial
  - ☐ Denial "explanation of benefits"
  - ☐ Reason for use of POSLUMA, PET, and/or both
  - ☐ Documentation supporting medical necessity

POSLUMA Scheduling Tip Sheet

This resource is provided to support patient access to POSLUMA as prescribed. This is not a guide or instruction. The processes outlined here do not guarantee payment. Providers must use independent medical judgment in determining whether an POSLUMA PET scan is appropriate for the patient. The provider has the responsibility to ensure correct prior authorization, appeal, and denial policies are followed.

POSLUMA is covered by Medicare where reasonable and necessary

POSLUMA® (flotufolastat F 18) injection is indicated for positron emission tomography (PET) imaging of prostate-specific membrane antigen (PSMA) positive lesions in men with

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

IS THIS PATIENT APPROPRIATE FOR POSLUMA IMAGING?

- ☐ **Patient has a new diagnosis of prostate cancer with Unfavorable Intermediate, High or Very High risk for metastatic disease**
- ☐ **Patient has prior history of prostate cancer**
- ☐ **Patient was treated for prostate cancer**
- ☐ **Patient has elevated PSA levels following prior treatment**

DO I HAVE WHAT I NEED TO SCHEDULE THE PATIENT?

- ☐ **Physician order for POSLUMA PET scan**
- ☐ **Patient's insurance information and prior authorization number, if available**
- ☐ **If performing authorization, documentation of:**
  - ☐ Medical necessity
  - ☐ Patient history
  - ☐ Information on POSLUMA PET scans

PATIENT PREPARATION AND PRECAUTIONS

Preparing for a POSLUMA scan

- Patients should drink water prior to POSLUMA administration and continue drinking and voiding frequently for first few hours after administration.
- Patients should void immediately prior to imaging.
- Scan duration is approximately 20 minutes.

POSLUMA Scheduling Tip Sheet

CODING FOR POSLUMA PET SCANS

Healthcare Common Procedure Coding System (HCPCS)

Code	Descriptor
A9597	Positron Emission Tomography radiopharmaceutical, diagnostic, for tumor identification, not otherwise classified, 1 unit

*List **one** unit of service in the 2400/SV1-04 data element or in item 24G of the CMS 1500 form. Do not quantity-bill NOC drugs and biologicals even if multiple units are provided. Medicare determines the proper payment of NOC drugs and biologicals by the narrative information, not the number of units billed. https://www.cms.gov/medicare-coveragedatabase/view/article.aspx?articleid=59073&ver=27&=

Potential CPT codes for POSLUMA

Code	Descriptor
78811	Positron emission tomography (PET) imaging; limited area (e.g., 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) imaging with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; limited area (e.g., chest, head/neck)
78815	Positron emission tomography (PET) imaging with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; skull base to mid-thigh
78816	Positron emission tomography (PET) imaging with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; whole body

The Current Procedural Terminology (CPT®) codes for PET imaging are 78811- 78816. Providers should choose the code that accurately describes the procedure performed and is supported by documentation in the medical record.

ICD-10 codes most commonly used for POSLUMA PET scans

Code	Descriptor
R97.20	Elevated prostate-specific antigen (PSA)
R97.21	Rising PSA following treatment for malignant neoplasm of the prostate
Z85.46	Personal history of malignant neoplasm of prostate
C61	Malignant neoplasm of prostate
Z19.1	Hormone sensitive malignancy status
Z19.2	Hormone resistant malignancy status

The above codes are representative. Providers should choose the code(s) that accurately describes the diagnoses.

POSLUMA PET Imaging Program Implementation Checklist

A proactive approach regarding reimbursement can help your patients successfully obtain coverage for POSLUMA as prescribed. The checklist below outlines key potential steps to help facilitate coverage if you determine POSLUMA is appropriate for your patient. Please review individual insurer requirements, as the specific steps may vary based on the patient's insurer.

- ☐ **HOSPITALS ONLY** Confirm/add PET or PET/CT procedure codes and "NOC" HCPCS code A9597 to charge master
- ☐ **HOSPITALS ONLY** Confirm both current APC and revenue codes for PET scanning are set up in charge master
- ☐ **IDTF ONLY** Submit form 855B to add "NOC" HCPCS code A9597 (IDTF only) https://www.cms.gov/Medicare/CMS-Forms/CMS-Forms/Downloads/cms855b.pdf
- ☐ Obtain local MAC oncologic PET coverage policy and coding instructions for restaging/recurrence of prostate cancer
- ☐ Obtain oncologic PET coverage policies from commercial payers and Medicare Advantage plans
- ☐ Obtain publicly available RBM coverage criteria for oncologic imaging
- ☐ Review commercial payer contracts and submit contract addendum to add separate reimbursement for "NOC", HCPCS Level II code A9597 to current contract. Please note, such contract addenda may take 60 days or more to process
- ☐ Check with private payers to confirm code sets for oncologic PET are included in privileging criteria
- ☐ Credentialing—you may need to update your office/practice profile with your payers

Abbreviations: APC, ambulatory payment classification; HCPCS, Healthcare Common Procedure Coding System; IDTF, independent diagnostic testing facility; MAC, Medicare Administrative Contractor; RBM, radiology benefits manager.

If you have questions, your Blue Earth Diagnostics Field Reimbursement Manager is available to provide a reimbursement training overview.

This training will provide information relevant to departments including, but not limited to:

- Scheduling department
- Benefit investigation
- Prior authorization
- Charge master
- Finance department
- Billing and patient financial services
- Third-party billing company (if utilizing)
- Prostate cancer nurse navigators

Topics for this training session will include:

- Review of POSLUMA Reimbursement Resource Guide
- Review of publicly available local MAC and private payer coverage policies
- Review of publicly available RBM coverage criteria and prior-authorization requirements
- Q&A session

Template:
Letter of Medical Necessity

[Date]

[Contact at Health insurer]
[His/Her Title]
[Name of health Insurance Company]
[Address]
[City, State, ZIP code]

Regarding: Letter of Medical Necessity for POSLUMA® (fluciclovine F 18) injection

Insured: [Name]
Patient: [Name]
Patient Date of Birth: [DOB]
Insurance ID number: [Policy Number]

Dear [Name of Contact]:

I am writing on behalf of my patient, [name of patient], to request that [name of insurance company] approve coverage for a POSLUMA® (flotufolostat F 18) injection which is used in Positron Emission Tomography (PET) imaging. POSLUMA, an ^{18}F-labeled Prostate-Specific Membrane Antigen (PSMA) agent is the first and only commercially available radiohybrid™ (rh) F 18 PET diagnostic radiopharmaceutical which was approved by the Food and Drug Administration (FDA) on May 25th, 2023[1]. POSLUMA is 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

Patient's Medical History

[This is where you should summarize your rationale as to why a POSLUMA® PET scan is appropriate and medically necessary for your patient. Consider including the following information. provide patient information regarding condition, symptoms and history related to his prostate cancer:]

- Description of patient's condition, date of original diagnosis and history related to his Prostate CA
- Current symptoms
- Circumstances surrounding care, need for diagnostic imaging with POSLUMA®
- Previous diagnostic tests, therapies, and any complications
- Any other relevant information

Based on the above information, I hope that you will agree that a POSLUMA PET scan is indicated and medically necessary for the detection and localization of [name of patient's] [prostate cancer prior to initial therapy or suspected prostate cancer recurrence based on elevated blood prostate specific antigen (PSA) level, select the reason for approval][3,4].

If you have any further questions, please contact me at [physicians' telephone number]. Thank you in advance for your immediate attention to this request.

Sincerely
[Physician's Name]
[Physician's Practice Name]
[Practice Address]

References: 1. POSLUMA. Package insert. Blue Earth Diagnostics Ltd; 2023. **2.** Fendler WP, et al. PSMA PET/CT: joint EANM procedure guideline/SNMMI procedure standard for prostate cancer imaging 2.0. *Eur J Nucl Med Mol Imaging* 2023; https://doi.org/10.1007/s00259-022-06089-w **3.** Jani AB, et al. Diagnostic performance and safety of 18F-rhPSMA-7.3 PET in men with suspected prostate cancer recurrence: results from a Phase 3, prospective, multicenter study (SPOTLIGHT). *J Urol.* Published online April 26, 2023: doi/10.1097/JU.0000000000003493 **4.** Chapin B; LIGHTHOUSE Study Group. Diagnostic performance and safety of 18F-rhPSMA-7.3 PET in patients with newly diagnosed prostate cancer: results from a phase 3, prospective, multicenter study (LIGHTHOUSE). Poster presented at: 23rd Annual Meeting of the Society of Urologic Oncology. December 1, 2022. San Diego, CA. **5.** Wurzer A, Di Carlo D, Schmidt A, et al. Radiohybrid ligands: a novel tracer concept exemplified by 18F- or 68Ga-labeled rhPSMA inhibitors. *J Nucl Med.* 2020;61(5):735-742.

