| KAISER PERMANENTE® Mid-Atlantic States | **Sipuleucel-T (Provenge)**<br>**Medical Coverage Policy** |
|---|---|

**Utilization *ALERT***

- Prior to use of this MCP for evaluation of medical necessity, benefit coverage MUST be verified in the member's EOC or benefit document.
- For Medicare members, please refer to CMS guidelines through Medicare Coverage Database requirements.
- Note: After searching the Medicare Coverage Database, if no NCD/LCD/LCA is found, then use the policy referenced above for coverage guidelines

**I. Procedure/Service: Sipuleucel-T (Provenge®)**

**II. Specialty:** Cellular Immunotherapy, Oncology

**III. Clinical Indications for Referral**

The use of Sipuleucel-T (Provenge®) therapy is considered medically necessary in the treatment of an FDA-approved indication and when the patient meets **ALL** the following criteria:

A. For the treatment of first-line or second-line treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer (mCRPC);
B. There is no evidence of small cell or neuroendocrine prostate cancer;
C. The Prostate-Specific Antigen (PSA) concentration is less than or equal to 22.1 ng/mL;
D. No evidence of spinal cord compression or visceral metastasis
*E.* There is no prior chemotherapy regimen which included docetaxel or cabazitaxel and no chemotherapy within three months of planned treatment; *and*
F. There is documented clinical contraindication to treatment with secondary hormonal therapies, abiraterone acetate AND enzalutamide

**IV. Limitation**

A. Sipuleucel-T (Provenge®) is for autologous use only.
B. Infusion of more than a single course of Sipuleucel-T therapy (a series of 3 complete doses) is considered not medically necessary.
C. Careful evaluation should be made for patients who were or are currently on immunosuppressive agents prior to Sipuleucel-T therapy as immunosuppressive agents may alter Sipuleucel-T's safety and efficacy. Determination of medical appropriateness to reduce or discontinue the immunosuppressive agent is needed before starting Sipuleucel-T's treatment.

## V. Exclusion

A. The use of Sipuleucel-T in combination with other therapeutic agents such as abiraterone acetate (Zytiga®), enzalutamide (Xtandi®), or ipilimumab (Yervoy®) is considered *experimental and investigational.*
B. Sipuleucel-T therapy is considered *experimental and investigational* in all other indications except those cited in section IV due to lack of evidence to support its' efficacy and safety including but not limited to the following:
   1. Prevention of prostate cancer;
   2. Treatment of other indications such as :
      a. Stage I to III prostate cancer;
      b. Small cell neuroendocrine prostate cancer;
      c. Localized prostate cancer;
      d. Urogenital malignancies such as urinary bladder cancer;
      e. Glioblastoma;
      *f.* Germ cell tumors; *or*
      g. Sarcoma

## VI. Background

**Cellular immunotherapy** is an innovative therapy where the patient's own cells are taken, processed, multiplied & sometimes reengineered in the laboratory by harnessing the body's own immune system to fight cancer.

**Sipuleucel-T (Provenge®)** is an autologous cellular immunotherapy, manufactured by Dendreon Corp and approved by FDA in 2010 for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer. This first-line biologic is designed to stimulate the patient's own immune system against cancer, targeted against prostatic acid phosphatase (PAP), an antigen expressed in most prostate cancers.

- The process requires the patient's own autologous white blood cells to be collected by leukapheresis and processed through two buoyant density separations intended-b(4)-red blood cells and granulocytes while retaining leukocytes.
- The CD54 cells (such as the white blood cells called dendritic cells, T-lymphocytes and mononuclear cells) are subsequently cultured and activated in the presence of **PAP-GM-CSF** recombinant protein for 36-44 hours, washed and suspended in lactated ringer's solution for infusion back to the patient to treat prostate cancer.
- **PAP** linked to **GM-CSF protein** acts as an adjuvant in cancer immunotherapy by targeting the PAP protein to autologous Antigen Presenting Cells (APC) and activating those cells.
- A single dose of Sipuleucel-T is produced for each cycle of leukapheresis, contains a minimum of 50 million autologous CD54.
- A total single course of Sipuleucel-T therapy is administered intravenously as a series of 3 complete

doses at approximately two-week intervals.

**Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF)** is a potent cytokine which can be used as an immunostimulatory adjuvant to elicit antitumor immunity and essential for the differentiation of dendritic cells, which are responsible for processing and presenting tumor antigens for the priming of antitumor cytotoxic T lymphocytes.

**Prostatic Acid Phosphatase (PAP)** is a protein expressed in prostate cancer tissue which provides the antigen to direct the immune system to target prostate cancer.

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## Approval History

Effective June 01, 2016, state filing is no longer required per Maryland House Bill HB 798 – Health Insurance – Reporting

| Date approved by RUMC | Date of Implementation |
|---|---|
| 04/16/2021 | 04/16/2021 |
| 04/25/2022 | 04/25/2022 |
| 03/22/2023 | 03/22/2023 |
| 03/19/2024 | 03/19/2024 |

*The Regional Utilization Management Committee received delegated authority in 2011 to review and approve designated Utilization Management and Medical Coverage Policies by the Regional Quality Improvement Committee.

Note: Kaiser Permanente Mid-Atlantic States (KPMAS) include referral and authorization criteria to support primary care and specialty care practitioners, as appropriate, in caring for members with selected conditions. Medical Coverage Policies are not intended or designed as a substitute for the reasonable exercise of independent clinical judgment by a practitioner in any particular set of circumstances for an individual member.