PLUVICTO®
lutetium Lu 177 vipivotide tetraxetan
INJECTION FOR INTRAVENOUS USE

MENU

NOW APPROVED FOR PATIENTS WITHOUT PRIOR CHEMOTHERAPY*

EFFICACY AND SAFETY MONITORING IN PLUVICTO CLINICAL TRIALS

PLUVICTO is FDA approved to treat patients with or without prior chemotherapy, based on results from the PSMAfore and VISION trials*

*The PSMAfore trial included chemotherapy-naive patients with PSMA+ mCRPC who were considered appropriate to delay taxane-based chemotherapy. The VISION trial included chemotherapy-experienced patients with PSMA+ mCRPC.[1]

Indication

PLUVICTO® (lutetium Lu 177 vipivotide tetraxetan) is indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibition (ARPI) therapy, and

- are considered appropriate to delay taxane-based chemotherapy, or
- have received prior taxane-based chemotherapy

IMPORTANT SAFETY INFORMATION

Risk From Radiation Exposure

PLUVICTO contributes to a patient's long-term cumulative radiation exposure, which is associated with an increased risk for cancer.

Minimize radiation exposure to patients, medical personnel, and others during and after treatment with PLUVICTO consistent with institutional practices, patient treatment procedures, Nuclear Regulatory Commission patient-release guidance, and instructions to the patient for follow-up radiation protection.

Please see additional Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

NEXT

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MENU

IT TAKES THE EXPERTISE OF MULTIPLE SPECIALISTS, LIKE YOU, TO MANAGE ADVANCED PROSTATE CANCER CARE BEFORE, DURING, AND AFTER TREATMENT[2]

Observed benefits of multidisciplinary care*:

↑ INCREASED

- Adherence to practice guidelines[3]
- Patient engagement[4]
- Shared decision-making[5,6]
- Patient satisfaction and retention[7,8]

↓ REDUCED

- Time to diagnosis and treatment initiation[6,9]
- Physician bias during care[5,6]
- Racial disparity during care[6,10]

*Information based on multiple studies in MDT care. For details on study authors and sources, please refer to the reference list on page 25.

PATIENTS WITH ADVANCED PROSTATE CANCER BENEFIT FROM MULTIDISCIPLINARY CARE

MDT care can directly benefit patients with advanced prostate cancer[3,7]

More than 90% of patients had a **positive experience** with MDT treatment, based on a 15-year MDT care retrospective review performed by the National Cancer Institute[7]

Nearly 50% of patients received a **comprehensive treatment plan with MDT care**[11,*]

*Data based on a prospective study that investigated the impact of MDT on prostate cancer clinical management.

PSMAfore: A study of PLUVICTO after only 1 ARPI

MONITORING FOR TUMOR RESPONSE

Radiologic assessment in PSMAfore

In the PSMAfore trial, tumor response was monitored at regular intervals via CT scan with contrast or MRI and bone scan.[1,13,14]

CT scan with contrast or MRI[13]

Tumor assessments included evaluations of the chest, abdomen, and pelvis

Bone scan with technetium-99m labeled diphosphonate[13,*]

Disease progression by bone scan was defined as:

- Two new bone lesions at the first posttreatment scan, with at least 2 additional lesions on the next scan **outside the 12-week flare window,** by BICR
- For scans after the 12-week flare window, first observation of at least 2 new lesions relative to the baseline scan must be confirmed on a subsequent scan at least 6 weeks later

Patients underwent imaging at the following intervals[13]:

- **Baseline**
- **Every 8 weeks** for the first 24 weeks of treatment
- **Every 12 weeks** thereafter until the end of treatment
- **Every 3 months** during follow-up

Trial design: PSMAfore was an open-label, multicenter, randomized phase 3 clinical trial evaluating PLUVICTO in 468 adult taxane-naive patients with PSMA+ mCRPC previously treated with 1 ARPI, who were considered appropriate to delay taxane-based chemotherapy. Participants were randomized in a 1:1 ratio to receive PLUVICTO (7.4 GBq every 6 weeks for 6 cycles) or a change in ARPI. The primary end point was rPFS.[1,13,14]

*If the second scan confirmed the metastasis, then the date of progression was the date of the scan when the first 2 new metastases were documented.[13]

IMPORTANT SAFETY INFORMATION (continued)

Risk From Radiation Exposure (continued)

Ensure patients increase oral fluid intake and advise them to void as often as possible to reduce bladder radiation.