Template:
Letter for Appeal of Denial

[Date]

[Contact at Health insurer]
[His/Her Title]
[Name of health Insurance Company]
[Address]
[City, State, ZIP code]

Insured: [Name]
Patient: [Name]
Patient Date of Birth: [DOB]
Insurance ID number: [Policy Number]
Claim Number: [Insert Claim #]

Dear [Medical Director]

I am writing this letter to formally request a reconsideration of the adverse determination for a POSLUMA® (flotufolostat F 18) PET scan in the above-referenced claim. It is my understanding based on your letter of denial dated [insert date] that this procedure has been denied because: [quote the specific reason for the denial stated in denial letter].

[If the denial criteria is unclear, you may consider requesting additional information such as:]

1. Name of the board-certified physician who reviewed this claim and a description of any applicable advanced training or experience this reviewer has related to this type of care.
2. Board certified physician's recommendation regarding alternative diagnostic assessment or work up and care.
3. A copy of applicable internal clinical guideline, source of the guideline and the date of development.
4. An outline of the specific records reviewed and a description of any records which would be necessary to justify coverage of this treatment.
5. Copies of any peer-reviewed literature, technical assessments or expert medical opinions reviewed by your company regarding treatment of this nature and its efficacy.

On May 25th, 2023, the Food and Drug Administration approved POSLUMA® (flotufolastst F 18) injection, an F 18 labeled Prostate-Specific Membrane Antigen (PSMA) agent that is the first and only commercially available radiohybrid™ (rh) F 18 PET diagnostic radiopharmaceutical. POSLUMA (flotufolastat F 18) injection is 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

On behalf of the patient, I am requesting reconsideration of the use of POSLUMA PET imaging to [describe intended clinical use].

Patient's Medical History
[provide patient information regarding condition, symptoms and history related to his prostate cancer]

Clinical Rationale / Supporting Information
[provide clinical rationale for ordering POSLUMA scan and supporting documentation]

I respectfully request that you review the information provided and reevaluate your coverage of POSLUMA PET imaging for [patient name]. If you have any further questions about this request, please contact me at [insert practice phone number]. I look forward to your reconsideration.

Thank you in advance for your immediate attention to this request.

Sincerely
[Physician's Name]
[Physician's Practice Name]
[Practice Address]

Template:
Letter for Appeal of Denial

Enclosure

1. POSLUMA FDA Approval Letter
2. POSLUMA. Package insert. Blue Earth Diagnostics Ltd; 2023.

[Enclose additional documents as specifically required by payer in appeal procedures or supportive of use.]

May also include:

- Copy of the original claim
- Designated payer-specific appeal form
- Copy of the denial notification from the payer
- Patient's complete medical history

References: 1. Fendler WP, et al. PSMA PET/CT: joint EANM procedure guideline/SNMMI procedure standard for prostate cancer imaging 2.0. *Eur J Nucl Med Mol Imaging* 2023; https://doi.org/10.1007/s00259-022-06089-w **2.** Wurzer A, Di Carlo D, Schmidt A, et al. Radiohybrid ligands: a novel tracer concept exemplified by 18F- or 68Ga-labeled rhPSMA inhibitors. *J Nucl Med*. 2020;61(5):735-742. **3.** Jani AB, et al. Diagnostic performance and safety of 18F-rhPSMA-7.3 PET in men with suspected prostate cancer recurrence: results from a Phase 3, prospective, multicenter study (SPOTLIGHT). *J Urol*. Published online April 26, 2023: doi/10.1097/JU.0000000000003493 **4.** Chapin B; LIGHTHOUSE Study Group. Diagnostic performance and safety of 18F-rhPSMA-7.3 PET in patients with newly diagnosed prostate cancer: results from a phase 3, prospective, multicenter study (LIGHTHOUSE). Poster presented at: 23rd Annual Meeting of the Society of Urologic Oncology. December 1, 2022. San Diego, CA. **5.** Gafita A, et al. Measuring response in metastatic castration resistant prostate cancer using PSMA PET/CT: comparison of RECIST 1.1, aPCWG3, aPERCIST, PPP, and RECIP 1.0 criteria. *Eur J Nuc Med Mol Imaging* **6.** Karimzadeh A, et al. 177Lu-PSMA-I&T for treatment of metastatic castration resistant prostate cancer: prognostic value of scintigraphic and clinical biomarkers. *J Nucl Med* 2023; 64:402-9 **7.** Langbein T, et al. Utility of 18F-rhPSMA-7.3 PET for imaging of primary prostate cancer and preoperative efficacy in N-staging of unfavorable intermediate- to very high-risk patients validated by histopathology. *J Nucl Med* 2022;63:1334-42 **8.** Malaspina S, et al. Kinetic analysis and optimisation of 18F-rhPSMA-7.3 PET imaging of prostate cancer. *Eur J Nuc Med Mol Imaging* 2021;48:3723-31 **9.** Malaspina S, et al. Uptake of 18F-rhPSMA-7.3 in PET imaging of prostate cancer – a phase 1 proof-of-concept study. CBR. 2022; 37(3):205-213 **10.** Rauscher I, et al. Detection efficacy of 18F-rhPSMA-7.3 PET/CT and impact on management in patients with biochemical recurrence of prostate cancer after radical prostatectomy and before potential salvage treatment. *J Nucl Med* 2021;62:1719-26 **11.** Surasi DS, et al. Diagnostic performance and safety of positron emission tomography with 18F-rhPSMA-7.3 in patients with newly diagnosed unfavourable intermediate to very high-risk prostate cancer: results from a Phase 3, prospective, multicentre study (LIGHTHOUSE). *Eur Urol* 2023: under review **12.** Tolvanen T, et al. Safety, biodistribution, and radiation dosimetry of 18F-rhPSMA-7.3 in healthy adult volunteers. *J Nucl Med* 2021;62:679-84

POSLUMA Coding Information Sheet

Prior Authorization Helpful Tips

POSLUMA Scheduling Tip Sheet

POSLUMA PET Imaging Program Implementation Checklist

Letter Templates

Sample Billing Forms

POSLUMA Access and Reimbursement Information

Fillable Forms

POSLUMA Order Form

Patient Benefit Investigation Form

Template:
Medicare Advantage Denial Appeal

[Date]

[Contact at Health insurer]
[His/Her Title]
[Name of health Insurance Company]
[Address]
[City, State, ZIP code]

Patient: [Name]
Patient Date of Birth: [DOB]
Insurance ID number: [Policy Number]
Claim Number: [Insert Claim#

Re: POSLUMA® (flotufolastat F 18) injection PET Scan Denial

Dear [MA Plan Medical Director]:

I am writing this letter to formally request a reconsideration of the adverse determination for a POSLUMA® (flotufolastat F 18) injection PET scan for the above-referenced patient. It is my understanding based on your letter of denial dated [insert date] that this procedure has been denied because: [insert language from denial letter indicating initial treatment strategy is a non-covered indication].

As documented below, on May 25th, 2023, the Food and Drug Administration approved POSLUMA® (flotufolastat F 18) injection, an F 18 F Prostate-Specific Membrane Antigen (PSMA) agent that is the first and only commercially available radiohybrid™ (rh) F 18 PET diagnostic radiopharmaceutical. POSLUMA ®(flotufolastat F 18) injection is 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

Medicare currently has a National Coverage Determination (NCD) for Positron Emission Tomography (PET) Scans which allows local contractors to determine coverage for newly approved PET agents by the FDA. Specifically, NCD 220.6 (Jan. 1, 2022), available at https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=211, provides:

"Effective January 1, 2022, the Centers for Medicare & Medicaid Services removed the umbrella national coverage determination (NCD) for Positron Emission Tomography (PET) Scans. In the absence of an NCD, coverage determinations for all oncologic and nononcologic uses of PET that are not included in another NCD under section 220.6 will be made by the Medicare Administrative Contractors under section 1862(a)(1)(A) of the Social Security Act. All PET indications currently covered or non-covered under NCDs under section 220.6 remain unchanged and MACs shall not alter coverage for indications covered under NCDs."

