

**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-naïve patients with PSMA+ mCRPC who were considered appropriate to delay taxane-based chemotherapy. The VISION trial included chemotherapy-experienced patients with PSMA+ mCRPC.<sup>1</sup>

### **Indication**

PLUVICTO<sup>®</sup> (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](#).

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# IT TAKES THE EXPERTISE OF MULTIPLE SPECIALISTS, LIKE YOU, TO MANAGE ADVANCED PROSTATE CANCER CARE BEFORE, DURING, AND AFTER TREATMENT<sup>2</sup>

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## Observed benefits of multidisciplinary care\*:

-  **INCREASED**
- Adherence to practice guidelines<sup>3</sup>
  - Patient engagement<sup>4</sup>
  - Shared decision-making<sup>5,6</sup>
  - Patient satisfaction and retention<sup>7,8</sup>
- 

-  **REDUCED**
- Time to diagnosis and treatment initiation<sup>6,9</sup>
  - Physician bias during care<sup>5,6</sup>
  - Racial disparity during care<sup>6,10</sup>

\*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

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MDT care can directly benefit patients with  
advanced prostate cancer<sup>3,7</sup>

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<sup>7</sup>

Nearly  
**50%**  
of patients

received a comprehensive  
treatment plan with MDT care<sup>11,\*</sup>

\*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.<sup>1,13,14</sup>



#### CT scan with contrast or MRI<sup>13</sup>

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



#### Bone scan with technetium-99m labeled diphosphonate<sup>13,\*</sup>

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<sup>13</sup>:

- **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.<sup>1,13,14</sup>

\*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.<sup>13</sup>

## 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<sup>15</sup>

- **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<sup>13</sup>:

- A  $\geq 25\%$  increase and  $\geq 2$  ng/mL above the nadir confirmed by a second value  $\geq 3$  weeks later if there is PSA decline from baseline
- OR
- A  $\geq 25\%$  increase and  $\geq 2$  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<sup>15</sup>**

### 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<sup>13</sup>**

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.<sup>1</sup>

**FIRST CYCLE OF PLUVICTO: SCHEDULE OF ASSESSMENTS<sup>13</sup>**

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Hematology <sup>a</sup>	✓	✓	✓	✓	✓	✓
Chemistry <sup>a</sup>	✓	✓	✓	✓	✓	✓
Coagulation panel	✓	✓	✓	✓	✓	✓

**CYCLES 2-6 OF PLUVICTO: SCHEDULE OF ASSESSMENTS<sup>13</sup>**

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	After Cycle 6
Hematology <sup>a</sup>	✓		✓		✓		Monitor every 12 weeks (± 28 days)
Chemistry <sup>a</sup>	✓		✓		✓		
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<sup>15</sup>

**Long-term safety follow-up was conducted every 3 months (± 1 month) and assessed for<sup>13</sup>:**

- AEs
- Hematology
- Chemistry
- Coagulation panel

<sup>a</sup>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](#).

PSMAfore: A study of PLUVICTO after only 1 ARPI

## LABORATORY TESTS

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

### LABORATORY TESTS ACROSS CATEGORIES<sup>13</sup>

<b>Hematology</b>	Hematocrit	Platelets	
	Hemoglobin	White blood cells	
	Red blood cells	Differential (basophils, eosinophils, lymphocytes, monocytes, neutrophils, bands)	
<b>Chemistry</b>	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	
<b>Urinalysis</b>	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)		
<b>Coagulation</b>	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<sup>1,14</sup>

### Grade $\geq 3$ AE rates were lower in the PLUVICTO group with a longer median duration of exposure<sup>14</sup>

- Incidence of grade  $\geq 3$  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 $\geq 10\%$ INCIDENCE IN PATIENTS WHO RECEIVED PLUVICTO<sup>1,a</sup>

