

<b>CMS Manual System</b>	<b>Department of Health &amp; Human Services (DHHS)</b>
<b>Pub 100-03 Medicare National Coverage Determinations</b>	<b>Centers for Medicare &amp; Medicaid Services (CMS)</b>
<b>Transmittal 140</b>	<b>Date: January 6, 2012</b>
	<b>Change Request 7431</b>

**NOTE: Transmittal 136, dated November 2, 2011, is being rescinded and replaced with Transmittal 140 dated January 6, 2012. The changes include additional clarification under the Policy section regarding payment for administration of PROVENGE®, deletion of original business requirements (BRs) 8, 8.1, 9, and 9.1 relating to Common Working File frequency edits, and a date change from April 2, 2012, to July 2, 2012, in current BR 9 as it relates to Pub. 100-04 (BR). Language in current BR 7 has been revised to align with the policy changes made that allow separate payment for the cost of administration. This instruction is being re-communicated to revise the title of manual instruction of Pub. 100-03, section 110.22. The transmittal number, date issued and all other information remains the same.**

**SUBJECT: Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer**

**I. SUMMARY OF CHANGES:** Effective for services performed on or after June 30, 2011, The Centers for Medicare and Medicaid Services (CMS) proposes that the evidence is adequate to conclude that the use of autologous cellular immunotherapy treatment - sipuleucel-T; PROVENGE, improves health outcomes for Medicare beneficiaries with asymptomatic or minimally symptomatic metastatic castrate-resistant (hormone refractory) prostate cancer, and thus is reasonable and necessary for this on-label indication under 1862(a)(1)(A) of the Social Security Act.

This revision [to the Medicare National Coverage Determinations Manual] is a national coverage determination (NCD). NCDs are binding on all carriers, fiscal intermediaries, [contractors with the Federal government that review and/or adjudicate claims, determinations, and/or decisions], quality improvement organizations, qualified independent contractors, the Medicare appeals council, and administrative law judges (ALJs) (see 42 CFR section 405.1060(a)(4) (2005)). An NCD that expands coverage is also binding on a Medicare advantage organization. In addition, an ALJ may not review an NCD. (See section 1869(f)(1)(A)(i) of the Social Security Act.)

**EFFECTIVE DATE: June 30, 2011**

**IMPLEMENTATION DATE: August 8, 2011**

*Disclaimer for manual changes only: The revision date and transmittal number apply only to red italicized material. Any other material was previously published and remains unchanged. However, if this revision contains a table of contents, you will receive the new/revised information only, and not the entire table of contents.*

**II. CHANGES IN MANUAL INSTRUCTIONS:** (N/A if manual is not updated)

R=REVISED, N=NEW, D=DELETED-*Only One Per Row.*

R/N/D	CHAPTER / SECTION / SUBSECTION / TITLE
N	110.22/Autologous Cellular Immunotherapy Treatment

**III. FUNDING:**

**For Fiscal Intermediaries (FIs), Regional Home Health Intermediaries (RHHIs) and/or Carriers:**

No additional funding will be provided by CMS; Contractor activities are to be carried out within their operating budgets.

**For Medicare Administrative Contractors (MACs):**

The Medicare Administrative Contractor is hereby advised that this constitutes technical direction as defined in your contract. CMS does not construe this as a change to the MAC Statement of Work. The contractor is not obligated to incur costs in excess of the amounts allotted in your contract unless and until specifically authorized by the Contracting Officer. If the contractor considers anything provided, as described above, to be outside the current scope of work, the contractor shall withhold performance on the part(s) in question and immediately notify the Contracting Officer, in writing or by e-mail, and request formal directions regarding continued performance requirements.

**IV. ATTACHMENTS:**

**Business Requirements**

**Manual Instruction**

*\*Unless otherwise specified, the effective date is the date of service.*

# Attachment - Business Requirements

Pub. 100-03	Transmittal:140	Date: January 6, 2012	Change Request: 7431
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**SUBJECT: Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer**

**EFFECTIVE DATE: June 30, 2011**

**IMPLEMENTATION DATE: August 8, 2011**

## **I. GENERAL INFORMATION**

**A. Background:** Prostate cancer is the most common non-cutaneous cancer in men in the United States. In 2009 an estimated 192,280 new cases of prostate cancer were diagnosed and an estimated 27,360 deaths were reported. Once the patient has castration-resistant, metastatic prostate cancer the median survival is less than two years.