In addition, according to Medicare's "Managed Care Manual", Chapter 4 - Benefits and Beneficiary Protections, Section 10.2 - "Basic Rule", https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/

mc86c04.pdf, "An MAO offering a MA plan must provide enrollees in that plan with all Part A and Part B original Medicare services, if the enrollee is entitled to benefits under both parts, and Part B services if the enrollee is a grandfathered "Part B only" enrollee. The MAO fulfills its obligation of providing original Medicare benefits by furnishing the benefits directly, through arrangements, or by paying for the benefits on behalf of enrollees."

Because Medicare's Managed Care Manual provides that a Medicare Advantage Organization must provide enrollees with same services as are covered under original Medicare, [MA Plan] must cover POSLUMA® — whether for initial treatment strategy or subsequent treatment strategy — where medically reasonable and necessary for the patient.

It is my opinion that based on my patient's clinical history, as outlined below, the use of POSLUMA PET Imaging is appropriate and medically necessary for [patient name] and should be covered by [MA Plan].

POSLUMA Coding Information Sheet
Prior Authorization Helpful Tips
POSLUMA Scheduling Tip Sheet
POSLUMA PET Imaging Program Implementation Checklist
Letter Templates
Sample Billing Forms
POSLUMA Access and Reimbursement Information
Fillable Forms
POSLUMA Order Form
Patient Benefit Investigation Form

Template:
Medicare Advantage Denial Appeal

[This is where you should summarize your rationale as to why a POSLUMA PET scan is appropriate and medically necessary for the patient. Consider including the following information:]

- Description of patient's condition, date of original diagnosis and history related to his Prostate CA
- Current symptoms
- Circumstances surrounding care, need for diagnostic imaging with POSLUMA
- Previous diagnostic tests, therapies, and any complications
- Any other relevant information

I respectfully request that you review the information provided and re-evaluate your coverage of POSLUMA PET Imaging for [patient name]. If you have any further questions about this request, please contact me at [insert practice phone number].

Thank you in advance for your immediate attention to this request. I look forward to your reconsideration.
Sincerely,
[Physician's Name]
[Physician's Practice Name]
[Practice Address]
[Phone Number]

Enclosure

1. POSLUMA FDA Approval Letter
2. POSLUMA. Package insert. Blue Earth Diagnostics Ltd; 2023.

[Enclose additional documents as specifically required by payer in appeal procedures or supportive of use.]

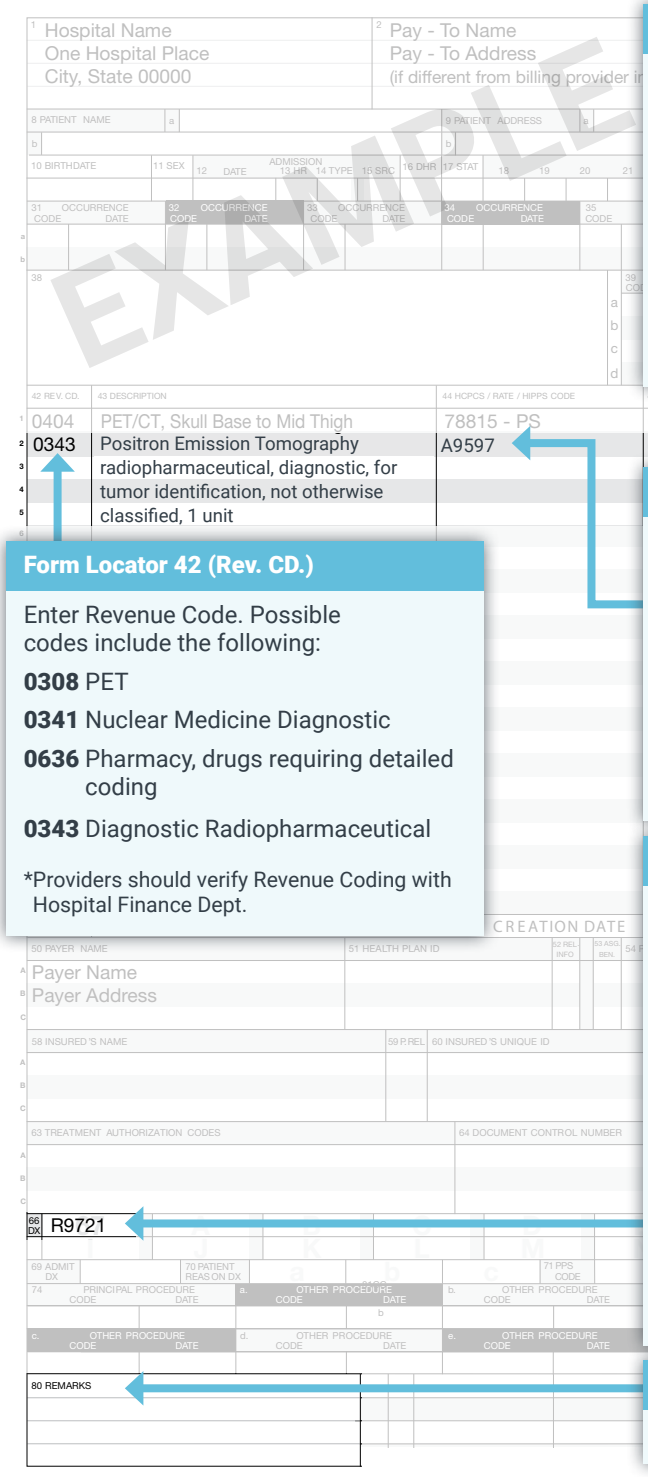
May also include:

- Copy of the original claim
- Designated payer-specific appeal form
- Copy of the denial notification from the payer
- Patient's complete medical history
- ACR Appropriate Use Criteria

References: 1. Fendler WP, et al. PSMA PET/CT: joint EANM procedure guideline/SNMMI procedure standard for prostate cancer imaging 2.0. *Eur J Nucl Med Mol Imaging* 2023; https://doi.org/10.1007/s00259-022-06089-w **2.** Wurzer A, Di Carlo D, Schmidt A, et al. Radiohybrid ligands: a novel tracer concept exemplified by 18F- or 68Ga-labeled rhPSMA inhibitors. *J Nucl Med.* 2020;61(5):735-742. **3.** Jani AB, et al. Diagnostic performance and safety of 18F-rhPSMA-7.3 PET in men with suspected prostate cancer recurrence: results from a Phase 3, prospective, multicenter study (SPOTLIGHT). *J Urol.* Published online April 26, 2023: doi/10.1097/JU.0000000000003493 **4.** Chapin B; LIGHTHOUSE Study Group. Diagnostic performance and safety of 18F-rhPSMA-7.3 PET in patients with newly diagnosed prostate cancer: results from a phase 3, prospective, multicenter study (LIGHTHOUSE). Poster presented at: 23rd Annual Meeting of the Society of Urologic Oncology. December 1, 2022. San Diego, CA. **5.** Gafita A, et al. Measuring response in metastatic castration resistant prostate cancer using PSMA PET/CT: comparison of RECIST 1.1, aPCWG3, aPERCIST, PPP, and RECIP 1.0 criteria. *Eur J Nuc Med Mol Imaging* **6.** Karimzadeh A, et al. 177Lu-PSMA-I&T for treatment of metastatic castration resistant prostate cancer: prognostic value of scintigraphic and clinical biomarkers. *J Nucl Med* 2023; 64:402-9 **7.** Langbein T, et al. Utility of 18F-rhPSMA-7.3 PET for imaging of primary prostate cancer and preoperative efficacy in N-staging of unfavorable intermediate- to very high-risk patients validated by histopathology. *J Nucl Med* 2022;63:1334-42 **8.** Malaspina S, et al. Kinetic analysis and optimisation of 18F-rhPSMA-7.3 PET imaging of prostate cancer. *Eur J Nuc Med Mol Imaging* 2021;48:3723-31 **9.** Malaspina S, et al. Uptake of 18F-rhPSMA-7.3 in PET imaging of prostate cancer – a phase 1 proof-of-concept study. CBR. 2022; 37(3):205-213 **10.** Rauscher I, et al. Detection efficacy of 18F-rhPSMA-7.3 PET/CT and impact on management in patients with biochemical recurrence of prostate cancer after radical prostatectomy and before potential salvage treatment. *J Nucl Med* 2021;62:1719-26 **11.** Surasi DS, et al. Diagnostic performance and safety of positron emission tomography with 18F-rhPSMA-7.3 in patients with newly diagnosed unfavourable intermediate to very high-risk prostate cancer: results from a Phase 3, prospective, multicentre study (LIGHTHOUSE). Eur Urol 2023: under review **12.** Tolvanen T, et al. Safety, biodistribution, and radiation dosimetry of 18F-rhPSMA-7.3 in healthy adult volunteers. *J Nucl Med* 2021;62:679-84

Sample Hospital Setting Billing
UB-04

Key components of this form are illustrated on the sample form below.



