# Medical Drug Clinical Criteria

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| **Subject:** | Provenge (sipuleucel-T) | | |
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## Table of Contents



## Overview

This document addresses the use of Provenge (Sipuleucel-T). Provenge is a product used to treat castrate-resistant prostate cancer (also known as androgen-independent prostate cancer [AIPC] or hormone-resistant [or recurrent or refractory] prostate cancer [HRPC]), a form of prostate cancer that is resistant to standard hormone treatment, and is further defined as follows:

> Disease progression evidenced by a progressively rising prostate specific antigen (PSA) (defined as a PSA rise by 2 ng/ml or more above the nadir PSA) or an increase in tumor mass on bone scan, X-ray, computerized tomography (CT) scan or magnetic resonance image (MRI) despite a castrate level of testosterone less than 20 ng/dl.

The precise mechanism of action of Provenge is not known. Provenge is a type of autologous cellular immunotherapy, also referred to as a vaccine, which is intended to activate an individual's immune system to respond to prostate tumor antigens. It is designed to direct an immune response by targeting against prostatic acid phosphatase (PAP), an antigen expressed in most prostate cancers. Autologous peripheral blood mononuclear cells, including antigen presenting cells (APCs) collected by leukapheresis are activated during culture with PAP and granulocyte-macrophage colony-stimulating factor (GM-CSF), an immune cell activator. The final product contains a minimum of 50 million autologous CD54+ cells activated with PAP-GM-CSF as well as T cells, B cells, natural killer (NK) cells and other cells.

The FDA approved indication for Provenge states that it is indicated for asymptomatic or minimally symptomatic metastatic castrate-resistant prostate cancer. The pivotal clinical trial included specific inclusion parameters such as evidence of progression after surgical or medical castration, baseline testosterone levels < 50 ng/mL, and life expectancy greater than 6 months. Individuals with ECOG (Eastern Cooperative Oncology Group) performance status ≥2 were excluded as well as those with visceral metastasis, those with pathologic long bone fracture or spinal cord compression, and prior chemotherapy within 3 months or systemic glucocorticoids, external-beam radiation (EBRT), surgery, or systemic therapy for prostate cancer (except medical or surgical castration) within 28 days. Exclusions related to recent chemotherapy and systemic corticosteroids were specified to address the concern that treatments which impact the immune system could also interfere with the subject's immunologic function and response to Provenge treatment. Accordingly, it is appropriate to discontinue these treatments prior to beginning a course of Provenge.

At the August 2019 Hematology/Oncology Committee Meeting, criteria for baseline testosterone levels less than 50 ng/mL and prior chemotherapy within 3 months was removed per specialty committee consensus opinion.

A prospective registry of men with metastatic CRPC, PROCEED, followed 1976 patients from 2011 to 2017 for a median of 46.6 months. The safety and tolerability of Provenge were consistent with previous findings and the median overall survival was 30.7 months (95%CI, 28.6-32.2 months).

The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for Provenge only for asymptomatic or minimally symptomatic individuals without liver metastases, life expectancy >6 mo, and ECOG performance status 0–1. Benefit with Provenge (sipuleucel-T) has not been reported in patients with visceral metastases and is not recommended if visceral metastases are present. Provenge also is not recommended for patients with small cell/NEPC. Provenge has been shown in a phase 3 clinical trial to extend mean survival from 21.7 months in the control arm to 25.8 months in the treatment arm, which constitutes a 22% reduction in mortality risk.

**Definitions and Measures**
Chemotherapy: Medical treatment of a disease, particularly cancer, with drugs or other chemicals.

Disease Progression: Cancer that continues to grow or spread.

ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:

- 0 = Fully active, able to carry on all pre-disease performance without restriction
- 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light house work, office work
- 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
- 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
- 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
- 5 = Dead

Hormonal therapy: Treatment that adds, blocks, or removes hormones. Agents that slow or stop the growth of certain cancers, synthetic hormones or other drugs may be given to block the body's natural hormones.

Progressive Disease (PD): Cancer that is growing, spreading, or getting worse.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Stable disease: Cancer that is not decreasing or increasing in extent or severity.

Unresectable: Unable to be removed with surgery.

## Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

**Provenge (sipuleucel-T)**

Requests for Provenge (sipuleucel-T) may be approved if the following criteria are met:

I. Individual has a diagnosis of prostate cancer (Label, NCCN 1, 2A); **AND**
II. Individual has metastatic castrate-resistant or hormone refractory disease; **AND**
III. Individual meets all of the following (Kantoff 2010):
    A. Asymptomatic or minimally symptomatic; **AND**
    B. ECOG (Eastern Cooperative Oncology Group) performance status 0-1; **AND**
    C. No visceral metastasis; **AND**
    D. No pathologic long bone fracture, or spinal cord compression within the last 3 months; **AND**
    E. Life expectancy of greater than 6 months; **AND**
    F. No treatment within the previous 28 days with systemic glucocorticoids, external-beam radiation (EBRT), surgery, or systemic therapy for prostate cancer (except medical or surgical castration); **AND**
    G. Progressive disease documented by either of the following:
        1. Serum prostate-specific antigen (PSA) level increasing; **OR**
        2. Osseous metastases on imaging with objective evidence of progression regardless of PSA levels.

Requests for Provenge (sipuleucel-T) may not be approved for the following:

I. Small cell/neuroendocrine prostate cancer (NCCN Prostate Cancer Guidelines); **OR**
II. When the above criteria are not met and for all other indications.

## Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

**HCPCS**

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| Q2043 | Sipuleucel-T, minimum of 50 million autologous CD54+ cells activated with PAP-GM-CSF, including leukapheresis and all other preparatory procedures, per infusion |

**ICD-10 Diagnosis**

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| C61 | Malignant neoplasm of prostate |
| R97.20 | Elevated prostate specific antigen [PSA] |
| R97.21 | Rising PSA following treatment for malignant neoplasm of prostate |
| Z19.2 | Hormone resistant malignancy status |
| Z51.12 | Encounter for antineoplastic immunotherapy |

## Document History

Reviewed: 05/19/2023
Document History:

- 05/19/2023 – Annual Review: Minor wording and formatting updates. Coding Reviewed: No changes.
- 05/20/2022 – Annual Review: No changes. Coding Reviewed: No changes.
- 05/21/2021– Annual Review: No changes. Coding Reviewed: No changes.
- 05/15/2020 – Annual Review: Update Provenge may not be approved criteria to exclude use in those with small cell/neurodendocrine prostate cancer. Coding review: No changes
- 08/16/2019 – Select Review: Remove criteria regarding testosterone levels and previous chemotherapy; update language around progressive disease. Coding Reviewed: No changes.
- 05/17/2019 – Annual Review: First review of Provenge clinical criteria. Wording and formatting updates. Add reference for off label criteria. Coding reviewed: No changes.

## References


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2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
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; 363(5):411-422.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
6. NCCN Clinical Practice Guidelines in Oncology™. © 2022 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on April 14, 2023.
    a. Prostate Cancer. V1.2023. Revised September 16, 2022.


Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.