Please see additional Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

PSMAfore: A study of PLUVICTO after only 1 ARPI

MONITORING FOR TUMOR RESPONSE (continued)

PSA assessment in PSMAfore

Please follow your own institution's protocols/clinical judgment when making monitoring decisions.

PSA levels were measured consistently in PSMAfore[15]

- **Baseline**
- **During Cycle 1:** Not measured
- **During Cycles 2-6:** Measured every 6 weeks

PSA progression was an exploratory end point

PSA progression was defined as the date of[13]:

- A ≥25% increase and ≥2 ng/mL above the nadir confirmed by a second value ≥3 weeks later if there is PSA decline from baseline

OR

- A ≥25% increase and ≥2 ng/mL increase from baseline beyond 12 weeks if there is no PSA decline from baseline

63% of patients in the PSMAfore trial received 6 cycles of PLUVICTO[15]

IMPORTANT SAFETY INFORMATION (continued)

Risk From Radiation Exposure (continued)

To minimize radiation exposure to others, advise patients to limit close contact (less than 3 feet) with household contacts for 2 days or with children and pregnant women for 7 days, to refrain from sexual activity for 7 days, and to sleep in a separate bedroom from household contacts for 3 days, from children for 7 days, or from pregnant women for 15 days.

Please see additional Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

PSMAfore: A study of PLUVICTO after only 1 ARPI

MONITORING FOR SAFETY

Safety was assessed in the PSMAfore trial at consistent intervals[13]

The intervals below were used to assess safety in the PSMAfore trial. Please follow your own institution's protocols/clinical judgment when making decisions on assessment intervals.

Each cycle of PLUVICTO is 6 weeks.[1]

FIRST CYCLE OF PLUVICTO: SCHEDULE OF ASSESSMENTS[13]

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Hematology[a]	✓	✓	✓	✓	✓	✓
Chemistry[a]	✓	✓	✓	✓	✓	✓
Coagulation panel	✓	✓	✓	✓	✓	✓

CYCLES 2-6 OF PLUVICTO: SCHEDULE OF ASSESSMENTS[13]

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	After Cycle 6
Hematology[a]	✓		✓		✓		Monitor every 12 weeks (± 28 days)
Chemistry[a]	✓		✓		✓		
Coagulation panel	✓		✓		✓		

- **For Cycles 2-6** of PLUVICTO, assessments for hematology and chemistry were performed within 3 days prior to Days 1, 15, and 29[15]

Long-term safety follow-up was conducted every 3 months (± 1 month) and assessed for[13]:

- AEs
- Hematology
- Chemistry
- Coagulation panel

[a] Central labs for hematology, chemistry and coagulation results must all be assessed prior to dosing. If central lab results are not available in time to review prior to dosing, local labs may be additionally sent to expedite clearing the patient for treatment.

IMPORTANT SAFETY INFORMATION (continued)

Myelosuppression

PLUVICTO can cause severe and life-threatening myelosuppression. In the PSMAfore study, grade 3 or 4 decreased hemoglobin (7%), decreased leukocytes (4.4%), decreased neutrophils (3.5%), and decreased platelets (2.7%) occurred in patients treated with PLUVICTO.

Please see additional Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

LABORATORY TESTS

Patients were monitored in the PSMAfore trial for safety through laboratory tests

LABORATORY TESTS ACROSS CATEGORIES[13]

Hematology	Hematocrit	Platelets	
	Hemoglobin	White blood cells	
	Red blood cells	Differential (basophils, eosinophils, lymphocytes, monocytes, neutrophils, bands)	
Chemistry	Bicarbonate	Albumin	Amylase
	Calcium	ALP	Lipase
	Chloride	ALT	Magnesium
	Creatinine	AST	Phosphate
	Creatinine kinase	Bilirubin (direct)	Uric acid
	Glucose	Bilirubin (total)	Urea nitrogen
	Potassium	GGT	eGFR
	Sodium	LDH	
Urinalysis	Macroscopic panel (Dipstick) (color, bilirubin, blood, glucose, ketones, leukocytes esterase, nitrite, pH, protein, specific gravity, urobilinogen)		
	Differential as needed (red blood cells, white blood cells, casts, crystals, bacteria, epithelial cells)		
Coagulation	International normalized ratio		
	Activated partial thromboplastin time		

IMPORTANT SAFETY INFORMATION (continued)

Myelosuppression (continued)

One death occurred due to bone marrow failure during long-term follow-up in a patient who received PLUVICTO. In the VISION study, 4 myelosuppression-related deaths occurred.

Perform complete blood counts before and during treatment with PLUVICTO. Withhold, reduce dose, or permanently discontinue PLUVICTO based on severity of myelosuppression.