Form Locator 46 (Units of Service)

Important: List **one** unit of service in the 2400/SV1-04 data element or in item 24G of the CMS 1500 form. Do not quantity-bill NOC drugs and biologicals even if multiple units are provided. Medicare determines the proper payment of NOC drugs and biologicals by the narrative information, not the number of units billed. https://www.cms.gov/medicare-coveragedatabase/view/article.aspx?articleid=59073&ver=27&=

Form Locator 42 (Rev. CD.)

Enter Revenue Code. Possible codes include the following:

0308 PET

0341 Nuclear Medicine Diagnostic

0636 Pharmacy, drugs requiring detailed coding

0343 Diagnostic Radiopharmaceutical

*Providers should verify Revenue Coding with Hospital Finance Dept.

Form Locator 44 (HCPCS/Rate/HIPPS Code)

Enter the CPT® or HCPCS code for the procedure, radiopharmaceutical, and drug. Possible codes include the following:

78815 PET/CT imaging, skull base to mid-thigh (most common procedure code used for oncologic PET imaging)

A9597 Positron Emission Tomography radiopharmaceutical, diagnostic, for tumor identification, not otherwise classified, 1 unit

Form Locator 67 (Principal Diagnosis Code)

Enter the ICD-10 code for the principal diagnoses. Possible codes include the following:

R97.21 Rising PSA following prior treatment for malignant neoplasm of the prostate

Z85.46 Personal history of malignant neoplasm of prostate

C61 Malignant neoplasm of prostate

Z19.1 Hormone sensitive malignancy status

Z19.2 Hormone resistant malignancy status

Special note: Do not use the decimal point on the claim form, as it may cause rejection of the claim. Up to 8 additional diagnoses that coexist with the principal diagnosis can be reported in FL 67 A-H.

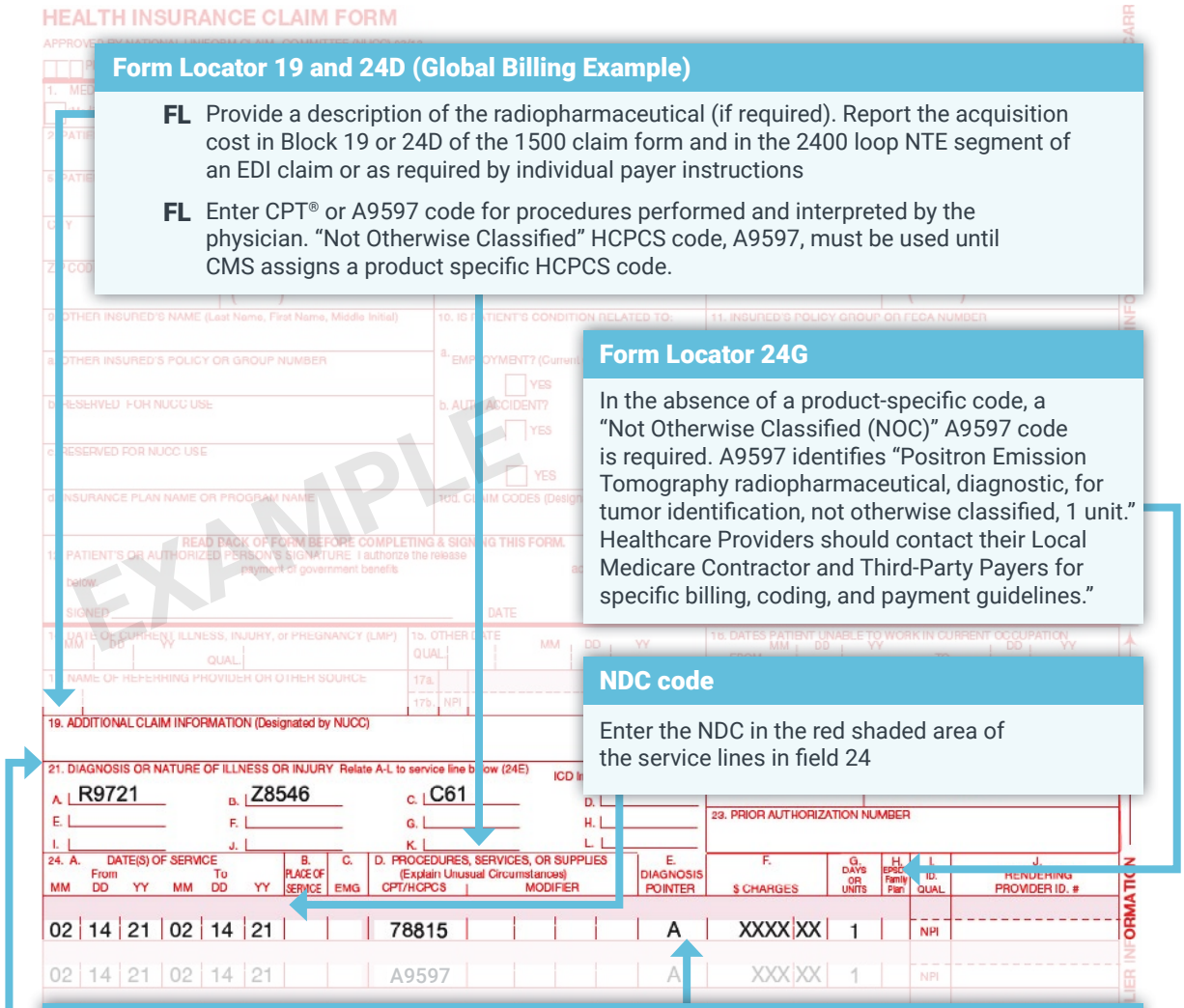
Form Locator 80 (Drug Identifying information)

Enter the NDC in Form Locator 80

Sample Physician Billing Global Nonhospital Outpatient Setting

CMS-1500

Key components of this form are illustrated on the sample form below.



Form Locator 19 and 24D (Global Billing Example)

FL Provide a description of the radiopharmaceutical (if required). Report the acquisition cost in Block 19 or 24D of the 1500 claim form and in the 2400 loop NTE segment of an EDI claim or as required by individual payer instructions

FL Enter CPT® or A9597 code for procedures performed and interpreted by the physician. "Not Otherwise Classified" HCPCS code, A9597, must be used until CMS assigns a product specific HCPCS code.

Form Locator 24G

In the absence of a product-specific code, a "Not Otherwise Classified (NOC)" A9597 code is required. A9597 identifies "Positron Emission Tomography radiopharmaceutical, diagnostic, for tumor identification, not otherwise classified, 1 unit." Healthcare Providers should contact their Local Medicare Contractor and Third-Party Payers for specific billing, coding, and payment guidelines."

NDC code

Enter the NDC in the red shaded area of the service lines in field 24

Form Locator 21 and 24E

FL 21 Enter **ICD-10** code for principal diagnosis in FL 21. Possible codes include the following:

R97.21 Rising PSA following prior treatment for malignant neoplasm of the prostate

Z85.46 Personal history of malignant neoplasm of prostate

C61 Malignant neoplasm of prostate

Z19.1 Hormone sensitive malignancy status

Z19.2 Hormone resistant malignancy status

FL 24E Enter the letter corresponding to the diagnosis code for the procedure in FL 24E

Special note: Do not use the decimal point on the claim form, as it may cause rejection of the claim.

POSLUMA® (flotufolastat F 18) Access and Reimbursement Information

The purpose of this resource is to offer information to providers and payers regarding reimbursement for POSLUMA® (flotufolastat F 18). Reimbursement information and processes will evolve over time, as they do with any prescription drug.