In 2010 the Food and Drug Administration (FDA) approved sipuleucel-T (®; APC8015) for patients with castration-resistant, metastatic prostate cancer. The posited mechanism of action, immunotherapy, is different from that of anti-cancer chemotherapy such as docetaxel. This is the first immunotherapy for prostate cancer to receive FDA approval. The goal of immunotherapy is to stimulate the body's natural defenses (such as the white blood cells called dendritic cells, T-lymphocytes and mononuclear cells) in a specific manner so that they attack and destroy, or at least prevent the proliferation of, cancer cells. Specificity is attained by intentionally exposing a patient's white blood cells to a particular protein (called an antigen) associated with the prostate cancer. This exposure "trains" the white blood cells to target and attack the prostate cancer cells. Clinically this is expected to result in a decrease in the size and/or number of cancer sites, an increase in the time to cancer progression, and/or an increase in survival of the patient.

**B. Policy:** Effective for services performed on or after June 30, 2011, The Centers for Medicare and Medicaid Services (CMS) proposes that the evidence is adequate to conclude that the use of autologous cellular immunotherapy treatment - sipuleucel-T; PROVENGE® improves health outcomes for Medicare beneficiaries with asymptomatic or minimally symptomatic metastatic castrate-resistant (hormone refractory) prostate cancer, and thus is reasonable and necessary for this on-label indication under 1862(a)(1)(A) of the Social Security Act.

**NOTE:** Contractors shall continue to process claims for PROVENGE® as they do currently between June 30, 2011, and July 5, 2011, when the new code will be implemented. During this timeframe, practitioners may continue to submit claims for this service using Not Otherwise Classified code(s) J3590 or J3490 or C9273, or they may hold their claims and submit them using Q2043 on or after July 1, 2011.

**NOTE:** Please note the new Q2043 code will be implemented in the July 2011 Update of Quarterly HCPCS Drug/Biological Code Changes (CR 7303) with a July 1, 2011, effective date. Editing for the code will be implemented July 2, 2012, with a July 1, 2011 effective date. Additionally, the Ambulatory Surgical Center (ASC) Fee Schedule will be updated to reflect these coding changes. These changes will be announced in the ASC Quarterly Update CR for July 2011.

**II. BUSINESS REQUIREMENTS TABLE**

Number	Requirement	Responsibility (place an "X" in each applicable column)								
		A / B  M A C	D M E  M A C	F I  M A C	C A R R I E R	R H H I	Shared-System Maintainers			
						F I S S	M C S	V M S	C W F	
7431-03.1	Effective for services performed on and after June 30, 2011, contractors shall allow payment for nationally covered for asymptomatic or minimally symptomatic metastatic castrate-resistant (hormone refractory) prostate cancer according to NCD 110.22, provided the claim contains the following elements specified in the companion 100-04 Business Requirements.	X		X	X					

**III. PROVIDER EDUCATION TABLE**

Number	Requirement	Responsibility (place an "X" in each applicable column)								
		A / B  M A C	D M E  M A C	F I  M A C	C A R R I E R	R H H I	Shared-System Maintainers			
						F I S S	M C S	V M S	C W F	
7431-03.2	A provider education article related to this instruction will be available at <a href="http://www.cms.hhs.gov/MLNMattersArticles">http://www.cms.hhs.gov/MLNMattersArticles</a> shortly after the CR is released. You will receive notification of the article release via the established "MLN Matters" listserv. Contractors shall post this article, or a direct link to this article, on their Web site and include information about it in a listserv message within one week of the availability of the provider education article. In addition, the provider education article shall be included in your next regularly scheduled bulletin.  Contractors are free to supplement MLN Matters articles with local information that would benefit their provider community in billing and administering the Medicare program correctly.	X		X	X					

**IV. SUPPORTING INFORMATION**

**Section A: for any recommendations and supporting information associated with listed requirements, use the box below: N/A**

X-Ref Requirement Number	Recommendations or other supporting information:

**Section B: For all other recommendations and supporting information, use this space: N/A**

**V. CONTACTS**

**Pre-Implementation Contact(s):** Leslye Fitterman, coverage, 410-786-1806, [leslye.fitterman3@cms.hhs.gov](mailto:leslye.fitterman3@cms.hhs.gov), Wanda M. Belle, coverage, 410-786-7491, [wanda.belle@cms.hhs.gov](mailto:wanda.belle@cms.hhs.gov), Cheryl Gilbreath, coverage, 410-786-5919, [cheryl.gilbreath@cms.hhs.gov](mailto:cheryl.gilbreath@cms.hhs.gov), William Ruiz, institutional claims processing, 410-786-9283, [william.ruiz@cms.hhs.gov](mailto:william.ruiz@cms.hhs.gov), Thomas Dorsey, practitioner claims processing, 410-786-7434, [thomas.dorsey@cms.hhs.gov](mailto:thomas.dorsey@cms.hhs.gov), Mark Baldwin, practitioner claims processing, 410-786-8139, [mark.baldwin@cms.hhs.gov](mailto:mark.baldwin@cms.hhs.gov), Felicia Rowe, supplier claims processing, 410-786-5655, [felicia.rowe@cms.hhs.gov](mailto:felicia.rowe@cms.hhs.gov).