Please see additional Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

PSMAfore: A study of PLUVICTO after only 1 ARPI

PLUVICTO HAS A FAVORABLE SAFETY PROFILE[1,14]

Grade ≥3 AE rates were lower in the PLUVICTO group with a longer median duration of exposure[14]

- Incidence of grade ≥3 TEAEs: 36% with PLUVICTO (n=81) vs 48% with a change in ARPI (n=112)
- Median duration of exposure: 8.4 months with PLUVICTO vs 6.5 months with a change in ARPI

PSMAfore: ADVERSE REACTIONS OCCURRING AT ≥10% INCIDENCE IN PATIENTS WHO RECEIVED PLUVICTO[1,a]

	PLUVICTO (n=227)		Change in ARPI (n=232)	
Adverse reactions	**All grades (%)**	**Grades 3 or 4 (%)**	**All grades (%)**	**Grades 3 or 4 (%)**
Gastrointestinal disorders				
Dry mouth[b]	61	0.9	2.6	0
Nausea	32	0	12	0.4
Constipation	22	0.4	14	0
Diarrhea	17	0	9	0.4
Vomiting	11	0	4.7	0
Chemistry				
Fatigue[b]	53	1.3	53	5
Metabolism and nutrition disorders				
Decreased appetite	22	0	19	0.4
Musculoskeletal and connective tissue disorders				
Arthralgia	20	0	23	0.4
Back pain	14	1.3	20	1.6

[a] National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0.[13]
[b] Includes multiple similar terms.[1]

- Clinically relevant ARs in <10% of patients who received PLUVICTO included dysgeusia, abdominal pain, peripheral edema, headache, acute kidney injury, weight decreased, urinary tract infection, dry eye, dizziness, dry skin, oral fungal infection, gastroesophageal reflux disease, pyrexia, vertigo, stomatitis, dysphagia, esophagitis, pancytopenia, and bone marrow failure[1]

Please see Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

PSMAfore: A study of PLUVICTO after only 1 ARPI

LABORATORY ABNORMALITIES

SELECT LABORATORY ABNORMALITIES (≥10%) THAT WORSENED FROM BASELINE IN PATIENTS WHO RECEIVED PLUVICTO (BETWEEN-ARM DIFFERENCE OF ≥5% ALL GRADES) IN PSMAfore[1]

	PLUVICTO[a]		Change in ARPI[b]	
Laboratory abnormalities	All grades (%)	Grades 3 or 4 (%)	All grades (%)	Grades 3 or 4 (%)
Hematology				
Decreased lymphocytes	78	27	57	12
Decreased hemoglobin	67	7[c]	50	7[c]
Decreased neutrophils	38	3.5	18	1.3
Decreased platelets	30	2.7	11	1.7
Chemistry				
Increased alkaline phosphatase	31	8	50	10[c]
Decreased estimated glomerular filtration rate (eGFR)	23	0.9[c]	22	3.5
Increased magnesium	19	0.9[c]	28	0[c]
Decreased calcium	18	0.9	11	0.9
Decreased sodium	11	0[c]	18	0[c]
Decreased potassium	6	0.9[c]	18	2.6

[a] The denominator used to calculate the rate for each laboratory parameter was based on 226 patients with a baseline value and at least one posttreatment value.

[b] The denominator used to calculate the rate for each laboratory parameter varied from 231 to 232 based on the number of patients with a baseline value and at least one posttreatment value.

[c] No grade 4 laboratory abnormalities worsening from baseline were reported.

- To enroll in the PSMAfore trial, patients were required to have adequate bone marrow reserve[13]
  - ANC ≥1.5 x 10^9/L
  - Platelets ≥100 x 10^9/L
  - Hemoglobin ≥9 g/dL
- In the PSMAfore clinical trial, bone marrow failure was considered a clinically relevant adverse reaction (<10%) with PLUVICTO[1]
- In the PSMAfore study, the following grade 3 or 4 adverse reactions occurred in patients treated with PLUVICTO: decreased hemoglobin (7%), decreased leukocytes (4.4%), decreased neutrophils (3.5%), and decreased platelets (2.7%)[1]

No unexpected laboratory abnormalities were reported in the PSMAfore trial.[1]

Please see Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

PSMAfore: A study of PLUVICTO after only 1 ARPI

PLUVICTO HAS A FAVORABLE SAFETY PROFILE AND PROVEN TOLERABILITY[1,14]

Median duration of exposure to PLUVICTO was 8.4 months[14]

TEAEs led to discontinuation in 6% (n=13) of patients treated with PLUVICTO vs 5% with a change in ARPI (n=12)[1,14]