Adverse reactions	PLUVICTO (n=227)		Change in ARPI (n=232)	
	All grades (%)	Grades 3 or 4 (%)	All grades (%)	Grades 3 or 4 (%)
<b>Gastrointestinal disorders</b>				
Dry mouth <sup>b</sup>	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
<b>Chemistry</b>				
Fatigue <sup>b</sup>	53	1.3	53	5
<b>Metabolism and nutrition disorders</b>				
Decreased appetite	22	0	19	0.4
<b>Musculoskeletal and connective tissue disorders</b>				
Arthralgia	20	0	23	0.4
Back pain	14	1.3	20	1.6

<sup>a</sup>National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0.<sup>13</sup>

<sup>b</sup>Includes multiple similar terms.<sup>1</sup>

- 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<sup>1</sup>

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 ( $\geq 10\%$ ) THAT WORSENEDED FROM BASELINE IN PATIENTS WHO RECEIVED PLUVICTO (BETWEEN-ARM DIFFERENCE OF $\geq 5\%$ ALL GRADES) IN PSMAfore<sup>1</sup>

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

<sup>a</sup> 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.

<sup>b</sup> 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.

<sup>c</sup> 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<sup>13</sup>
  - ANC  $\geq 1.5 \times 10^9/L$
  - Platelets  $\geq 100 \times 10^9/L$
  - Hemoglobin  $\geq 9$  g/dL
- In the PSMAfore clinical trial, bone marrow failure was considered a clinically relevant adverse reaction ( $< 10\%$ ) with PLUVICTO<sup>1</sup>
- 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%)<sup>1</sup>

**No unexpected laboratory abnormalities were reported in the PSMAfore trial.<sup>1</sup>**

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<sup>1,14</sup>



**Median duration of exposure to PLUVICTO was 8.4 months<sup>14</sup>**



**TEAEs led to discontinuation in 6% (n=13) of patients treated with PLUVICTO vs 5% with a change in ARPI (n=12)<sup>1,14</sup>**

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



**47% of patients treated with PLUVICTO received subsequent chemotherapy<sup>14</sup>**

- 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.<sup>16</sup>



#### CT scan with contrast or MRI<sup>16</sup>

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



#### Bone scan with technetium-99m labeled diphosphonate<sup>16</sup>

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.<sup>1,17</sup>

\*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.<sup>16</sup>

## 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<sup>16</sup>:**

- **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<sup>16</sup>:**

- **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.<sup>16</sup>



**Patients in the VISION trial received a median of 5 cycles of PLUVICTO<sup>17</sup>**

### 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<sup>16</sup>**

### **PSA progression was a secondary end point**

- PSA progression was defined as the date that a  $\geq 25\%$  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<sup>16</sup>

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 <sup>a</sup>	✓					

- **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 <sup>b</sup>	✓		✓		✓		Monitor every 8 weeks (± 1 week)
Chemistry <sup>b</sup>	✓		✓		✓		
Serum testosterone <sup>a</sup>	✓						

<sup>a</sup>Serum testosterone was evaluated to assess the adequacy of ADT treatment in patients.

<sup>b</sup>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<sup>16</sup> (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  $<3.0 \times 10^9/L$ , ANC  $<1.5 \times 10^9/L$ , platelet count  $<100 \times 10^9/L$ , or hemoglobin level  $<9 \text{ g/dL}$  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  $\geq 2$  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 ( $\pm 1$  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 ( $\geq 20\%$ ) 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<sup>16</sup>

### LABORATORY TESTS ACROSS CATEGORIES

<b>Hematology</b>	Complete blood count (white blood cell count and differential)	Hematocrit	
	Red blood cell count	Platelet count	
	Hemoglobin		
<b>Chemistry</b>	Bicarbonate	Albumin	Blood urea nitrogen
	Calcium	ALP	Phosphorus
	Creatinine	ALT	Total protein
	Glucose	Bilirubin (direct)	Phosphate
	Potassium	Bilirubin (total)	Urate
	Sodium	LDH	
<b>Urinalysis</b>	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<sup>1,a</sup>

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

<sup>a</sup>National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0.