**Post-Implementation Contact(s):** Contact your Contracting Officer’s Technical Representative (COTR) or Contractor Manager, as applicable.

**VI. FUNDING**

**Section A: For Fiscal Intermediaries (FIs), Regional Home Health Intermediaries (RHHIs), and/or Carriers:**

No additional funding will be provided by CMS; contractor activities are to be carried out within their operating budgets.

**Section B: For Medicare Administrative Contractors (MACs):**

The Medicare Administrative Contractor is hereby advised that this constitutes technical direction as defined in your contract. CMS does not construe this as a change to the MAC Statement of Work. The contractor is not obligated to incur costs in excess of the amounts allotted in your contract unless and until specifically authorized by the Contracting Officer. If the contractor considers anything provided, as described above, to be outside the current scope of work, the contractor shall withhold performance on the part(s) in question and immediately notify the Contracting Officer, in writing or by e-mail, and request formal directions regarding continued performance requirements.

## ***110.22 – Autologous Cellular Immunotherapy Treatment (Effective June 30, 2011)***

***(Rev.140, Issued: 01-06-12, Effective: 06-30-11, Implementation: 08-08-11)***

### ***A. General***

*Prostate cancer is the most common non-cutaneous cancer in men in the United States. In 2009, an estimated 192,280 new cases of prostate cancer were diagnosed and an estimated 27,360 deaths were reported. The National Cancer Institute states that prostate cancer is predominantly a cancer of older men; the median age at diagnosis is 72 years. Once the patient has castration-resistant, metastatic prostate cancer the median survival is generally less than two years.*

*In 2010 the Food and Drug Administration (FDA) approved sipuleucel-T (PROVENGE®; APC8015), for patients with castration-resistant, metastatic prostate cancer. The posited mechanism of action, immunotherapy, is different from that of anti-cancer chemotherapy such as docetaxel. This is the first immunotherapy for prostate cancer to receive FDA approval.*

*The goal of immunotherapy is to stimulate the body's natural defenses (such as the white blood cells called dendritic cells, T-lymphocytes and mononuclear cells) in a specific manner so that they attack and destroy, or at least prevent, the proliferation of cancer cells. Specificity is attained by intentionally exposing a patient's white blood cells to a particular protein (called an antigen) associated with the prostate cancer. This exposure "trains" the white blood cells to target and attack the prostate cancer cells. Clinically, this is expected to result in a decrease in the size and/or number of cancer sites, an increase in the time to cancer progression, and/or an increase in survival of the patient.*

*Sipuleucel-T differs from other infused anti-cancer therapies. Most such anti-cancer therapies are manufactured and sold by a biopharmaceutical company and then purchased by and dispensed from a pharmacy. In contrast, once the decision is made to treat with sipuleucel-T, a multi-step process is used to produce sipuleucel-T. Sipuleucel-T is made individually for each patient with his own white blood cells. The patient's white blood cells are removed via a procedure called leukapheresis. In a laboratory the white blood cells are exposed to PA2024, which is a molecule created by linking prostatic acid phosphatase (PAP) with granulocyte/macrophage-colony stimulating factor (GM-CSF). PAP is an antigen specifically associated with prostate cancer cells; GM-CSF is a protein that targets a receptor on the surface of white blood cells. Hence, PAP serves to externally manipulate the immunological functioning of the patient's white blood cells while GM-CSF serves to stimulate the white blood cells into action. As noted in the FDA's clinical review, each dose of sipuleucel-T contains a minimum of 40 million treated white blood cells, however there is "high inherent variability" in the yield of sipuleucel-T from leukapheresis to leukapheresis in the same patient as well as from patient to patient. The treated white blood cells are then infused back into the same patient. The FDA-approved dosing regimen is three doses with each dose administered two weeks apart.*

## ***Indications and Limitations of Coverage***

### ***B. Nationally Covered Indications***

*Effective for services performed on or after June 30, 2011, The Centers for Medicare and Medicaid Services (CMS) proposes that the evidence is adequate to conclude that the use of autologous cellular immunotherapy treatment - sipuleucel-T; PROVENGE® improves health outcomes for Medicare beneficiaries with asymptomatic or minimally symptomatic metastatic castrate-resistant (hormone refractory) prostate cancer, and thus is reasonable and necessary for this on-label indication under 1862(a)(1)(A) of the Social Security Act.*

### ***C. Nationally Non-Covered Indications***

*N/A*

### ***D. Other***

*Effective for services performed on or after June 30, 2011, coverage of all off-label uses of autologous cellular immunotherapy treatment – sipuleucel-T; PROVENGE® for the treatment of prostate cancer is left to the discretion of the local Medicare Administrative Contractors.*

*(NCD last reviewed June 2011.)*