- Dose modification due to an AE: 4% with PLUVICTO (n=8) vs 16% with change in ARPI (n=36)[14]
- Dose interruption due to an AE: 12% with PLUVICTO (n=28) vs 19% with change in ARPI (n=45)[14]

47% of patients treated with PLUVICTO received subsequent chemotherapy[14]

- Additional subsequent treatments included radiotherapy (19%), hormonal therapy (13%), and other anticancer therapies (<5%)

IMPORTANT SAFETY INFORMATION (continued)

Renal Toxicity

PLUVICTO can cause severe renal toxicity. In the PSMAfore study, grade 3 or 4 acute kidney injury (1.3%) occurred in patients treated with PLUVICTO.

Please see additional Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

VISION: A study of PLUVICTO after ARPI and chemo

MONITORING FOR TUMOR RESPONSE

Radiologic assessment in VISION

In the VISION trial, tumor response was monitored at regular intervals via CT scan with contrast or MRI and bone scan.[16]

CT scan with contrast or MRI[16]

Tumor assessments included evaluations of the chest, abdomen, and pelvis

Bone scan with technetium-99m labeled diphosphonate[16]

Disease progression by bone scan was defined as at least 2 new bone lesions at the first posttreatment scan, with at least 2 additional lesions on the next scan*

The VISION trial was first initiated in 2018. In 2018, a CT scan with contrast/MRI and bone scans were considered standard-of-care imaging practices. Please follow your own institution's protocols/clinical judgment when making monitoring decisions.

Trial design: VISION was an international, prospective, open-label, multicenter, randomized phase 3 clinical trial evaluating PLUVICTO in 831 adult patients with PSMA+ mCRPC previously treated with at least 1 ARPI and 1 or 2 taxane regimens. Participants were randomized in a 2:1 ratio to receive PLUVICTO (7.4 GBq every 6 weeks for up to 6 cycles) + protocol-permitted BSOC or BSOC alone. Alternate primary end points included OS and rPFS.[1,17]

*For scans after the first posttreatment scan, at least 2 new lesions relative to the first posttreatment scan confirmed on a subsequent scan. If the second scan confirmed the metastasis, then the date of progression was the date of the scan when the first 2 new metastases were documented.[16]

IMPORTANT SAFETY INFORMATION (continued)

Renal Toxicity (continued)

Advise patients to remain well hydrated and to urinate frequently before and after administration of PLUVICTO. Perform kidney function laboratory tests, including serum creatinine and calculated creatinine clearance (CrCl), before and during treatment. Withhold, reduce dose, or permanently discontinue PLUVICTO based on severity of renal toxicity.

Please see additional Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

VISION: A study of PLUVICTO after ARPI and chemo

MONITORING FOR TUMOR RESPONSE (continued)

Radiographic imaging interval schedule in VISION

Patients underwent imaging at the following intervals[16]:

- **Baseline**
- **Every 8 weeks** for the first 24 weeks of treatment
- **Every 12 weeks** thereafter until the end of treatment
- **Every 3 months** during follow-up

After 4 cycles, investigators determined if patients responding to treatment could receive additional doses based on[16]:

- **Evidence of response** based on radiological, PSA, and clinical benefit markers
- **Signs of residual disease** on CT with contrast/MRI or bone scan
- **Tolerated** treatment with PLUVICTO

Patients who met the above criteria were administered 2 further cycles, for a total of 6 doses of PLUVICTO.[16]

Patients in the VISION trial received a median of 5 cycles of PLUVICTO[17]

IMPORTANT SAFETY INFORMATION (continued)

Embryo-Fetal Toxicity

The safety and efficacy of PLUVICTO have not been established in females. Based on its mechanism of action, PLUVICTO can cause fetal harm. No animal studies using lutetium Lu 177 vipivotide tetraxetan have been conducted to evaluate its effect on female reproduction and embryo-fetal development; however, radioactive emissions, including those from PLUVICTO, can cause fetal harm. Advise males with female partners of reproductive potential to use effective contraception during treatment with PLUVICTO and for 14 weeks after the last dose.

Please see additional Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

VISION: A study of PLUVICTO after ARPI and chemo

MONITORING FOR PSA RESPONSE

PSA levels were monitored every 6 weeks in VISION[16]

PSA progression was a secondary end point

- PSA progression was defined as the date that a ≥25% increase in PSA and an absolute increase of 2 ng/mL or more from the nadir is documented and confirmed by a second consecutive value obtained 3 or more weeks later

In the VISION trial, treatment response of PLUVICTO was measured through radiologic assessment and PSA responses.

