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NCCN Guidelines Panel: Prostate Cancer

On behalf of Dendreon Corporation, I would like to request that the NCCN Prostate Cancer Panel re-evaluate the guidelines for sipuleucel-T (PROVENGE®) in light of the FDA approved label and the recent National Coverage Determination by the Center for Medicare and Medicaid Services (CMS). While the NCCN Guidelines are intended to serve only as guidance to physicians who must individualize their treatment decisions, in practice the NCCN Guidelines are frequently used as the basis for health care payer coverage criteria. We are concerned that the current NCCN Guidelines may lead to some patients who might be appropriate candidates for sipuleucel-T being denied access.

FDA and CMS Indications for sipuleucel-T. The FDA approved indication for sipuleucel-T is for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer. On June 30th 2011, CMS announced that the evidence is adequate to conclude that the use of sipuleucel-T improves health outcomes for Medicare beneficiaries within the FDA label indication, and thus is reasonable and necessary. No restrictions of coverage beyond the FDA label indication, e.g., restrictions based on the clinical trial criteria, were included.

Current NCCN Guidelines. The current NCCN Prostate Cancer Guidelines state:"Sipuleucel-T was added as a category 1 recommendation for patients with metastatic CRPC. However, this treatment is only recommended for patients who have good performance level (ECOG 0-1), estimated life expectancy greater than 6 months, no visceral disease, and no or minimal symptoms."

Change Requested. We request that NCCN consider revising the guideline language to be consistent with the FDA approved label for sipuleucel-T and remove the statement that sipuleucel-T is only recommended for patients who meet criteria pertaining to performance status, life expectancy and presence of visceral disease.

Rationale. Eligibility criteria for clinical trials serve many methodologic purposes that are not necessarily relevant to the determination of which patients would be expected to benefit.

- Performance Status. A patient's likelihood of benefiting from sipuleucel-T is likely a function of his immune status, rather than performance status per se. Patients with asymptomatic or minimally symptomatic disease would be expected to have a reasonable performance status. A diminished performance status in an asymptomatic or minimally symptomatic patient may be due to reasons other than prostate cancer, and some of these patients may still have a reasonable prognosis and immune status, and still benefit from sipuleucel-T.

- Life expectancy. Life expectancy is included as a clinical trial eligibility criterion to increase the probability that patients will live long enough to experience a benefit from the treatment. However, even in the clinical trial setting it is difficult to reliably predict or verify life expectancy prospectively. Patients with a asymptomatic or minimally symptomatic disease

would generally expected to have a life expectancy greater than 6 months. Including this as a requirement for treatment should not therefore be necessary, and runs the risk that some patients will be denied coverage retrospectively if they do not survive more than 6 months.

- Visceral Disease. Visceral metastases are not common in men with asymptomatic or minimally symptomatic prostate cancer. Requiring physicians to rule out the presence of visceral metastases would lead to additional imaging studies which are not part of routine care. Whether or not abnormalities on imaging studies represent metastatic disease is frequently uncertain, and could lead to further work-up, including biopsies which are costly and place the patient at risk for complications. Lung nodules observed on chest x-rays, for example, are relatively common in an elderly patient population. While visceral disease is a negative prognostic indicator in general, certain subgroups of patients, e.g., those with only lung visceral metastases and/or those with more indolent disease progression kinetics, may do as well as other patients without visceral metastases.

Summary. The FDA label and the CMS coverage criteria specify that candidates for sipuleucel-T should have asymptomatic or minimally symptomatic metastatic CRPC. The restriction of sipuleucel-T based on symptomatology adequately defines the group of patients who were included in the sipuleucel-T clinical trials, who have a more favorable prognosis, and who are likely to benefit from treatment with sipuleucel-T. Most patients who are candidates for sipuleucel-T treatment will have a good performance status, no visceral metastases and an anticipated life expectancy greater than 6 months, but there are patients who do not meet one or more of these criteria who may still benefit from treatment. Patients would best be served by allowing physicians the flexibility to use their clinical judgment as to which patients with asymptomatic or minimally symptomatic, metastatic CRPC are candidates for treatment with sipuleucel-T.

Attachments. The following references are submitted in support of this proposed change. We would like to thank the NCCN panel members for their consideration of this change.

1. PROVENGE® (sipuleucel-T) prescribing information. Dendreon Corporation: Seattle, WA. 2011.
2. Decision memo for autologous cellular immunotherapy treatment of metastatic prostate cancer (CAG-00422N). Centers for Medicare & Medicaid Services. 2011