

Corporate Medical Policy

Cellular Immunotherapy for Prostate Cancer

File Name:	cellular_immunotherapy_for_prostate_cancers
Origination:	6/2010
Last CAP Review:	8/2018
Next CAP Review:	8/2019
Last Review:	8/2018

Description of Procedure or Service

Sipuleucel-T (Provenge®) is a class of therapeutic agent used in the treatment of asymptomatic or minimally symptomatic, androgen-independent (castration-resistant), metastatic prostate cancer. The agent consists of specially treated dendritic cells obtained from the patient with leukapheresis. The cells are then exposed in vitro to proteins that contain prostate antigens and immunologic stimulating factors, and are then reinfused back into the patient. The proposed mechanism of action is that the treatment stimulates the patient's own immune system to resist spread of the cancer.

Background

Prostate cancer is the second leading cause of cancer-related deaths among American men with an estimated incidence of 164,690 cases and an estimated number of 29,430 deaths in 2018. In most cases, prostate cancer is diagnosed at a localized stage and is treated with prostatectomy or radiation therapy. However, some patients are diagnosed with metastatic disease or recurrent disease after treatment of localized disease. Androgen ablation is the standard treatment for metastatic or recurrent disease. However, most patients who survive long enough eventually develop androgen-independent prostate cancer. At this stage of metastatic disease, docetaxel, a chemotherapeutic agent, has been demonstrated to confer a survival benefit of 1.9 to 2.4 months in randomized clinical trials (RCTs). Chemotherapy with docetaxel causes adverse effects in large proportions of patients, including alopecia, fatigue, neutropenia, neuropathy, and other symptoms. The trials evaluating docetaxel included both asymptomatic and symptomatic patients, and results suggested a survival benefit for both groups. Because of the burden of treatment and its side effects, most patients therefore defer docetaxel treatment until the cancer recurrence is symptomatic.

Cancer immunotherapy has been investigated as a treatment which might be instituted at the point of detection of androgen-independent metastatic disease before significant symptomatic manifestations have occurred. The quantity of cancer cells in the patient during this time interval is thought to be relatively low, and it is thought that an effective immune response against the cancer during this time period could effectively delay or prevent progression. Such a delay could allow effective chemotherapy such as docetaxel to be deferred or delayed until necessary, thus providing an overall survival benefit.

Regulatory Status

On April 29, 2010, the U.S. Food and Drug Administration (FDA) approved Provenge® (sipuleucel-T, Dendreon Corp, now Sanpower) via a Biologics Licensing Application (BLA) for "the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer (for autologous use only)." Approval was contingent on agreement of the manufacturer to conduct a postmarketing study, based on a registry design, to assess the risk of cerebrovascular events in 1,500 patients with prostate cancer who receive sipuleucel-T.

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Related Policies

Gene-Based Tests for Screening, Detection, and/or Management of Prostate Cancer

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will cover cellular immunotherapy for prostate cancer when determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Cellular Immunotherapy for Prostate Cancer is covered

Sipuleucel-T therapy may be considered medically necessary in the treatment of asymptomatic or minimally symptomatic, androgen-independent (castration-resistant) metastatic prostate cancer.

Use of cellular immunotherapy for prostate cancer may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, see Policy Guidelines); **OR**
- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached

When Cellular Immunotherapy for Prostate Cancer is not covered

Sipuleucel-T therapy is considered **investigational** in all other situations, including but not limited to treatment of hormone-responsive prostate cancer, treatment of moderate to severe symptomatic metastatic prostate cancer, and treatment of visceral (liver, lung or brain) metastases.

Cellular immunotherapy for prostate cancer is considered investigational when used for:

1. Non-cancer indications; **OR**
2. When criteria are not met regarding FDA labeling **OR** strong endorsement/support by nationally recognized compendia, as stated under "When Cellular Immunotherapy for Prostate Cancer is covered."

Policy Guidelines

For individuals who have asymptomatic or minimally symptomatic, metastatic, castration-resistant prostate cancer who receive sipuleucel-T (Provenge), the evidence includes 3 randomized, controlled trials (RCTs) and a systematic review of these RCTs. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related morbidity. The 2 earlier RCTs of sipuleucel-T were not specifically designed to demonstrate a

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difference in overall mortality but did show a survival difference. The third RCT, which was designed to demonstrate a mortality difference, showed a similar improvement in overall survival. All 3 studies were consistent in demonstrating that sipuleucel-T treatment does not delay time to a measurable progression of the disease. A meta-analysis of the 3 RCTs found significantly improved overall survival, but not the time to progression, with sipuleucel-T compared with placebo. Serious adverse events did not increase in the sipuleucel-T group. However, the available data suggested, but did not confirm, an increase in stroke risk; this risk is being evaluated in a postmarketing study. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have nonmetastatic, androgen-dependent prostate cancer who receive sipuleucel-T (Provenge), the evidence includes a RCT. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related morbidity. The RCT did not find a statistically significant difference between sipuleucel-T and a control in time to biochemical failure. The RCT was not designed to evaluate the impact of sipuleucel-T on mortality. The evidence is insufficient to determine the effects of the technology on health outcomes.