Rises in PSA within the first 12 weeks of treatment with PLUVICTO were dismissed in the absence of other evidence of disease progression

IMPORTANT SAFETY INFORMATION (continued)

Infertility

The recommended cumulative dose of 44.4 GBq of PLUVICTO results in a radiation-absorbed dose to the testes within the range where PLUVICTO may cause temporary or permanent infertility.

Please see additional Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

VISION: A study of PLUVICTO after ARPI and chemo

MONITORING FOR SAFETY

Safety was assessed in the VISION trial at consistent intervals[16]

The below intervals were used to assess safety in the VISION trial. Please follow your own institution's protocols/clinical judgment when making decisions on assessment intervals.

Each cycle of PLUVICTO is 6 weeks. For all cycles, assessment for serum testosterone was performed within 3 days prior to Day 1.

FIRST CYCLE OF PLUVICTO: SCHEDULE OF ASSESSMENTS

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Hematology	✓	✓	✓	✓	✓	✓
Chemistry	✓	✓	✓	✓	✓	✓
Serum testosterone[a]	✓					

- **For Cycle 1** of PLUVICTO, assessments for hematology and chemistry were performed within 3 days prior to Days 1, 8, 15, 22, 29, and 36

CYCLES 2-6 OF PLUVICTO: SCHEDULE OF ASSESSMENTS

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	After Cycle 6
Hematology[b]	✓		✓		✓		Monitor every 8 weeks (± 1 week)
Chemistry[b]	✓		✓		✓		
Serum testosterone[a]	✓						

[a] Serum testosterone was evaluated to assess the adequacy of ADT treatment in patients.
[b] Within 3 days prior to Days 1, 15, and 28.

Please see Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

VISION: A study of PLUVICTO after ARPI and chemo

MONITORING FOR SAFETY (continued)

Safety was assessed in the VISION trial at consistent intervals[16] (continued)

- **For Cycles 2-6** of PLUVICTO, assessments for hematology and chemistry were performed within 3 days prior to Days 1, 15, and 28
- **During Cycles 2-6,** patients with certain lab results were monitored more frequently
  - For patients with WBC count <3.0 x 10^9/L, ANC <1.5 x 10^9/L, platelet count <100 x 10^9/L, or hemoglobin level <9 g/dL at any time, hematologic parameters (ie, CBC with differential analysis) were done no less frequently than once each week until resolution to grade 1 or baseline
  - For patients with a grade ≥2 related chemistry lab result, chemistry was done no less frequently than once each week until resolution to grade 1 or baseline

Patients with abnormal hematologic and/or chemistry labs had their doses modified according to the chart on pages 21-22.

Long-term safety follow-up was conducted every 3 months (± 1 month) and assessed for:

- AEs
- Hematology
- Chemistry

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions and Laboratory Abnormalities

In the pooled safety population for the PSMAfore and VISION studies (N=756), the most common (≥20%) adverse reactions, including laboratory abnormalities, were decreased lymphocytes (83%), decreased hemoglobin (65%), fatigue (49%), dry mouth (46%), decreased platelets (40%), decreased estimated glomerular filtration rate (37%), nausea (35%), decreased neutrophils (31%), decreased calcium (29%), decreased sodium (27%), increased aspartate aminotransferase (26%), increased alkaline phosphatase (24%), arthralgia (22%), decreased appetite (21%), increased potassium (21%), constipation (21%), and back pain (21%).

Please see additional Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

VISION: A study of PLUVICTO after ARPI and chemo

LABORATORY TESTS

Patients were monitored in the VISION trial for safety through laboratory tests[16]

LABORATORY TESTS ACROSS CATEGORIES

Hematology	Complete blood count (white blood cell count and differential)	Hematocrit	
	Red blood cell count	Platelet count	
	Hemoglobin		
Chemistry	Bicarbonate	Albumin	Blood urea nitrogen
	Calcium	ALP	Phosphorus
	Creatinine	ALT	Total protein
	Glucose	Bilirubin (direct)	Phosphate
	Potassium	Bilirubin (total)	Urate
	Sodium	LDH	
Urinalysis	Appearance & color	Specific gravity	
	Urine pH	Ketones	
	Protein content	Glucose	

IMPORTANT SAFETY INFORMATION

Risk From Radiation Exposure

PLUVICTO contributes to a patient's long-term cumulative radiation exposure, which is associated with an increased risk for cancer.

Minimize radiation exposure to patients, medical personnel, and others during and after treatment with PLUVICTO consistent with institutional practices, patient treatment procedures, Nuclear Regulatory Commission patient-release guidance, and instructions to the patient for follow-up radiation protection.

