HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all of the information needed to use PROVENGE® (sipuleucel-T) safely and effectively. See Full Prescribing Information for PROVENGE.

PROVENGE® (sipuleucel-T)
Suspension for Intravenous Infusion
Initial U.S. Approval: 2010

- - - - - - - INDICATIONS AND USAGE - - - - - - -

PROVENGE is an autologous cellular immunotherapy indicated for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer. (1)

- - - - - DOSAGE AND ADMINISTRATION - - - -

- **For Autologous Use Only**.
- Administer 3 doses at approximately 2-week intervals. (2.1)
- Premedicate patients with oral acetaminophen and an antihistamine such as diphenhydramine. (2.2)
- Before infusion, confirm that the patient's identity matches the patient identifiers on the infusion bag. (2.6)
- **Do not initiate infusion of expired PROVENGE**. (2.7)
- Infuse PROVENGE intravenously over a period of approximately 60 minutes. **Do Not Use a Cell Filter.** (2.7)
- Interrupt or slow infusion for acute infusion reactions, depending on the severity of the reaction. (2.8)

- - - - DOSAGE FORMS AND STRENGTHS - - - -

Each dose of PROVENGE contains a minimum of 50 million autologous $CD54^+$ cells activated with PAP-GM-CSF, suspended in 250 mL of Lactated Ringer's Injection, USP in a sealed, patient-specific infusion bag. (3)

- - - - - - - - - CONTRAINDICATIONS - - - - - - - -

- None. (4)

- - - - - WARNINGS AND PRECAUTIONS - - - - -

- PROVENGE is intended solely for autologous use. (5)
- Acute infusion reactions have been observed in patients treated with PROVENGE. In the event of an acute infusion reaction, the infusion rate may be decreased, or the infusion stopped, depending on the severity of the reaction. Appropriate medical therapy should be administered as needed. Closely monitor patients with cardiac or pulmonary conditions. (2.8, 5.1)
- PROVENGE is **not** routinely tested for transmissible infectious diseases and may transmit diseases to health care professionals handling the product. Universal precautions should be followed. (2.3, 5.2)
- Concomitant use of chemotherapy and immunosuppressive medications with PROVENGE has not been studied. (5.3)

- - - - - - - - - ADVERSE REACTIONS - - - - - - - - -

- The most common adverse reactions (incidence ≥ 15%) are chills, fatigue, fever, back pain, nausea, joint ache, and headache. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Dendreon Corporation at 1-877-336-3736 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revision date: Month/Year

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the Full Prescribing Information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

PROVENGE® (sipuleucel-T) is an autologous cellular immunotherapy indicated for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer.

2 DOSAGE AND ADMINISTRATION

For Autologous Use Only.

For Intravenous Use Only. Do Not Use a Cell Filter.

Do Not Initiate Infusion of Expired Product.

2.1 Dose and Schedule

Each dose of PROVENGE contains a minimum of 50 million autologous $CD54^+$ cells activated with PAP-GM-CSF [*see Description (11)*].

The recommended course of therapy for PROVENGE is 3 complete doses, given at approximately 2-week intervals. In controlled clinical trials, the median dosing interval between infusions was 2 weeks (range 1 to 15 weeks); the maximum dosing interval has not been established.

If, for any reason, the patient is unable to receive a scheduled infusion of PROVENGE, the patient will need to undergo an additional leukapheresis procedure if the course of treatment is to be continued. Patients should be advised of this possibility prior to initiating treatment.

2.2 Premedication

To minimize potential acute infusion reactions such as chills and/or fever, it is recommended that patients be premedicated orally with acetaminophen and an antihistamine such as diphenhydramine approximately 30 minutes prior to administration of PROVENGE [*see Warnings and Precautions (5.1)]*.

2.3 Handling Precautions for Control of Infectious Disease

PROVENGE is **not** routinely tested for transmissible infectious diseases. Therefore, patient leukapheresis material and PROVENGE may carry the risk of transmitting infectious diseases to health care professionals handling the product. Employ universal precautions in handling leukapheresis material or PROVENGE. [*See How Supplied/Storage and Handling (16)*.]

