Provenge® (sipuleucel-T)
(Intravenous)

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Document Number: EOCCO-0412

Last Review Date: 05/03/2021
Chapter 1 Date of Origin: 01/07/2019
Dates Reviewed: 01/2019, 05/2019, 05/2020, 05/2021

I. Length of Authorization

Coverage will be provided for 3 doses only

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Provenge suspension for injection: 1 pre-made bag every 14 days for 3 doses only

B. Max Units (per dose and over time) [HCPCS Unit]:

- 1 billable unit every 14 days x 3 doses only

III. Initial Approval Criteria [1-4]

Coverage is provided in the following conditions:

Prostate Cancer † ‡ [4,1e-8e]

- Patient has castration-resistant metastatic disease; **AND**
- Patient has an ECOG Performance status of 0-1; **AND**
- Patient has no hepatic metastases; **AND**
- Must not be used in combination with chemotherapy; **AND**
- Patient's life expectancy is estimated to be greater than 6 months; **AND**
- Patient is asymptomatic or minimally symptomatic; **AND**
- Patient has not previously received therapy with sipuleucel-T

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s); ‡ Compendia recommended indication(s)

IV. Renewal Criteria [1]

Coverage cannot be renewed.

V. Dosage/Administration [1]

Indication	Dose
Prostate Cancer	Infuse the contents of 1 pre-made bag (containing at least 50 million autologous CD54+ cells activated with PAP-GM-CSF) over 60 minutes. Administer 3 doses over approximately 2-week intervals

VI. Billing Code/Availability Information

HCPCS code:

- Q2043 – Sipuleucel-T, minimum of 50 million autologous CD54+ cells activated with PAP-GM-CSF, including leukapheresis and all other preparatory procedures, per infusion
  - 1 billable unit = 1 dose (Code Price is per 250 mL)

NDC(s):

- Provenge suspension for injection: 30237-8900-xx

VII. References (STANDARD)

1. Provenge [package insert]. Seattle, WA; Dendreon Corporation; July 2017. Accessed April 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Sipuleucel-T. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed by Magellan Rx April 2021.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Prostate Cancer 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed by Magellan Rx April 2021.
4. Kantoff PW, Higano CS, Shore ND, et al; IMPACT Study Investigators. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. N Engl J Med. 2010 Jul 29;363(5):411-22. doi: 10.1056/NEJMoa1001294.

5. 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. 2006 Jul 1;24(19):3089-94. doi: 10.1200/JCO.2005.04.5252.
6. Noridian Healthcare Solutions, LLC. Local Coverage Article for SIPULEUCEL-T (Provenge®) - Coverage Criteria for Prostate Cancer – Clarification (A52926; A55719). Centers for Medicare & Medicaid Services, Inc. Updated on 09/29/2020 with effective date 10/19/2018. Accessed April 2021.
7. National Coverage Determination (NCD) for Autologous Cellular Immunotherapy Treatment (110.22). Centers for Medicare & Medicaid Services, Inc. Updated 01/06/2012 with effective date 06/30/2011. Accessed April 2021.

VIII. References (ENHANCED)

1e. Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus Prednisone or Mitoxantrone plus Prednisone for Advanced Prostate Cancer. N Engl J Med 2004; 351:1502-1512.
2e. Berthold DR, Pond GR, Soban F, de Wit R, Eisenberger M, Tannock IF. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer: updated survival in the TAX 327 study. J Clin Oncol. 2008 Jan 10;26(2):242-5. doi: 10.1200/JCO.2007.12.4008.
3e. Ryan CJ, Smith MR, Fizazi K, et al. Abiraterone acetate plus prednisone versus placebo plus prednisone in chemotherapy-naive men with metastatic castration-resistant prostate cancer (COU-AA-302): final overall survival analysis of a randomised, double-blind, placebo-controlled phase 3 study. Lancet Oncol. 2015 Feb;16(2):152-60. doi: 10.1016/S1470-2045(14)71205-7. Epub 2015 Jan 16.
4e. Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in Metastatic Prostate Cancer before Chemotherapy. N Engl J Med. 2014 Jul 31; 371(5): 424–433.
5e. Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in Men with Chemotherapy-naïve Metastatic Castration-resistant Prostate Cancer: Extended Analysis of the Phase 3 PREVAIL Study. Eur Urol. 2017 Feb; 71(2): 151–154.
6e. Fizazi K, Scher HI, Molina A, et al. Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study. Lancet Oncol. 2012 Oct;13(10):983-92. doi: 10.1016/S1470-2045(12)70379-0. Epub 2012 Sep 18.
7e. Scher H, Fizazi K, Saad F, et al. Increased Survival with Enzalutamide in Prostate Cancer after Chemotherapy. N Engl J Med 2012; 367:1187-1197.
8e. de Bono JS, Oudard S, Ozguroglu M, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. Lancet. 2010 Oct 2;376(9747):1147-54. doi: 10.1016/S0140-6736(10)61389-X.

9e. Marabelle A, Le DT, Ascierto PA, et al. Efficacy of Pembrolizumab in Patients With Noncolorectal High Microsatellite Instability/Mismatch Repair-Deficient Cancer: Results From the Phase II KEYNOTE-158 Study. J Clin Oncol. 2020 Jan 1;38(1):1-10. doi: 10.1200/JCO.19.02105. Epub 2019 Nov 4.