Please see additional Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

VISION: A study of PLUVICTO after ARPI and chemo

PLUVICTO HAS AN ESTABLISHED SAFETY PROFILE

ADVERSE REACTIONS OCCURRING AT ≥10% INCIDENCE IN PATIENTS WHO RECEIVED PLUVICTO + BSOC IN VISION[1,a]

	PLUVICTO + BSOC (n=529)		BSOC (n=205)	
Adverse reactions	**All grades (%)**	**Grades 3 or 4 (%)**	**All grades (%)**	**Grades 3 or 4 (%)**
General disorders				
Fatigue[b]	48	7	29	2.4
Decreased appetite	21	1.9	15	0.5
Weight decreased	11	0.4	10	0.5
Peripheral edema[b]	10	0.4	7	1
Gastrointestinal disorders				
Dry mouth[b]	39	0	1	0
Nausea	36	1.3	17	0.5
Constipation	20	1.1	11	0.5
Vomiting[b]	19	0.9	6	0.5
Diarrhea	19	0.8	2.9	0.5
Abdominal pain[b]	12	1.3	6	0.5
Musculoskeletal and connective tissue disorders				
Back pain	14	1.3	20	2.6
Arthralgia	20	0	23	0.4
Bone pain[b]	11	2.5	8	2.4
Renal and urinary disorders				
Urinary tract infection[b]	12	3.8	1	0.5

[a] National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0.
[b] Includes multiple similar terms.

- 12% of patients discontinued PLUVICTO + BSOC due to any treatment-related adverse events[18]
- Clinically relevant ARs in <10% of patients who received PLUVICTO + BSOC included acute kidney injury, dizziness, dysgeusia, headache, pyrexia, dry eye, oral fungal infection, vertigo, gastroesophageal reflux disease, stomatitis, pancytopenia, dry skin, dysphagia, esophagitis, and bone marrow failure[1]

Please see Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

VISION: A study of PLUVICTO after ARPI and chemo

LABORATORY ABNORMALITIES

SELECT LABORATORY ABNORMALITIES (≥10%) THAT WORSENED FROM BASELINE IN PATIENTS WHO RECEIVED PLUVICTO + BSOC (BETWEEN-ARM DIFFERENCE OF ≥5% ALL GRADES) IN VISION[1]

	PLUVICTO + BSOC[a]		BSOC[b]	
Laboratory abnormalities	All grades (%)	Grades 3 or 4 (%)	All grades (%)	Grades 3 or 4 (%)
Hematology				
Decreased lymphocytes	85	47	51	18
Decreased hemoglobin	64	15[c]	34	7[c]
Decreased platelets	45	9	20	2.5
Decreased neutrophils	28	4.7	9	0.5
Chemistry				
Decreased eGFR	43	3.6	28	2.5
Decreased sodium	34	0.6[c]	23	1
Decreased calcium	34	1.9	18	1.5
Increased AST	29	1.1	18	1[c]
Increased potassium	24	0.6	18	0.5[c]
Increased sodium	11	0[c]	5	0[c]

[a] The denominator used to calculate the rate for each laboratory parameter varied from 506 to 529 based on the number of patients with a baseline value and at least 1 posttreatment value.

[b] The denominator used to calculate the rate for each laboratory parameter varied from 194 to 198 based on the number of patients with a baseline value and at least one posttreatment value.

[c] No grade 4 laboratory abnormalities worsening from baseline were reported.

No unexpected laboratory abnormalities were reported in the VISION trial.

Please see Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

VISION: A study of PLUVICTO after ARPI and chemo

PLUVICTO HAS PROVEN TOLERABILITY

Median duration of exposure to PLUVICTO was 7.8 months[1]

TEAEs led to PLUVICTO discontinuation in 12% of patients[18]

- 6% had a dose modification due to an AE; 16% had a dose interruption due to an AE

After treatment discontinuation, use of taxane-based chemotherapy was balanced between groups: 17% in patients treated with PLUVICTO + BSOC vs 22% with BSOC alone[18]

Please see Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

RECOMMENDED DOSE MODIFICATIONS OF PLUVICTO FOR ADVERSE REACTIONS

Management of adverse reactions may require temporary dose interruption, dose reduction, or permanent discontinuation of treatment with PLUVICTO[1]