Please visit https://www.prostatecancer-blueearthdx.com/insights-and-resources#access-support periodically for the most up-to-date information.

REIMBURSEMENT SUPPORT HELPLINE

Telephone
1-855-495-9200

Hours of Operation: Telephone support is available Monday through Friday, from 9 AM to 8 PM EST.

Fax
1-877-309-7514

Email
reimbursement@blueearthdx.com

NEW REIMBURSEMENT SUPPORT TO HELP PATIENTS ACCESS POSLUMA

- **Benefit investigation:** Investigation of patient insurance benefits, including deductible and copayments, and coverage status for POSLUMA and PET/CT, including insurance requirements and possible coverage restrictions
- **Prior authorization (PA) assistance:** Information on PA requirements*
- **Appeal assistance:** Information on appeals requirements for denied prior authorizations or denied claims†

ADDITIONAL SUPPORT OFFERED

- **Billing, coding, and claims information:** Assistance with questions specific to billing, coding, and claims submission for POSLUMA and PET
- **Patient support:** Support with issues related to reimbursement coverage, claim submission, and payment denials

Patient enrollment	Benefit investigation	Prior authorization assistance	Appeal assistance
Practice submits patient enrollment form to helpline and is contacted within 24 hours	Helpline conducts benefit investigation and notifies practice within 24 to 48 hours	Helpline assists practice in understanding PA requirements, submits and follows up within 48 to 72 hours*	Helpline assists practice in understanding appeal requirements for a denied PA or claim

*Prior Authorization response time varies by payer.

†Helpline provides information about PA/appeals requirements, and, at the provider's option, submits PA forms completed by the provider to the payer.

POSLUMA
flotufolastat F 18 injection

POSLUMA Order Form

If you would like to refer a patient for a POSLUMA PET/CT scan, please complete this form and fax it to a POSLUMA imaging site. To locate an POSLUMA imaging site, visit www.POSLUMA.com/imaging-center-locator.

PATIENT INFORMATION

Patient name	Date of birth	Phone

Primary insurance	Subscriber ID	Prior authorization #

Secondary insurance	Subscriber ID	Prior authorization #

CLINICAL SIGNS/SYMPTOMS

ICD-10

☐ R97.20 ☐ C61
☐ R97.21 ☐ Z19.1
☐ Z85.46 ☐ Z19.2

Other

_____
_____
_____

CPT Code

☐ 78811 ☐ 78814
☐ 78812 ☐ 78815
☐ 78813 ☐ 78816

PRIOR TREATMENT

Radical prostatectomy ☐ Yes ☐ No

Physician | Date

Radiation therapy to prostate ☐ Yes ☐ No

Physician | Date

Currently undergoing ADT ☐ Yes ☐ No

Physician | Date

PATIENT PREPARATION AND PRECAUTIONS

Preparing for an POSLUMA scan

- **Patients should drink water prior to POSLUMA administration and continue drinking and voiding frequently for first few hours after administration.**
- Patient should void immediately prior to imaging.
- Scan duration is approximately 20 minutes.

PREVIOUS SCANS

☐ CT Date: _____
☐ MR Date: _____
☐ Bone scan Date: _____
☐ Negative PSMA PET Scan Date: _____

I verify that the above information is complete and accurate to the best of my knowledge and that I have prescribed POSLUMA based on my independent professional judgment of medical necessity.

Physician or nurse practitioner signature | Date

BLUE EARTH DIAGNOSTICS
A Bracco Company

BEDPRC23-0072A 06/23

POSLUMA
flotufolastat F 18 injection

Patient Benefit Investigation Form

Phone: 1-855-495-9200 | Fax: 1-877-309-7514 | Email: reimbursement@blueearthdx.com

REQUESTED SERVICE

☐ Benefit investigation only
☐ Prior authorization assistance
☐ Appeal/denial assistance

The following information should be filled out by your healthcare provider

HCPCS: ☐ A9597

CPT® codes: ☐ 78815 ☐ Other: _____

☐ **Diagnosis code C61**
☐ **Diagnosis code Z85.46**
☐ **Diagnosis code R97.21**
☐ Other: _____
☐ **Diagnosis code R97.20**
☐ **Diagnosis code Z19.1**
☐ **Diagnosis code Z19.2**

For new diagnosis of prostate cancer: (please select the risk group that best describes the patient's condition)

☐ **Unfavorable Intermediate** ☐ **High** ☐ **Very High**

Suspicion of recurrent disease after previously treated prostate cancer: ☐ Yes ☐ No

Suspected recurrence based on:

Elevated PSA levels: _____

Prior studies/treatment: _____

Radical prostatectomy ☐ Yes ☐ No Date: _____

Radiation therapy to prostate ☐ Yes ☐ No Date: _____

Other treatments: _____ Date: _____

Previous imaging studies: ☐ CT ☐ MRI ☐ Bone scan
☐ Other: _____

I verify that the patient and physician information contained in this enrollment form is complete and accurate to the best of my knowledge and that I have prescribed POSLUMA based on my professional, independent judgment of medical necessity and it will be used as directed. I certify that I have received the appropriate permission from the patient and met any other applicable requirements imposed under the Health Insurance Portability and Accountability Act of 1996 and/or state law needed to release the above information to Blue Earth Diagnostics and its agents for the purposes of verifying the patient's insurance coverage, on my patient's behalf, and providing information on prior authorization and/or appeals for denials of claims. I authorize the Reimbursement Support Helpline Program to perform a preliminary assessment of insurance and benefit investigation for the above-named patient, and I further authorize and request that the Program provide to me information regarding POSLUMA for my reference in completing documentation as may be required by the patient's health plan. I further authorize POSLUMA Reimbursement Support to submit, at my request, information provided by me on this form and documentation completed by me to applicable health plans.

Prescriber signature required (no stamps) | Date

PATIENT DEMOGRAPHIC INFORMATION

First name _____ MI _____
Last name _____
Address _____
City _____ State _____ ZIP _____
Mobile phone # _____ Last 4 of SSN _____
Email _____ DOB _____
Primary insurance _____
Policy holder _____ Group # _____
Policy # _____ Phone # _____
Secondary insurance _____
Policy holder _____ Group # _____
Policy # _____ Phone # _____

NOTE: Copy of insurance card(s) acceptable in lieu of completing insurance information above. Please include both sides of card.

REFERRING PHYSICIAN INFORMATION

Physician name _____
Physician specialty _____
Practice name _____
Practice address _____
City _____ State _____ ZIP _____
TIN # _____ Medicare PTAN _____
NPI # _____
Contact person _____
Contact phone # _____ Fax # _____
Contact email _____

SITE OF POSLUMA PET/CT SCAN

☐ Hospital outpatient ☐ Physician practice
☐ Independent diagnostic testing facility
☐ Other: _____
Name of facility _____
TIN # _____ Medicare PTAN _____
NPI # _____
Facility contact name _____
Facility contact phone # _____
Facility contact email _____

BLUE EARTH DIAGNOSTICS
A Bracco Company

BEDPRC23-0072A 06/23

POSLUMA
flotufolastat F 18 injection

Patient Benefit Investigation Form

PATIENT AUTHORIZATION TO SHARE HEALTH INFORMATION

I understand that I must authorize the use and disclosure of certain personal health information ("PHI") before I can receive assistance through the Reimbursement Support Helpline Program (the "Program"). I hereby authorize my healthcare providers, pharmacies, and health plan(s) to disclose my PHI related to my medical condition and treatment, and all information provided on this patient enrollment form, to Blue Earth Diagnostics, the manufacturer of POSLUMA, and to its agents and the administrator of the Program (collectively, the "Recipients"). I further authorize the Recipients to use and disclose my PHI for the purposes of establishing my eligibility for benefits from my health plan or other programs, providing educational and reimbursement support, communicating with my healthcare providers and health plan(s), and for Blue Earth Diagnostics' internal business purposes, including quality control and compliance. I understand that signing this authorization is voluntary and that if I were to refuse to sign, that would not affect my eligibility for health plan benefits or ability to obtain treatment by my healthcare providers. I also understand, however, that if I refuse to sign, I will not have access to the services offered by the Program. I also understand that if I sign this authorization, I can cancel it at any time by notifying Blue Earth Diagnostics in writing at reimbursement@blueearthdx.com. Upon receiving my notice of cancellation, Blue Earth Diagnostics would stop using this authorization to access, use, or disclose my PHI, and would notify my healthcare providers and health plan(s) of the cancellation, but the cancellation would not invalidate reliance on the authorization prior to its cancellation. I understand that once disclosures of my PHI pursuant to this authorization have occurred, that PHI may no longer be protected by certain federal or state privacy laws and therefore could potentially be re-disclosed to others.