<sup>b</sup>Includes multiple similar terms.

- 12% of patients discontinued PLUVICTO + BSOC due to any treatment-related adverse events<sup>18</sup>
- 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<sup>1</sup>

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 ( $\geq 10\%$ ) THAT WORSENEDED FROM BASELINE IN PATIENTS WHO RECEIVED PLUVICTO + BSOC (BETWEEN-ARM DIFFERENCE OF $\geq 5\%$ ALL GRADES) IN VISION<sup>1</sup>

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

<sup>a</sup>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.

<sup>b</sup>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.

<sup>c</sup>No grade 4 laboratory abnormalities worsening from baseline were reported.

**No unexpected laboratory abnormalities were reported in the VISION trial.**

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VISION: A study of PLUVICTO after ARPI and chemo

## PLUVICTO HAS PROVEN TOLERABILITY



**Median duration of exposure to PLUVICTO was 7.8 months<sup>1</sup>**



**TEAEs led to PLUVICTO discontinuation in 12% of patients<sup>18</sup>**

- 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<sup>18</sup>**

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## 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<sup>1</sup>

Adverse reaction	Severity	Dosage modification
<b>Myelosuppression (anemia, thrombocytopenia, leukopenia, or neutropenia)</b>	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.
<b>Renal toxicity</b>	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.
<b>Dry mouth</b>	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<sup>16</sup>

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## 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<sup>1</sup>

Adverse reaction	Severity	Dosage modification
<b>Gastrointestinal toxicity</b>	Grade $\geq 3$ (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 $\geq 3$ gastrointestinal toxicity after 1 dose reduction	Permanently discontinue PLUVICTO.
<b>Fatigue</b>	Grade $\geq 3$	Withhold PLUVICTO until improvement to grade 2 or baseline.
<b>Electrolyte or metabolic abnormalities</b>	Grade $\geq 2$	Withhold PLUVICTO until improvement to grade 1 or baseline.
<b>AST or ALT elevation</b>	AST or ALT $>5$ times ULN in the absence of liver metastases	Permanently discontinue PLUVICTO.
<b>Other nonhematologic toxicity</b>	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**

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## INDICATION AND IMPORTANT SAFETY INFORMATION

### Indication

PLUVICTO<sup>®</sup> (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 ( $\geq 20\%$ ) 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.

