Sipuleucel-T (Provenge) **Policy Number:** M-0047

Payment will not be made for any use of these drugs outside of the criteria without prior authorization. The member may not be billed unless the member explicitly agrees in writing to be responsible for the charges in accordance with the contract/provider manual. Prior authorization will only be given if the provider demonstrates the intended use meets Medicare coverage guidelines.

Coverage Guidelines:

FDA

- Treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer

Coding Information:

HCPCS Code(s)

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-9 Code(s)

Each claim must contain two ICD-9 codes for Provenge, one of which must be: 185-Malignant neoplasm of prostate. The secondary ICD-9 codes included in the transmittal are listed below.

Primary ICD-9 Code	
185	Malignant neoplasm of prostate
Secondary ICD-9 Codes	
196.1	Secondary and unspecified malignant neoplasm of intrathoracic lymph nodes
196.2	Secondary and unspecified malignant neoplasm of intra-abdominal lymph nodes
196.5	Secondary and unspecified malignant neoplasm of lymph nodes of inguinal region and lower limb
196.6	Secondary and unspecified malignant neoplasm of intrapelvic lymph nodes
196.8	Secondary and unspecified malignant neoplasm of lymph nodes of multiple sites
196.9	Secondary and unspecified malignant neoplasm of lymph node site unspecified: The spread of cancer to and establishment in the lymph nodes

197.0	Secondary malignant neoplasm of lung: Cancer that has spread from the original (primary) tumor to the lung. The spread of cancer to the lung. This may be from a primary lung cancer or from a cancer at a distant site.
197.7	Malignant neoplasm of liver secondary: Cancer that has spread from the original (primary) tumor to the liver. A malignant neoplasm that has spread to the liver from another (primary) anatomic site. Such malignant neoplasms may be carcinomas (eg, breast, colon), lymphomas, melanomas, or sarcomas.
198.0	Secondary malignant neoplasm of kidney: The spread of cancer to the kidney. This may be from a primary kidney cancer involving the opposite kidney or from a cancer at a distant site
198.1	Secondary malignant neoplasm of other urinary organs
198.5	Secondary malignant neoplasm of bone and bone marrow: Cancer that has spread from the original (primary) tumor to the bone. The spread of a malignant neoplasm from a primary site to the skeletal system. The majority of metastatic neoplasms to the bone are carcinomas
198.7	Secondary malignant neoplasm of adrenal gland
198.82	Secondary malignant neoplasm of genital organs

Indications:

Sipuleucel-T may be indicated when **ALL** of the following are present:

- Metastatic prostate cancer
- Previous treatment with surgical or medical castration
- Serum testosterone level less than 50 ng/dL (1.74 nmol/L)
- Evidence of progressive disease, as indicated by **1 or more** of the following:
  - New metastases or progression of known lesions on imaging studies
  - Increase in PSA level of more than 25% over baseline, and total increase of at least 2 ng/mL (2 mcg/L) from nadir measurement
- Expected survival 6 months or longer
- No history of pathologic fractures in long bones
- No evidence of spinal cord compression
- No evidence of visceral metastases
- No chemotherapy within 3 months of planned treatment
- No prior treatment with more than 2 different chemotherapy regimens
- No treatment with systemic corticosteroids, radiation, surgery, or other systemic therapy (other than medical or surgical castration) within 28 days of planned treatment

- No initiation or discontinuation of bisphosphonates within 28 days of planned treatment

Limitations:

Coverage for Provenge®, Q2043, for asymptomatic or minimally symptomatic metastatic castrate-resistant (hormone refractory) prostate cancer is limited to one (1) treatment regimen in a patient's lifetime, consisting of three (3) doses with each dose administered approximately two (2) weeks apart for a total treatment period not to exceed 30 weeks from the first administration. Any claims for Provenge®, that are provided after 30 weeks from the date of the first Provenge® administration shall be denied.

Note: The off-label use of Provenge® for the treatment of prostate cancer is left to the discretion of the Medicare Administrative Contractors (MACs). For a local coverage determination by an individual MAC to cover PROVENGE® off-label for the treatment of prostate cancer, the primary ICD-9 diagnosis code must be either 233.4 (carcinoma in situ of prostate), or 185 (malignant neoplasm of prostate). Note that ICD-9 233.4 may not be used for on-label coverage claims.

Background:

Prostate cancer is the most common non-cutaneous cancer in men in the United States. In 2009, an estimated 192,280 new cases of prostate cancer were diagnosed and an estimated 27,360 deaths were reported. The National Cancer Institute states that prostate cancer is predominantly a cancer of older men; the median age at diagnosis is 72 years. Once the patient has castration-resistant, metastatic prostate cancer the median survival is generally less than two years.

In 2010 the Food and Drug Administration (FDA) approved sipuleucel-T (PROVENGE®; APC8015), for patients with castration-resistant, metastatic prostate cancer. The posited mechanism of action, immunotherapy, is different from that of anti-cancer chemotherapy such as docetaxel. This is the first immunotherapy for prostate cancer to receive FDA approval. The goal of immunotherapy is to stimulate the body's natural defenses (such as the white blood cells called dendritic cells, T-lymphocytes and mononuclear cells) in a specific manner so that they attack and destroy, or at least prevent, the proliferation of cancer cells. Specificity is attained by intentionally exposing a patient's white blood cells to a particular protein (called an antigen) associated with the prostate cancer. This exposure "trains" the white blood cells to target and attack the prostate cancer cells. Clinically, this is expected to result in a decrease in

the size and/or number of cancer sites, an increase in the time to cancer progression, and/or an increase in survival of the patient.

Sipuleucel-T differs from other infused anti-cancer therapies. Most such anti-cancer therapies are manufactured and sold by a biopharmaceutical company and then purchased by and dispensed from a pharmacy. In contrast, once the decision is made to treat with sipuleucel-T, a multi-step process is used to produce sipuleucel-T. Sipuleucel-T is made individually for each patient with his own white blood cells. The patient's white blood cells are removed via a procedure called leukapheresis. In a laboratory the white blood cells are exposed to PA2024, which is a molecule created by linking prostatic acid phosphatase (PAP) with granulocyte/macrophage-colony stimulating factor (GM-CSF). PAP is an antigen specifically associated with prostate cancer cells; GM-CSF is a protein that targets a receptor on the surface of white blood cells. Hence, PAP serves to externally manipulate the immunological functioning of the patient's white blood cells while GM-CSF serves to stimulate the white blood cells into action. As noted in the FDA's clinical review, each dose of sipuleucel-T contains a minimum of 40 million treated white blood cells, however there is "high inherent variability" in the yield of sipuleucel-T from leukapheresis to leukapheresis in the same patient as well as from patient to patient. The treated white blood cells are then infused back into the same patient. The FDA-approved dosing regimen is three doses with each dose administered two weeks apart. The total treatment period is four weeks.

Definitions:

HCPCS Code—Healthcare Common Procedure Coding System - A system of letter and number codes assigned to procedures, medications, supplies and equipment used for pricing and billing.

ICD-9 Code—International Classification of Disease, 9th edition. A standardized classification of disease, injuries, and causes of death, by etiology and anatomic localization and codified into a 6-digit number, which allows clinicians, statisticians, politicians, health planners and others to speak a common language, both US and internationally.

References:

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