This authorization will expire 5 years after the date it is signed below or at such earlier time as may be required by applicable state law. I have read this authorization or have had it explained to me. I understand that I will receive a copy of this authorization after I sign it.

Patient signature _____ Date _____

Printed name _____

Abbreviations: CPT, current procedural terminology; HCPCS, Healthcare Common Procedure Coding System.

BLUE EARTH DIAGNOSTICS
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BEDPRC23-0072A 06/23

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use POSLUMA® safely and effectively. See full prescribing information for POSLUMA.

POSLUMA (flotufolastat F 18) injection, for intravenous use
Initial U.S. Approval: 2023

----------INDICATIONS AND USAGE----------
POSLUMA 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. (1)

----------DOSAGE AND ADMINISTRATION----------
- Recommended amount of radioactivity of POSLUMA is 296 MBq (8 mCi) administered as an intravenous bolus injection. (2.2)
- Initiate imaging approximately 60 minutes after administration. Scanning should start from mid-thigh and proceed to base of skull. (2.4)
- See full prescribing information for additional preparation, handling, administration, imaging, and radiation dosimetry information. (2.3, 2.4)

----------DOSAGE FORMS AND STRENGTHS----------
Injection: 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 in a multiple-dose vial. (3)

----------CONTRAINDICATIONS----------
None. (4)

----------WARNINGS AND PRECAUTIONS----------
- Risk of Image Misinterpretation: Image interpretation errors can occur with POSLUMA imaging. Interpretation of POSLUMA PET may differ depending on imaging readers in patients with suspected recurrence of prostate cancer. Consider multidisciplinary consultation and histopathological confirmation. (5.1, 14.2)
- Radiation risk: POSLUMA contributes to a patient's long-term cumulative radiation exposure. Ensure safe handling to protect patients and health care workers from unintentional radiation exposure. (2.1, 5.2)

----------ADVERSE REACTIONS----------
The most common adverse reactions (≥0.4%) are diarrhea, blood pressure increase, and injection site pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Blue Earth Diagnostics Ltd at 1-844-POSLUMA (1-844-767-5862) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION

Revised: 5/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

POSLUMA is 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.

2 DOSAGE AND ADMINISTRATION

2.1 Radiation Safety - Drug Handling

Handle POSLUMA with safety measures to minimize radiation exposure *[*see *Warnings and Precautions (5.2)]*. Use waterproof gloves, effective radiation shielding, including syringe shields, and other appropriate safety measures when handling and administering POSLUMA.

Radiopharmaceuticals should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radionuclides, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.

2.2 Recommended Dose and Administration Instructions

Recommended Dose

The recommended amount of radioactivity to be administered in adults is 296 MBq (8 mCi) as an intravenous bolus injection.

Preparation and Administration Instructions

- Inspect POSLUMA visually for particulate matter and discoloration before administration. Do not use the drug if the solution contains particulate matter or is discolored.
- Use aseptic technique and radiation shielding when withdrawing and administering POSLUMA.
- Calculate the necessary volume to administer based on calibration time and required dose.
- The recommended maximum volume of undiluted POSLUMA is 5 mL.
- POSLUMA may be diluted with 0.9% Sodium Chloride Injection, USP.
- Assay the dose in a dose calibrator before administration.

Post Administration Instructions

- After the POSLUMA injection, administer an intravenous flush of sterile 0.9% Sodium Chloride Injection, USP to ensure full delivery of the dose.
- Dispose of any unused drug in a safe manner in compliance with applicable regulations.

2.3 Patient Preparation

Instruct patients to drink water prior to administration of POSLUMA to ensure adequate hydration and to continue drinking and voiding frequently for the first few hours following administration to reduce radiation exposure.

2.4 Image Acquisition

- Patients should void immediately prior to imaging.
- Position the patient supine with arms above the head.
- Begin image acquisition approximately 60 minutes after POSLUMA injection.
- Image acquisition should start from mid-thigh and proceed to the base of the skull.
- Scan duration is approximately 20 minutes depending on the number of bed positions and acquisition time per bed position (typically 3 minutes). Adapt imaging technique according to the equipment used and patient characteristics in order to obtain the best image quality possible.

2.5 Image Display and Interpretation

POSLUMA binds to PSMA. PET images obtained using POSLUMA indicate the presence of PSMA in tissues *[see Clinical Pharmacology (12.1)]*. 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. Tumors that do not express PSMA will not be visualized. Increased uptake in tumors is not specific for prostate cancer *[see Warnings and Precautions (5.1)]*.

2.6 Radiation Dosimetry

Estimated absorbed radiation doses for adult patients following intravenous injection of POSLUMA are shown in Table 1. The effective radiation dose resulting from the administration of the recommended activity of 296 MBq of POSLUMA is 4.1 mSv. The radiation absorbed doses to the critical organs of adrenal glands, kidneys, and submandibular glands for the recommended activity of 296 MBq are 54.3 mGy, 51 mGy, and 43.8 mGy, respectively. When PET/CT is performed, exposure to radiation will increase by an amount dependent on the settings used in the CT acquisition.

Table 1: Estimated Radiation Absorbed Doses in Organs/Tissues in Adults who Received POSLUMA

Organ/Tissue	Absorbed Dose per Unit Administered Activity (mGy/MBq)
	Mean
Adrenal glands	0.184
Brain	0.002
Breasts	0.004
Gallbladder wall	0.017
Lower large intestine wall	0.007
Upper large intestine wall	0.01
Heart wall	0.02
Kidneys	0.172
Lacrimal glands	0.08*
Liver	0.062
Lungs	0.01

Muscle	0.006
Osteogenic cells	0.012
Ovaries	0.005
Pancreas	0.028
Parotid glands	0.114*
Red bone marrow	0.01
Skin	0.002
Small intestine	0.012
Spleen	0.083
Stomach wall	0.012
Sublingual glands	0.065*
Submandibular glands	0.148*
Testes	0.005
Thymus gland	0.01
Thyroid	0.01
Urinary bladder wall	0.006**
Uterus	0.011
Effective dose (mSv/MBq)	**0.014****

*The absorbed dose value reflects self-irradiation only; no dose contribution from other regions to the glands is added. **A 1-hour bladder voiding interval is assumed.

3 DOSAGE FORMS AND STRENGTHS

Injection: 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 in a multiple-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Image Misinterpretation

Image interpretation errors can occur with POSLUMA PET. 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 POSLUMA for imaging metastatic pelvic lymph nodes in patients prior to initial definitive therapy seems to be affected by serum PSA levels and risk grouping *[See Clinical Studies (14.1)]*. The performance of POSLUMA for imaging patients with biochemical evidence of recurrence of prostate cancer seems to be affected by serum PSA levels *[See Clinical Studies (14.2)]*. Flotufolastat F 18 uptake is not specific for prostate cancer and may occur in other types of cancer, in non-malignant processes, and in normal tissues. Clinical correlation, which may include histopathological evaluation, is recommended.

Risk of Image Misinterpretation in Patients with Suspected Prostate Cancer Recurrence

The interpretation of POSLUMA PET may differ depending on imaging readers, particularly in the prostate/prostate bed region *[see Clinical Studies (14.2)]*. Because of the associated risk of false positive

interpretation, consider multidisciplinary consultation and histopathological confirmation when clinical decision-making hinges on flotufolastat F18 uptake only in the prostate/prostate bed region or only on uptake interpreted as borderline.

5.2 Radiation Risks

POSLUMA use contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer. Advise patients to hydrate before and after administration and to void frequently after administration. Ensure safe handling to minimize radiation exposure to the patient and health care providers *[see Dosage and Administration (2.1, 2.2)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of POSLUMA was evaluated in 747 patients with prostate cancer *[see Clinical Studies (14.1,14.2)]*. All patients received a single administration of POSLUMA with an administered radioactivity (mean ± SD) of 307 ± 23 MBq (8.3 ± 0.6 mCi). The mean age of patients was 67 years (range: 43 to 86 years); distribution by race was 78% White, 12% Black or African American, 2% other, and 7% unreported; and distribution by ethnicity was 5% Hispanic/Latino, 87% non-Hispanic/Latino, and 8% unreported.

