Policy:	**Oncology (Injectable) – Provenge Utilization Management Medical Policy** • Provenge® (sipuleucel-T intravenous infusion – Dendreon)
Date:	06/05/2025
Applicable Lines of Business:	Medicare Advantage - Medical
Applicable States:	All States
Applicable NCDs, LCDs, and/or LCAs	NCD 110.22, A52926, A55719

SUMMARY OF EVIDENCE

Provenge, an autologous cellular immunotherapy, is indicated for the treatment of asymptomatic or minimally symptomatic metastatic **castrate-resistant (hormone-refractory) prostate cancer (CRPC)**.[1]

Provenge consists of autologous peripheral blood mononuclear cells, including antigen presenting cells, that have been activated during a defined culture period with a recombinant human protein found on prostate cancer tissue, linked to an immune cell activator. Provenge is designed to induce an immune response targeted against an antigen expressed in most prostate cancer cells. Each dose of Provenge contains a minimum of 50 million autologous CD54-positive cells activated with prostatic acid phosphatase (PAP)-granulocyte-macrophage colony-stimulating factor (GM-CSF). As noted in the prescribing information, in controlled clinical trials, the median dosing interval between infusions was 2 weeks; however, the dosing interval range could elapse between 1 week to 15 weeks. The maximum dosing interval has not been established.

Guidelines

The National Comprehensive Cancer Network (NCCN) prostate cancer guidelines (version 2.2025 – April 16, 2025) lists Provenge as a category 1 recommended therapy under "Useful in Certain Circumstances" for metastatic CRPC for patients who have not received prior docetaxel or prior novel hormone therapy.[2,3] Provenge is also listed as an option (category 2A) for patients who have received either prior docetaxel or prior novel hormone therapy. It is noted that Provenge has not been studied in patients with visceral metastases and is not recommended if visceral metastases are present. Provenge is also not recommended for patients with small cell/neuroendocrine prostate cancer. The guidelines note that Provenge is only recommended for patients who meet the following: Eastern Cooperative Oncology Group performance status of 0 or 1; estimated life expectancy > 6 months; no hepatic metastases; and no or minimal disease symptoms.

ANALYSIS OF EVIDENCE

The information provided in the summary of evidence is supported by labeled indications, CMS-approved compendia, published clinical literature, clinical practice guidelines, and/or applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs). Refer to the Sources of Information section of this policy for additional information.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Provenge. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the Sources of Information section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Sources of Information section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

Indications with a ^ below are referenced in both the corresponding Standard Medical Utilization Management Internal Policy AND applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications may be internally developed and/or referenced in applicable NCDs, LCDs, and/or LCAs. For these indications, internally developed coverage criteria is denoted throughout the policy in the following manner: 1) IC-L (internal criteria supported by the labeled indication), 2) IC-COMP (internal criteria supported by CMS-approved compendia), 3) IC-ISGP (internal criteria intended to interpret or supplement general provisions outlined in applicable NCDs, LCDs, and/or LCAs), or 4) IC-EC (internal criteria intended to expand coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs). For these indications, coverage criteria that is NOT denoted with one of the above indicators is referenced in applicable NCDs, LCDs, and/or LCAs. Additional information supporting the rationale for determination of internal coverage criteria can be found via the Sources of Information section.

Indications with a @ below are referenced in the corresponding Standard Medical Utilization Management Internal Policy, but are NOT directly referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications is internally developed. These indications and their respective coverage criteria represent expanded coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs.

Indications with a # below are supported and referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs), but are NOT directly referenced in the corresponding Standard Medical Utilization Management Internal Policy. Coverage criteria for these indications is referenced in applicable NCDs, LCDs, and/or LCAs.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Provenge is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. Prostate Cancer. ^

Criteria. Approve for 3 months if the patient meets the following criteria (A, B, C, D and E):
A) Patient is ≥ 18 years of age; IC-COMP AND
B) The patient has metastatic castration-resistant (hormone-refractory) prostate cancer; AND
C) The patient has minimal or no disease symptoms, according to the prescriber; AND
D) The patient does not have liver metastasis; IC-COMP AND
E) The patient has not been previously treated with a complete course (3 doses) of Provenge for prostate cancer. IC-COMP

Dosing. Approve up to three doses, each dose containing a minimum of 50 million autologous CD54-positive cells activated with prostatic acid phosphatase (PAP)-granulocyte-macrophage colony-stimulating factor (GM-CSF) given at approximately 2-week intervals.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Provenge is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

SOURCES OF INFORMATION

1. Provenge® intravenous infusion [prescribing information]. Seal Beach, CA: Dendreon Pharmaceuticals; July 2017.
2. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 25, 2025. Search term: Sipuleucel-T.
3. The NCCN Prostate Cancer Clinical Practice Guidelines in Oncology (version 2.2025 – April 16, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 25, 2025.
4. Centers for Medicare and Medicaid Services. National Coverage Determination (NCD) for Autologous Cellular Immunotherapy Treatment (110.22). [Version Number 1, Effective date of version: 6/30/2011, Revision 01/2012]. Accessed on June 5, 2025.
5. Centers for Medicare and Medicaid Services. Noridian Healthcare Solutions, LLC. Local Coverage Article (LCA): Sipuleucel-T (PROVENGE®) - Coverage Criteria for Prostate Cancer – Clarification (A52926). [Original effective date 10/01/2015; Revision effective date 10/19/2018]. Accessed on June 5, 2025.
6. Centers for Medicare and Medicaid Services. Noridian Healthcare Solutions, LLC. Local Coverage Article (LCA): Sipuleucel-T (PROVENGE®) - Coverage Criteria for Prostate Cancer – Clarification (A55719). [Original effective date 10/01/2015; Revision effective date 10/19/2018]. Accessed on June 5, 2025.

HISTORY

Type of Revision	Summary of Changes*	Date
Policy created	New Medicare Advantage Medical Policy	02/20/2019
Policy revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific	1/30/2020

	lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	
Policy revision	Changed "prescribing physician" to "prescriber".	02/26/2020
Policy revision	Added the following to the Policy Statement "Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles."	04/03/2020
Policy revision	**Prostate Cancer:** A requirement that the patient is ≥ 18 years of age was added.	06/23/2022
Policy revision	**Prostate Cancer:** Dosing was reworded to include the dose information "each dose containing a minimum of 50 million autologous CD54-positive cells activated with prostatic acid phosphatase (PAP)-granulocyte-macrophage colony-stimulating factor (GM-CSF)".	08/01/2022
Policy review	No criteria changes	05/10/2023
Policy review	No criteria changes (based on review of commercial policy annual review)	05/31/2024
Policy revision	No criteria changes. Formatting and notation updates.	03/10/2025
Policy review	No criteria changes (based on review of commercial policy annual review)	06/05/2025