10e. Magellan Health, Magellan Rx Management. Provenge Clinical Literature Review Analysis. Last updated April 2021. Accessed April 2021.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C61	Malignant neoplasm of prostate

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

Jurisdiction(s): E	NCD/LCD Document (s): A55719
https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?Date=&DocID=A55719&SearchType=Advanced&bc=EgAAAAAAAAAA&	

Jurisdiction(s): F	NCD/LCD Document (s): A52926
https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?DocID=A52926&SearchType=Advanced&bc=EAAAAAAAAAAA&	

Jurisdiction(s): ALL	NCD/LCD Document (s): NCD 110.22
https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?DocID=110.22&bc=EAAAAAAAAAAA&&SearchType=Advanced	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Appendix 3 – CLINICAL LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate; RFS = relapse-free survival; mCRPC = metastatic castration-resistant prostate cancer; CSPC = castration-sensitive prostate cancer; ADT = androgen-deprivation therapy; SOC = standard of care

Prostate Cancer

Metastatic Castration-Resistant Prostate Cancer – No prior docetaxel/no prior novel hormone therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Sipuleucel-T	2A certain circumstances	Yes	Phase 3 (IMPACT), multicenter, randomized, double-blind	Placebo	OS	≤ 2 prior lines of chemotherapy (asymptomatic or minimally symptomatic, no visceral metastases)	• Sipuleucel-T prolonged OS among men with CRPC • However, sipuleucel-T had minimal effect on radiographic disease progression and PSA
Docetaxel (every 3 weeks [D3P] or weekly [D1P]) + prednisone	1	Yes	Phase 3 (TAX 327), randomized Extended follow-up	Mitoxantrone + prednisone (MP)	OS	First-line (chemotherapy naïve)	• Docetaxel every 3 weeks led to superior OS than mitoxantrone
Abiraterone+ prednisone	1 (castration-naïve disease or initial therapy without visceral metastases)	Yes	Phase 3 (COU-AA-302), randomized; double-blind, placebo-controlled	Placebo+ prednisone	PFS	First-line (chemotherapy naïve; asymptomatic or minimally symptomatic; no visceral metastases)	• Abiraterone prolonged OS compared with placebo
Enzalutamide	1 (secondary hormone therapy)	Yes	Phase 3 (PREVAIL), double-blind, randomized	Placebo	PFS OS	First-line (chemotherapy naïve;	• Enzalutamide significantly decreased the risk of disease progression and death

	2A (previously treated with abiraterone)		Extended analysis			with and without visceral metastases)	
Metastatic Castration-Resistant Prostate Cancer – Prior novel hormone therapy/no prior docetaxel							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Sipuleucel-T	2A preferred	Yes	Phase 3 (IMPACT), multicenter, randomized, double-blind	Placebo	OS	≤ 2 prior lines of chemotherapy (asymptomatic or minimally symptomatic, no visceral metastases)	• Sipuleucel-T prolonged OS among men with CRPC (only 18.2% had pre-treated disease) • However, sipuleucel-T had minimal effect on radiographic disease progression and PSA
Docetaxel (every 3 weeks [D3P] or weekly [D1P]) + prednisone	1	Yes	Phase 3 (TAX 327), randomized Extended follow-up	Mitoxantrone + prednisone (MP)	OS	First-line (chemotherapy naïve)	• Docetaxel every 3 weeks led to superior OS than mitoxantrone
Pembrolizumab	2A certain circumstances for MSI-H or dMMR	Solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options	Phase 2 (KEYNOTE-158)	N/A	ORR	Subsequent therapy	Pembrolizumab demonstrated a clinical benefit with an overall ORR of 34.3% in patients with previously treated unresectable or metastatic MSI-H/dMMR non-colorectal cancer. This study included 6 patients with cervical cancer.

Metastatic Castration-Resistant Prostate Cancer – Prior docetaxel/no prior novel hormone therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Sipuleucel-T	2A other	Yes	Phase 3 (IMPACT), multicenter, randomized, double-blind	Placebo	OS	≤ 2 prior lines of chemotherapy (asymptomatic or minimally symptomatic, no visceral metastases)	• Sipuleucel-T prolonged OS among men with CRPC (only 18.2% had pre-treated disease) • However, sipuleucel-T had minimal effect on radiographic disease progression and PSA
Abiraterone+ prednisone	1 (castration-naïve disease or initial therapy without visceral metastases)	Yes	Phase 3 (COU-AA-302), randomized; double-blind, placebo-controlled	Placebo+ prednisone	PFS	First-line (chemotherapy naïve; asymptomatic or minimally symptomatic; no visceral metastases)	• Abiraterone prolonged OS compared with placebo
Enzalutamide	1	Yes	Phase 3 (AFFIRM), double-blind, placebo-controlled	Placebo	OS	Second-line after chemotherapy	• Enzalutamide significantly prolonged the OS of men with mCRPC after chemotherapy
Cabazitaxel+ prednisone	1 (after docetaxel-based regimen)	Yes metastatic CRPC previously treated with a docetaxel-containing treatment regimen	Phase 3 (TROPIC), randomized, open-label, international, multi-center	Mitoxantrone +prednisone	OS	Second-line after docetaxel-containing regimen	• Cabazitaxel improved OS patients with metastatic castration-resistant prostate cancer whose disease has progressed during or after docetaxel-based therapy