The adverse reactions reported in ≥ 0.4% of patients are shown in Table 2.

Table 2: Adverse Reactions in ≥ 0.4% of Patients with Prostate Cancer Receiving POSLUMA

Adverse Reaction	**POSLUMA N = 747 n (%)**
Diarrhea	5 (0.7%)
Blood pressure increase	4 (0.5%)
Injection site pain	3 (0.4%)

7 DRUG INTERACTIONS

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

POSLUMA is not indicated for use in females. There are no available data on the use of POSLUMA in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with flotufolastat F 18. Radioactive drugs, including POSLUMA, have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of the radiation dose.

8.2 Lactation

Risk Summary

POSLUMA is not indicated for use in females. There are no data on the presence of flotufolastat F 18 in human milk, the effect on the breastfed infant, or the effect on milk production.

8.4 Pediatric Use

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

8.5 Geriatric Use

Among the total number of patients receiving POSLUMA in clinical studies of prostate cancer, 463 (62%) were 65 years of age and older, while 118 (16%) were 75 years of age and older *[see Clinical Studies (14.1,14.2)]*. No overall differences in safety or effectiveness were observed between these patients and younger adult patients.

10 OVERDOSAGE

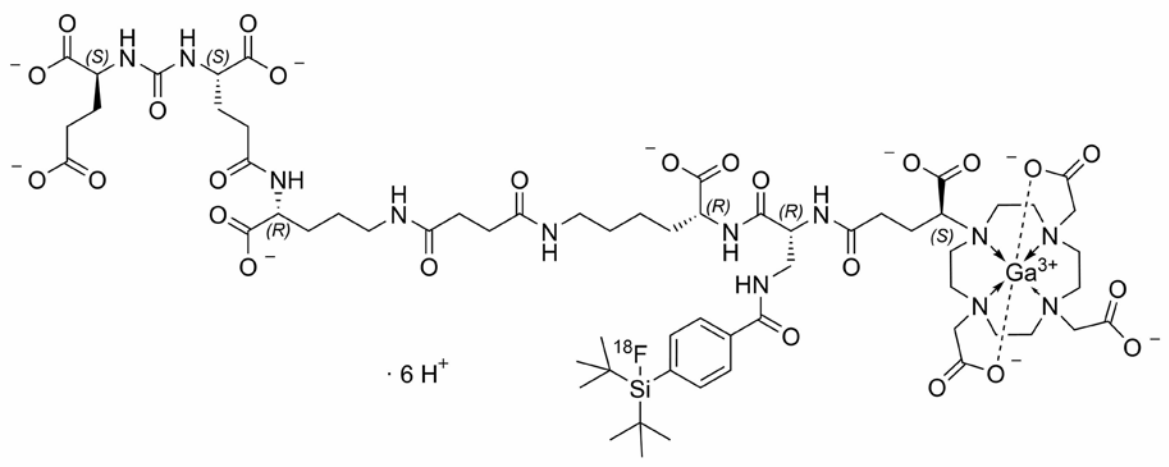
In the event of an overdose of POSLUMA, maintain hydration of the patient and frequent voiding to minimize radiation exposure. A diuretic might also be considered. If possible, an estimate of the radiation effective dose administered to the patient should be made.

11 DESCRIPTION

11.1 Chemical Characteristics

POSLUMA (flotufolastat F 18) injection is a radioactive diagnostic agent for intravenous use. The active ingredient of POSLUMA is flotufolastat F 18 gallium, of which the molecular structure includes a DOTAGA complex with nonradioactive gallium. Radioactive fluorine-18 is covalently bound to silicon.

Chemically, flotufolastat F 18 gallium is gallate(6-), [(4*S*,8*S*,13*R*,27*R*,30*R*,35*S*)-35-[4,10-bis[(carboxy-k*O*)methyl]-7-(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl-kN^{1},kN^{4},kN^{7},kN^{10}]-30-[[[4-[bis(1,1-dimethylethyl)fluoro-^{18}F-silyl]benzoyl]amino]methyl]-1,36-dihydroxy-1,6,11,18,21,29,32,36-octaoxo-5,7,12,17,22,28,31-heptaazahexatriacontane-4,8,13,27-tetracarboxylato(9-)]-, hydrogen (1:6). The molecular weight is 1537.3 g/mol and the structural formula is:



POSLUMA is a sterile, non-pyrogenic, clear, colorless, and isotonic solution. Each mL contains up to 20 mcg of flotufolastat gallium, up to 5,846 MBq (158 mCi) as flotufolastat F 18 gallium at end of synthesis, and the following inactive ingredients: not more than 10% (v/v) alcohol, 1.9 mg anhydrous citric acid, 7.2 mg sodium chloride, and 0.75 mg sodium hydroxide to adjust pH between 4 and 6. POSLUMA contains no preservative.

11.2 Physical Characteristics

POSLUMA contains fluorine-18 (F 18) which is a cyclotron produced radionuclide that decays by positron emission (β+ decay, 96.7%) and orbital electron capture (3.3%) to stable oxygen-18 with a physical half-life of 109.8 minutes (Table 3). The principal photons useful for diagnostic imaging are the coincident pair of 511 keV gamma photons, resulting from the interaction of the emitted positron with an electron (Table 4).

Table 3: Physical Decay Chart for Fluorine-18

Minutes	Fraction Remaining
0	1
15	0.909
30	0.826
60	0.683
110	0.5
220	0.25

Table 4: Principal Radiation Produced from Decay of Fluorine-18

	Energy (keV)	Abundance (%)
Positron	249.8	96.7
Gamma	511	193.5

11.3 External Radiation

The point source air-kerma coefficient for F 18 is 3.75×10^{-17} Gy m^2/(Bq s). The first half-value thickness of lead (Pb) for F 18 gamma rays is approximately 6 mm. The relative reduction of radiation emitted by F 18 that results from various thicknesses of lead shielding is shown in Table 5. The use of 8 cm of Pb will decrease the radiation transmission (i.e., exposure) by a factor of about 10,000.

Table 5: Radiation Attenuation of 511 keV Gamma Rays by Lead Shielding

Shield Thickness cm of Lead (Pb)	Coefficient of Attenuation
0.6	0.5
2	0.1
4	0.01
6	0.001
8	0.0001

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of action

Flotufolastat F 18 binds to PSMA (IC50 = 4.4 nM) expressed on cells, including prostate cancer cells, and is internalized. Prostate cancer cells usually overexpress PSMA. Fluorine-18 is a ß+ emitting radionuclide that can be detected using positron emission tomography.

12.2 Pharmacodynamics

The relationship between flotufolastat F 18 plasma concentrations and image interpretation has not been fully characterized.

12.3 Pharmacokinetics

Distribution

Following intravenous administration, flotufolastat F 18 distributes to liver (15.8% of administered activity), heart blood pool (7.4%), and kidneys (3.2%) and is cleared from the blood.

Elimination

Metabolism

Flotufolastat F 18 does not undergo metabolism up to 50 minutes post injection.

Excretion

Elimination is by urinary excretion. Approximately 7% of the administered activity was excreted in the urine in the first 2 hours post-injection with approximately 15% excreted by 4.5 hours post-injection.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies to assess the carcinogenicity or mutagenic potential of flotufolastat have not been conducted. However, flotufolastat F 18 has the potential to be mutagenic because of the F 18 radionuclide.

No studies in animals have been performed to evaluate potential impairment of fertility in males or females.

14 CLINICAL STUDIES

14.1 Imaging Prior to Initial Definitive Therapy of Prostate Cancer

The safety and efficacy of POSLUMA were evaluated in LIGHTHOUSE (NCT04186819), a prospective, multicenter, open-label, single-arm study in patients with prostate cancer who were candidates for initial definitive therapy.

The study enrolled 356 patients diagnosed with unfavorable intermediate-risk (32%) or high-/very high-risk prostate cancer (68%) who were candidates for radical prostatectomy and pelvic lymph node dissection (PLND). Unfavorable intermediate-risk was defined as having any ≥ 2 intermediate risk factors [T2b-T2c, Gleason score 7, PSA 10-20], Gleason pattern 4+3=7, or ≥ 50% of biopsy cores positive for prostate cancer. High or very high-risk was defined as having T3 or T4 disease, Gleason score ≥8, primary Gleason pattern 5, and/or PSA >20.