**References:** **1.** Pluvicto. Prescribing information. Novartis Pharmaceuticals Corp. **2.** Murphy DG, Hofman MS, Azad A, Violet J, Hicks RJ, Lawrentschuk N. Going nuclear: it is time to embed the nuclear medicine physician in the prostate cancer multidisciplinary team. *BJU Int.* 2019;124(4):551-553. **3.** Korman H, Lanni T Jr, Shah C, et al. Impact of a prostate multidisciplinary clinic program on patient treatment decisions and on adherence to NCCN guidelines: the William Beaumont Hospital experience. *Am J Clin Oncol.* 2013;36(2):121-125. **4.** Magnani T, Valdagni R, Salvioni R, et al. The 6-year attendance of a multidisciplinary prostate cancer clinic in Italy: incidence of management changes. *BJU Int.* 2012;110(7):998-1003. **5.** Aizer AA, Paly JJ, Zietman AL, et al. Multidisciplinary care and pursuit of active surveillance in low-risk prostate cancer. *J Clin Oncol.* 2012;30(25):3071-3076. **6.** Tang C, Hoffman KE, Allen PK, et al. Contemporary prostate cancer treatment choices in multidisciplinary clinics referenced to national trends. *Cancer.* 2020;126(3):506-514. **7.** Gomella LG, Lin J, Hoffman-Censits J, et al. Enhancing prostate cancer care through the multidisciplinary clinic approach: a 15-year experience. *J Oncol Pract.* 2010;6(6):e5-e10. **8.** Aizer AA, Paly JJ, Efstathiou JA. Multidisciplinary care and management selection in prostate cancer. *Semin Radiat Oncol.* 2013;23(3):157-164. **9.** Sciarra A, Gentile V, Panebianco V. Multidisciplinary management of Prostate Cancer: how and why. *Am J Clin Exp Urol.* 2013;1(1):12-17. Published 2013 Dec 25. **10.** Hurwitz LM, Cullen J, Elsamanoudi S, et al. A prospective cohort study of treatment decision-making for prostate cancer following participation in a multidisciplinary clinic. *Urol Oncol.* 2016;34(5):233.e17-233.e2.33E25. **11.** Reichard CA, Hoffman KE, Tang C, et al. Radical prostatectomy or radiotherapy for high- and very high-risk prostate cancer: a multidisciplinary prostate cancer clinic experience of patients eligible for either treatment. *BJU Int.* 2019;124(5):811-819. **12.** De Luca S, Fiori C, Tucci M, et al. Prostate cancer management at an Italian tertiary referral center: does multidisciplinary team meeting influence diagnostic and therapeutic decision-making process? A snapshot of the everyday clinical practice. *Minerva Urol Nefrol.* 2019;71(6):576-582. **13.** Morris MJ, Castellano D, Herrmann K, et al; PSMAfore Investigators. <sup>177</sup>Lu-PSMA-617 versus a change of androgen receptor pathway inhibitor therapy for taxane-naïve patients with progressive metastatic castration-resistant prostate cancer (PSMAfore): a phase 3, randomised, controlled trial. *Lancet.* 2024;404(10459)(suppl 2):1227-1239. doi:10.1016/S0140-6736(24)01653-2 **14.** Morris MJ, Castellano D, Herrmann K, et al; PSMAfore Investigators. <sup>177</sup>Lu-PSMA-617 versus a change of androgen receptor pathway inhibitor therapy for taxane-naïve patients with progressive metastatic castration-resistant prostate cancer (PSMAfore): a phase 3, randomised, controlled trial. *Lancet.* 2024;404(10459):1227-1239. **15.** Morris MJ, Castellano D, Herrmann K, et al; PSMAfore Investigators. <sup>177</sup>Lu-PSMA-617 versus a change of androgen receptor pathway inhibitor therapy for taxane-naïve patients with progressive metastatic castration-resistant prostate cancer (PSMAfore): a phase 3, randomised, controlled trial. *Lancet.* 2024;404(10459)(suppl 1):1227-1239. doi:10.1016/S0140-6736(24)01653-2 **16.** Sartor O, de Bono J, Chi KN, et al; VISION Investigators. *N Engl J Med.* 2021;385(12)(protocol):1091-1103. doi:10.1056/NEJMoa2107322 **17.** Sartor O, de Bono J, Chi KN, et al; VISION Investigators. *N Engl J Med.* 2021;385(12)(suppl):1091-1103. doi:10.1056/NEJMoa2107322 **18.** Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. *N Engl J Med.* 2021;385(12)(appendix):1091-1103.

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## EFFICACY WAS ASSESSED THROUGH COMPREHENSIVE MONITORING IN PSMAfore AND VISION<sup>13,15,16</sup>

-  Patients in PSMAfore received a median of 6 cycles of PLUVICTO<sup>1</sup>
-  Patients in VISION received a median of 5 cycles of PLUVICTO<sup>17</sup>
-  Response to PLUVICTO treatment was evaluated using both radiologic assessment and PSA monitoring<sup>13,15,16</sup>
-  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<sup>1</sup>

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

### IMPORTANT SAFETY INFORMATION

#### Risk From Radiation Exposure

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.

Please see additional Important Safety Information throughout and on pages [23-24](#) and full [Prescribing Information](#).