2.4 Storage

The PROVENGE infusion bag must remain within the insulated polyurethane container until the time of administration. Do not remove the insulated polyurethane container from the outer cardboard shipping box. [*See How Supplied/Storage and Handling (16).*]

2.5 Confirm Product Release Before Infusion

Do not infuse PROVENGE until confirmation of product release has been received from Dendreon. Dendreon will send a Cell Product Disposition Form containing the patient identifiers, expiration date and time, and the disposition status (approved for infusion or rejected), to the infusion site. [*See How Supplied/Storage and Handling (16).*]

2.6 Preparation for Infusion

***See How Supplied/Storage and Handling (16)* for full handling instructions.**

Confirm Patient Identity

PROVENGE is intended solely for autologous use. Confirm the proper product has been received according to the label on the outside of the insulated polyurethane container. Prior to PROVENGE infusion, match the patient's identity with the patient identifiers on the Cell Product Disposition Form and the PROVENGE infusion bag.

Inspect the Infusion Bag

Remove the infusion bag from the insulated polyurethane container and inspect the bag for signs of leakage. Do not administer if the bag leaks.

Contents of the bag will be slightly cloudy, with a cream-to-pink color. Gently mix and re-suspend the contents of the bag, inspecting for clumps and clots. Small clumps of cellular material should disperse with gentle manual mixing. Do not administer if the bag leaks during handling or if clumps remain in the bag.

2.7 Administration

Infusion must begin prior to the expiration date and time indicated on the Cell Product Disposition Form and Product Label. **Do not initiate infusion of expired PROVENGE**.

Administer PROVENGE via intravenous infusion over a period of approximately 60 minutes. **Do not use a cell filter.** PROVENGE is supplied in a sealed, patient-specific infusion bag; the entire volume of the bag should be infused.

Observe the patient for at least 30 minutes following each infusion.

2.8 Administration Modification for Infusion Reactions

Acute infusion reactions such as chills, fatigue, fever, nausea, and joint ache were frequently observed in studies of PROVENGE. To mitigate such reactions, premedication, consisting

of acetaminophen and an antihistamine such as diphenhydramine, was administered in clinical studies prior to infusion.

In the event of an acute infusion reaction, the infusion may be interrupted or slowed, depending on the severity of the reaction. Appropriate medical therapy should be administered as needed. In controlled clinical trials, symptoms of acute infusion reactions were treated with acetaminophen, intravenous H1 and/or H2 blockers, and low dose intravenous meperidine.

If the infusion of PROVENGE must be interrupted, the infusion should not be resumed if the PROVENGE infusion bag will be held at room temperature for more than 3 hours. **[***See How Supplied/Storage and Handling (16).*]

3 Dosage Forms and Strengths

Each dose of PROVENGE contains a minimum of 50 million autologous $CD54^+$ cells activated with PAP-GM-CSF, suspended in 250 mL of Lactated Ringer's Injection, USP in a sealed, patient-specific infusion bag.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

PROVENGE is intended solely for autologous use.

5.1 Acute Infusion Reactions

Acute infusion reactions (reported within 1 day of infusion) included, but were not limited to, fever, chills, respiratory events (dyspnea, hypoxia, and bronchospasm), nausea, vomiting, fatigue, hypertension, and tachycardia. In controlled clinical trials, 71.2% of patients in the PROVENGE group developed an acute infusion reaction. The most common events (≥ 20%) were chills, fever, and fatigue. In 95.1% of patients reporting acute infusion reactions, the events were mild or moderate. Fevers and chills generally resolved within 2 days (71.9% and 89.0%, respectively).

In controlled clinical trials, severe (Grade 3) acute infusion reactions were reported in 3.5% of patients in the PROVENGE group. Reactions included chills, fever, fatigue, asthenia, dyspnea, hypoxia, bronchospasm, dizziness, headache, hypertension, muscle ache, nausea, and vomiting. The incidence of severe events was greater following the second infusion (2.1% vs. 0.8% following the first infusion), and decreased to 1.3% following the third infusion. Some (1.2%) patients in the PROVENGE group were hospitalized within 1 day of infusion for management of acute infusion reactions. No Grade 4 or 5 acute infusion reactions were reported in patients in the PROVENGE group.

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