All patients received a single dose of POSLUMA with an administered radioactivity (mean ± SD) of 307 ± 23 MBq (8.3 ± 0.62 mCi), followed by PET/CT scan from mid-thigh to base of the skull. Three central readers blinded to clinical information independently interpreted each scan for lesions considered positive for prostate cancer in pelvic lymph nodes, categorized by subregion and left and right laterality *[see Dosage and Administration (2.5)]*. Positive lesions in the prostate gland, lymph nodes outside the pelvis, soft tissue/parenchyma, and bones were also recorded.

A total of 296 patients (83%) underwent standard-of-care prostatectomy and template PLND and had sufficient histopathology data for evaluation of the pelvic lymph nodes. The mean age was 65 years (range 46 to 82 years); distribution by race was 82% White, 8% Black or African American, 0.3% other, and 10% unreported; and distribution by ethnicity was 5% Hispanic/Latino, 86% non-Hispanic/Latino, and 9% unreported. The median serum PSA was 8.4 ng/mL. The total Gleason score was 7 for 45%, 8 for 26%, and 9 for 25% of the patients, with the remainder of the patients having Gleason scores of 6 or 10. Approximately 24% of patients had pelvic lymph node metastases based on histopathology.

POSLUMA performance was evaluated against histopathology after matching by hemipelvis. Table 6 shows the results, such that at least one true positive hemipelvis region defined a true positive patient.

Table 6: Patient-Level, Hemipelvis Region-Matched Performance of POSLUMA PET for Detection of Pelvic Lymph Node Metastasis (N1) in LIGHTHOUSE

N=296	Reader 1	Reader 2	Reader 3
True Positive	21	19	16

False Positive	16	14	7
True Negative	210	212	219
False Negative	49	51	54
Sensitivity, (%) [95% CI]	30% [20, 42]	27% [17, 39]	23% [14, 35]
Specificity, (%) [95% CI]	93% [89, 96]	94% [90, 97]	97% [94, 99]
Positive Predictive Value, (%) [95% CI]	57% [40, 73]	58% [39, 75]	70% [47, 87]
Negative Predictive Value, (%) [95% CI]	81% [76, 86]	81% [75, 85]	80% [75, 85]

CI= confidence interval

In exploratory analyses, there were numerical trends towards higher sensitivity among patients with PSA greater than or equal to the median value (8.4 ng/mL) and among patients with high-risk or very high-risk categorization.

POSLUMA-positive lesions outside of the prostate gland and pelvic lymph nodes (M1) were also evaluated. As a percentage of the 352 patients with an evaluable POSLUMA scan and of the 61 patients with at least one POSLUMA positive M1 lesion, 10% (95% CI: 7% to 13%) and 56% (95% CI: 42% to 68%), respectively, had at least one matching positive M1 lesion between the POSLUMA majority read and a reference standard consisting of other imaging evaluated by a separate consensus panel or histopathology.

14.2 Imaging for Suspected Recurrence of Prostate Cancer

The safety and efficacy of POSLUMA were evaluated in SPOTLIGHT (NCT04186845), a prospective, multicenter, open-label, single-arm study in patients with biochemical evidence of recurrent prostate cancer.

The study enrolled 391 patients with suspected recurrence defined by either serum PSA of at least 0.2 ng/mL after radical prostatectomy (with confirmatory PSA level also at least 0.2 ng/mL) or by an increase in serum PSA of at least 2 ng/mL above the nadir after other therapies.

All patients received a single dose of POSLUMA with an administered radioactivity (mean ± SD) of 306 ± 22 MBq (8.27 ±0.61 mCi), followed by PET/CT scan from mid-thigh to base of the skull. Three central readers blinded to clinical information independently interpreted each scan by region for the presence and location of lesions considered positive for prostate cancer *[see Dosage and Administration (2.5)]*. The regions interpreted were grouped into three for primary analysis: prostate/prostate bed; pelvic lymph nodes; and other (including extra-pelvic lymph nodes, bone, and soft tissue/parenchyma).

A total of 389 patients had an evaluable POSLUMA PET scan. The mean age was 68 years (range: 43 to 86 years); distribution by race was 75% White, 16% Black or African American, 4% other, and 5% unreported; and distribution by ethnicity 5% was Hispanic/Latino, 87% non-Hispanic/Latino, and 8% unreported. The median baseline serum PSA level was 1.1 ng/mL with 60% of patients having a baseline PSA <2.0 ng/mL. Prior treatment included radical prostatectomy in 79% of the patients.

POSLUMA-positive interpretations were compared to a reference standard of either histopathology or other imaging (CT, MRI, Technetium 99m bone scan, or fluciclovine F 18 PET) obtained within 90 days

of the POSLUMA scan using a lesion-to-lesion co-localization method and separate consensus panel. Reference standard information for negative interpretations was not collected.

At least one POSLUMA-positive lesion was detected by at least one reader in 366 patients (94%). Reference standard information consisted of imaging only (n=297) or histopathology (n=69). As a percentage of patients with an evaluable scan, 51% (95% CI: 46% to 56%) for reader 1, 48% (95% CI: 43% to 53%) for reader 2, and 49% (95% CI: 44% to 54%) for reader 3 had at least one matching positive region between the POSLUMA scan and the reference standard. Of all POSLUMA-positive regions, 46% (95% CI: 42% to 50%) for reader 1, 60% (95% CI: 55% to 66%) for reader 2, and 53% (95% CI: 48% to 58%) for reader 3 were categorized as positive by the reference standard.

Table 7 shows patient-level results from the majority read stratified by serum PSA level. Percent PET positivity was calculated as the percentage of patients with POSLUMA-positive lesions out of all patients with an evaluable PET scan. Percent PET positivity includes true and false positives and is not a measure of diagnostic performance.

Table 7: Patient-Level POSLUMA PET Results and Percent PET Positivity Stratified by Serum PSA Level in SPOTLIGHT by Majority Read (N=389)

PSA (ng/mL)	N	PET Positive Patients					PET Negative Patients	Percent PET Positivity [95% CI]
		Total	Histopathology		Imaging only[a]			
			PA	NPA	PA	NPA		
< 0.5	121	77	6	4	27	40	44	64% [54,72]
≥ 0.5 and < 1	67	51	7	3	24	17	16	76% [64,86]
≥ 1 and < 2	45	42	10	2	18	12	3	93% [82, 99]
≥ 2	156	152	33	3	84	32	4	97% [94, 99]
Total	389	322	56	12	153	101	67	83% [79, 86]

PSA = prostate-specific antigen, PA = positive agreement, NPA = no positive agreement, CI = confidence interval
[a]Imaging comprised of one or more of the following: CT, MRI, ^{99m}Tc Bone Scan, fluciclovine F 18 PET

Variable Interpretation in Patients with Suspected Prostate Cancer Recurrence

POSLUMA reader agreement was evaluated for the three central readers and 389 patients. Inter-reader Fleiss κ was 0.41 (95% CI: 0.39-0.43). The three readers agreed on the presence or absence of positive lesions across all five evaluated regions in 118 patients (30% unanimity) *[see Warning and Precautions (5.1)]*.

Given the level of inter-reader agreement observed overall, POSLUMA reader agreement was further evaluated by regional subgroup. The Fleiss κ for was 0.40 (95% CI: 0.33-0.46) in the prostate/prostate bed, 0.73 (95% CI: 0.67-0.78) in the pelvic lymph nodes, and 0.62 (95% CI: 0.58-0.65) across the other regions.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

POSLUMA injection is supplied as a clear, colorless solution in a multiple-dose glass vial (NDC 69932-002-50) 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.

Storage and Handling

Store POSLUMA at 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature]. Store POSLUMA in the original container in radiation shielding. The expiration date and time are provided on the container label. Use POSLUMA within 10 hours from end of synthesis.

Dispose of unused POSLUMA in compliance with applicable regulations.

This preparation is approved for use by persons under license by the Nuclear Regulatory Commission or the relevant regulatory authority of an Agreement State.

17 PATIENT COUNSELING INFORMATION

Adequate Hydration

Instruct patients to drink a sufficient amount of water to ensure adequate hydration before their PET study and urge them to drink and urinate as often as possible during the first hours following the administration of POSLUMA, in order to reduce radiation exposure *[see Dosage and Administration (2.3) and Warnings and Precautions (5.2)]*.

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