Adverse reaction	Severity	Dosage modification
Myelosuppression (anemia, thrombocytopenia, leukopenia, or neutropenia)	Grade 2	Withhold PLUVICTO until improvement to grade 1 or baseline.
	Grade ≥3	Withhold PLUVICTO until improvement to grade 1 or baseline. Reduce PLUVICTO dose by 20% to 5.9 GBq (160 mCi).
	Recurrent grade ≥3 myelosuppression after 1 dose reduction	Permanently discontinue PLUVICTO.
Renal toxicity	Defined as: • Confirmed serum creatinine increase grade ≥2 • Confirmed CrCl <30 mL/min; calculate using Cockcroft-Gault with actual body weight	Withhold PLUVICTO until improvement.
	Defined as: • Confirmed ≥40% increase from baseline serum creatinine, and • Confirmed >40% decrease from baseline CrCl; calculate using Cockcroft-Gault with actual body weight	Withhold PLUVICTO until improvement or return to baseline. Reduce PLUVICTO dose by 20% to 5.9 GBq (160 mCi).
	Grade ≥3 renal toxicity	Permanently discontinue PLUVICTO.
	Recurrent renal toxicity after 1 dose reduction	Permanently discontinue PLUVICTO.
Dry mouth	Grade 2	Withhold PLUVICTO until improvement or return to baseline. Consider reducing PLUVICTO dose by 20% to 5.9 GBq (160 mCi).
	Grade 3	Withhold PLUVICTO until improvement or return to baseline. Reduce PLUVICTO dose by 20% to 5.9 GBq (160 mCi).
	Recurrent grade 3 dry mouth after 1 dose reduction	Permanently discontinue PLUVICTO.

Transfusion recommendations from the VISION trial

- Transfusions may have been given as clinically indicated for anemia or thrombocytopenia[16]

Please see Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

RECOMMENDED DOSE MODIFICATIONS OF PLUVICTO FOR ADVERSE REACTIONS (continued)

Management of adverse reactions may require temporary dose interruption, dose reduction, or permanent discontinuation of treatment with PLUVICTO[1]

Adverse reaction	Severity	Dosage modification
Gastrointestinal toxicity	Grade ≥3 (not amenable to medical intervention)	Withhold PLUVICTO until improvement to grade 2 or baseline. Reduce PLUVICTO dose by 20% to 5.9 GBq (160 mCi).
	Recurrent grade ≥3 gastrointestinal toxicity after 1 dose reduction	Permanently discontinue PLUVICTO.
Fatigue	Grade ≥3	Withhold PLUVICTO until improvement to grade 2 or baseline.
Electrolyte or metabolic abnormalities	Grade ≥2	Withhold PLUVICTO until improvement to grade 1 or baseline.
AST or ALT elevation	AST or ALT >5 times ULN in the absence of liver metastases	Permanently discontinue PLUVICTO.
Other nonhematologic toxicity	Any unacceptable toxicity	Permanently discontinue PLUVICTO.
	Any adverse reaction that requires treatment delay of >4 weeks	Permanently discontinue PLUVICTO.
	Any recurrent grade 3 or 4 or persistent and intolerable grade 2 adverse reaction after 1 dose reduction	Permanently discontinue PLUVICTO.

Grading according to most current CTCAE.

GET IN TOUCH WITH YOUR NOVARTIS ONCOLOGY SPECIALIST TO LEARN MORE

Please see Important Safety Information throughout and on pages 23-24 and full Prescribing Information.

INDICATION AND IMPORTANT SAFETY INFORMATION

Indication

PLUVICTO® (lutetium Lu 177 vipivotide tetraxetan) is indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibition (ARPI) therapy, and

- are considered appropriate to delay taxane-based chemotherapy, or
- have received prior taxane-based chemotherapy

IMPORTANT SAFETY INFORMATION

Risk From Radiation Exposure

PLUVICTO contributes to a patient's long-term cumulative radiation exposure, which is associated with an increased risk for cancer.

Minimize radiation exposure to patients, medical personnel, and others during and after treatment with PLUVICTO consistent with institutional practices, patient treatment procedures, Nuclear Regulatory Commission patient-release guidance, and instructions to the patient for follow-up radiation protection.

Ensure patients increase oral fluid intake and advise them to void as often as possible to reduce bladder radiation.

To minimize radiation exposure to others, advise patients to limit close contact (less than 3 feet) with household contacts for 2 days or with children and pregnant women for 7 days, to refrain from sexual activity for 7 days, and to sleep in a separate bedroom from household contacts for 3 days, from children for 7 days, or from pregnant women for 15 days.