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), “Investigational (Experimental) Services.”

Please refer to CMP “Investigational (Experimental) Services” for a summary of evidence standards from nationally recognized compendia.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: Q2043, S0353, S0354

The following codes may be submitted for reimbursement of this service: C9399, J9999, J3590, J3490, 36511, 96413, 96415, and 96365.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

U.S. Food and Drug Administration. Press release: FDA Approves a Cellular Immunotherapy for Men with Advanced Prostate Cancer. Available online at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm210174.htm>. Last accessed May 2010.

Dendreon Corporation. Provenge® (sipuleucel-T) prescribing information. Seattle, WA; April 2010. Available online at <http://www.provenge.com/pdf/prescribing-information.pdf>. Last accessed May 2010.

Senior Medical Director – 5/2010

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.53, 5/13/2010

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Specialty Matched Consultant Advisory Panel – 8/2011

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.53, 8/11/2011

Specialty Matched Consultant Advisory Panel – 8/2012

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.53, 8/9/2012

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.53, 7/11/2013

Specialty Matched Consultant Advisory Panel – 8/2013

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.53, 7/10/2014

Specialty Matched Consultant Advisory Panel- 8/2014

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.53, 7/9/2015

Specialty Matched Consultant Advisory Panel-8/2015

Specialty Matched Consultant Advisory Panel-8/2016

Medical Director review 8/2016

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.53, 7/13/2017

Specialty Matched Consultant Advisory Panel-8/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.53, 7/12/2018

Specialty Matched Consultant Advisory Panel-8/2018

Policy Implementation/Update Information

- 6/22/10 New policy. Reviewed by Senior Medical Director 5/26/10. “Sipuleucel-T therapy may be considered medically necessary in the treatment of asymptomatic or minimally symptomatic, metastatic, androgen-independent (hormone-refractory) prostate cancer.” “Sipuleucel-T therapy is considered investigational in all other situations, including but not limited to treatment of hormone-responsive prostate cancer, treatment of those with moderate to severe symptomatic metastatic prostate cancer, and those with visceral (liver, lung or brain) metastases.” (btw)
- 2/1/10 Added HCPCS code “C9273” to “Billing/Coding” section. (btw)
- 7/1/11 Added new HCPCS code, “Q2043” to Billing/Coding” section and removed deleted code “C9273”. (btw)
- 9/30/11 Specialty Matched Consultant Advisory Panel review August 31, 2011. No change to policy statement. References added. (btw)
- 9/4/12 Specialty Matched Consultant Advisory Panel review August 15, 2012. Description section revised. Slight wording changes to the When and When Not Covered sections, no change to policy intent. Reference added. (btw)

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- 10/30/12 Reference added. (btw)
- 9/10/13 Specialty Matched Consultant Advisory Panel review 8/21/2013. Policy Guidelines updated. No change to policy intent. Reference added. (btw)
- 9/9/14 Specialty Matched consultant advisory panel review 8/26/2014. No change to policy intent. Reference added. (lpr)
- 10/1/15 Description and Policy Guidelines sections updated. “Hormone-refractory” changed to clinically accepted term “castration-resistant” throughout the policy. No change to policy intent. Reference added. Specialty Matched Consultant Advisory Panel review 8/26/2015. (lpr)
- 12/30/16 Specialty Matched Consultant Advisory Panel review 8/31/2016. No change to policy statement. Medical Director review 8/2016. Added HCPCS codes S0353, S0354 to Billing/Coding section. Notification given 12/30/16 for effective date 4/1/17. (lpr)
- 9/15/17 Updated Policy Guidelines section. Reference added. Specialty Matched Consultant Advisory Panel review 8/30/2017. No change to policy statement. (lpr)
- 3/9/18 Added the following statement to “When Covered” section: “Use of cellular immunotherapy for prostate cancer may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either: In accordance with FDA label (when clinical benefit has been established, see Policy Guidelines); OR In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached”. Under “When Not Covered” section, added the statement “Cellular immunotherapy for prostate cancer is considered investigational when used for: 1)Non-cancer indications; **OR** 2) When criteria are not met regarding FDA labeling **OR** strong endorsement/ support by nationally recognized compendia, as stated under “When Cellular immunotherapy for prostate cancer is covered.” Added the following statements under “Policy Guidelines” section: 1)Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy, Investigational (Experimental) Services.” 2) Please refer to CMP “Investigational (Experimental) Services” for a summary of evidence standards from nationally recognized compendia. No change to policy statement. (lpr)
- 10/26/18 Minor edits made to Description and Policy Guidelines sections for clarity. References added. Specialty Matched Consultant Advisory Panel review 8/22/2018. No change to policy intent. (krc)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.