MASSACHUSETTS

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Medical Policy

Cellular Immunotherapy for Prostate Cancer

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Policy Number: 268

BCBSA Reference Number: 8.01.53

Related Policies

None

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

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

Sipuleucel-T therapy is **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.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required**.
Commercial PPO and Indemnity	Prior authorization is **not required**.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes

There is no specific CPT code for this service.

HCPCS Codes

HCPCS codes:	Code Description
Q2043	Sipuleucel-T, minimum of 50 million autologous cd54+ cells activated with PAP-GM-CSF, including leukapheresis and all other preparatory procedures, per infusion

Description

Prostate Cancer

Prostate cancer is the second leading cause of cancer-related deaths among American men, with an estimated incidence of 164690 cases and an estimated number of 29430 deaths in 2018.[1,] In most cases, prostate cancer is diagnosed at a localized stage and is treated with prostatectomy or radiotherapy. However, some patients are diagnosed with metastatic or recurrent disease after treatment of localized disease.

Treatment

Androgen ablation is the standard treatment for metastatic or recurrent disease. Most patients who survive long enough eventually develop androgen-independent (castration-resistant) prostate cancer. At this stage of metastatic disease, docetaxel, a chemotherapeutic agent, has demonstrated a survival benefit of 1.9 to 2.4 months in randomized clinical trials.[2,3,] Chemotherapy with docetaxel causes adverse events in large proportions of patients, including alopecia, fatigue, neutropenia, neuropathy, and other symptoms. Trials evaluating docetaxel included both asymptomatic and symptomatic patients, and results have suggested a survival benefit for both groups. Because of the burden of treatment and its adverse events, most patients defer docetaxel treatment until cancer recurrence is symptomatic.

Cancer immunotherapy has been investigated as a treatment that could 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 is thought to be relatively low, and it is thought that an effective immune response to cancer during this interval could effectively delay or prevent progression. Such a delay could allow a course of effective chemotherapy, such as docetaxel, to be deferred or delayed until necessary, thus providing an overall survival benefit.

Summary

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

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 (OS), 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 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 OS. All 3 studies were consistent in demonstrating that sipuleucel-T does not delay time to a measurable progression of the disease. A meta-analysis of the 3 RCTs found significantly improved OS 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 an RCT. Relevant outcome are OS, disease-specific survival, change in disease status, and treatment-related morbidity. The RCT did not find a statistically significant difference between sipuleucel-T and 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.

Policy History

Date	Action
8/2021	BCBSA National medical policy review. Description, summary, and references updated. Policy statements unchanged.
1/2021	Medicare information removed. See MP #132 Medicare Advantage Management for local coverage determination and national coverage determination reference.
9/2020	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
9/2019	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
9/2018	BCBSA National medical policy review. No changes to policy statements. New references added. Background and summary clarified.
8/2017	New references added from BCBSA National medical policy.
9/2015	BCBSA National policy review. “Hormone-refractory” changed to the current clinically accepted term “castration-resistant” in the medically necessary policy statement and throughout the policy. Policy statements otherwise unchanged. 9/1/2015.
10/2014	Hormone refractory cancer clarified.
9/2014	New references added from BCBSA National medical policy.
10/2013	New references from BCBSA National medical policy.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
9/2011	Reviewed - Medical Policy Group – Urology, Obstetrics and Gynecology. No changes to policy statements.
7/2011	Reviewed - Medical Policy Group – Hematology and Oncology. No changes to policy statements.
1/1/2011	Medical Policy 268 effective 1/1/2011 describing covered and non-covered indications.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References

1. National Cancer Institute, Surveillance Epidemiology and End Results Program. Cancer Stat Fact: Prostate Cancer. n.d.; https://seer.cancer.gov/statfacts/html/prost.html. Accessed June 25, 2021

2. Berry DL, Moinpour CM, Jiang CS, et al. Quality of life and pain in advanced stage prostate cancer: results of a Southwest Oncology Group randomized trial comparing docetaxel and estramustine to mitoxantrone and prednisone. J Clin Oncol. Jun 20 2006; 24(18): 2828-35. PMID 16782921
3. Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Engl J Med. Oct 07 2004; 351(15): 1502-12. PMID 15470213
4. Food and Drug Administration (FDA). April 29, 2010 Approval Letter - Provenge. 2010; https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/provenge-sipuleucel-t. Accessed June 25, 2021.
5. Yi R, Chen B, Duan P, et al. Sipuleucel-T and Androgen Receptor-Directed Therapy for Castration-Resistant Prostate Cancer: A Meta-Analysis. J Immunol Res. 2016; 2016: 4543861. PMID 28058266
6. Dendreon Corporation. Provenge (sipuleucel-T) suspension for intravenous infusion prescribing information. n.d.; http://www.provenge.com/. Accessed June 25, 2021.
7. Small EJ, Schellhammer PF, Higano CS, et al. Placebo-controlled phase III trial of immunologic therapy with sipuleucel-T (APC8015) in patients with metastatic, asymptomatic hormone refractory prostate cancer. J Clin Oncol. Jul 01 2006; 24(19): 3089-94. PMID 16809734
8. Higano CS, Schellhammer PF, Small EJ, et al. Integrated data from 2 randomized, double-blind, placebo-controlled, phase 3 trials of active cellular immunotherapy with sipuleucel-T in advanced prostate cancer. Cancer. Aug 15 2009; 115(16): 3670-9. PMID 19536890
9. Kantoff PW, Higano CS, Shore ND, et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. N Engl J Med. Jul 29 2010; 363(5): 411-22. PMID 20818862
10. Food and Drug Administration (FDA). Summary Basis for Regulatory Action: Provenge (sipuleucel T). 2010; https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/provenge-sipuleucel-t. Accessed June 26, 2021.
11. Schellhammer PF, Chodak G, Whitmore JB, et al. Lower baseline prostate-specific antigen is associated with a greater overall survival benefit from sipuleucel-T in the Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) trial. Urology. Jun 2013; 81(6): 1297-302. PMID 23582482
12. Small EJ, Higano CS, Kantoff PW, et al. Time to disease-related pain and first opioid use in patients with metastatic castration-resistant prostate cancer treated with sipuleucel-T. Prostate Cancer Prostatic Dis. Sep 2014; 17(3): 259-64. PMID 24957547
13. Beer TM, Bernstein GT, Corman JM, et al. Randomized trial of autologous cellular immunotherapy with sipuleucel-T in androgen-dependent prostate cancer. Clin Cancer Res. Jul 01 2011; 17(13): 4558-67. PMID 21558406
14. Cookson MS, Roth BJ, Dahm P, et al. Castration-resistant prostate cancer: AUA Guideline. J Urol. Aug 2013; 190(2): 429-38. PMID 23665272
15. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: prostate cancer. Version 2.2021. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed June 25, 2021.
16. Center for Medicare and Medicaid Services. National Coverage Determination (NCD) for Autologous Cellular Immunotherapy Treatment (110.22). 2011; https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=344&ncdver=1&bc=AAAAIAAAAAAA&. Accessed June 25, 2021.