Myelosuppression

PLUVICTO can cause severe and life-threatening myelosuppression. In the PSMAfore study, grade 3 or 4 decreased hemoglobin (7%), decreased leukocytes (4.4%), decreased neutrophils (3.5%), and decreased platelets (2.7%) occurred in patients treated with PLUVICTO. One death occurred due to bone marrow failure during long-term follow-up in a patient who received PLUVICTO. In the VISION study, 4 myelosuppression-related deaths occurred.

Perform complete blood counts before and during treatment with PLUVICTO. Withhold, reduce dose, or permanently discontinue PLUVICTO based on severity of myelosuppression.

Please see full Prescribing Information.

IMPORTANT SAFETY INFORMATION (continued)

Renal Toxicity

PLUVICTO can cause severe renal toxicity. In the PSMAfore study, grade 3 or 4 acute kidney injury (1.3%) occurred in patients treated with PLUVICTO.

Advise patients to remain well hydrated and to urinate frequently before and after administration of PLUVICTO. Perform kidney function laboratory tests, including serum creatinine and calculated creatinine clearance (CrCl), before and during treatment. Withhold, reduce dose, or permanently discontinue PLUVICTO based on severity of renal toxicity.

Embryo-Fetal Toxicity

The safety and efficacy of PLUVICTO have not been established in females. Based on its mechanism of action, PLUVICTO can cause fetal harm. No animal studies using lutetium Lu 177 vipivotide tetraxetan have been conducted to evaluate its effect on female reproduction and embryo-fetal development; however, radioactive emissions, including those from PLUVICTO, can cause fetal harm. Advise males with female partners of reproductive potential to use effective contraception during treatment with PLUVICTO and for 14 weeks after the last dose.

Infertility

The recommended cumulative dose of 44.4 GBq of PLUVICTO results in a radiation-absorbed dose to the testes within the range where PLUVICTO may cause temporary or permanent infertility.

Adverse Reactions and Laboratory Abnormalities

In the pooled safety population for the PSMAfore and VISION studies (N=756), the most common (≥20%) adverse reactions, including laboratory abnormalities, were decreased lymphocytes (83%), decreased hemoglobin (65%), fatigue (49%), dry mouth (46%), decreased platelets (40%), decreased estimated glomerular filtration rate (37%), nausea (35%), decreased neutrophils (31%), decreased calcium (29%), decreased sodium (27%), increased aspartate aminotransferase (26%), increased alkaline phosphatase (24%), arthralgia (22%), decreased appetite (21%), increased potassium (21%), constipation (21%), and back pain (21%).

Please see full Prescribing Information.

REFERENCES AND DEFINITIONS

Definitions: ADT, androgen deprivation therapy; AEs, adverse events; ALP, alkaline phosphatase; ALT, alanine aminotransferase; ANC, absolute neutrophil count; ARPI, androgen receptor pathway inhibitor; ARs, adverse reactions; AST, aspartate aminotransferase; BICR, Blinded Independent Central Review; BSOC, best standard of care; CBC, complete blood count; CrCl, creatinine clearance; CT, computed tomography; CTCAE, common terminology criteria for adverse events; eGFR, estimated glomerular filtration rate; FDA, US Food and Drug Administration; GBq, gigabecquerel; GGT, gamma-glutamyl transferase; LDH, lactate dehydrogenase; mCi, millicurie; mCRPC, metastatic castration-resistant prostate cancer; MDT, multidisciplinary team; MRI, magnetic resonance imaging; OS, overall survival; PSA, prostate-specific antigen; PSMA+, prostate-specific membrane antigen positive; rPFS, radiographic progression-free survival; TEAEs, treatment-emergent adverse events; ULN, upper limit of normal; WBC, white blood cell.

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PLUVICTO®
lutetium Lu 177 vipivotide tetraxetan
INJECTION FOR INTRAVENOUS USE

MENU

EFFICACY WAS ASSESSED THROUGH COMPREHENSIVE MONITORING IN PSMAfore AND VISION[13,15,16]

- **Patients in PSMAfore received a median of 6 cycles of PLUVICTO[1]**
- **Patients in VISION received a median of 5 cycles of PLUVICTO[17]**
- **Response to PLUVICTO treatment was evaluated using both radiologic assessment and PSA monitoring[13,15,16]**
- **Dose modifications based on AEs, such as temporary dose interruptions, were performed in the PSMAfore and VISION trials so appropriate patients could continue PLUVICTO treatment as long as possible[1]**

STAY CONNECTED WITH YOUR PATIENTS BEFORE, DURING, AND AFTER TREATMENT THROUGH EFFICACY AND SAFETY MONITORING

IMPORTANT SAFETY INFORMATION

Risk From Radiation Exposure

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PREVIOUS