Medical Drug Clinical Criteria

Subject:	Melanoma Vaccines		
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Overview

This document addresses the use of Melanoma Vaccines. Therapeutic cancer vaccines try to refresh the immune system's memory to recognize cancer cells for removal by the body. Melanoma vaccines are immunotherapies which attempt to stimulate and enhance the individual's own immune system to respond to tumor related antigens. They function by creating antibodies or activated T lymphocytes with intended destruction of tumor cells and regression of the melanoma.

Imlygic (talimogene laherparepvec), also known as T-VEC, is currently the only FDA approved melanoma vaccine. It is live, attenuated herpes simplex virus (HSV-1) that has been genetically modified to express human granulocyte macrophage colony-stimulating factor (huGM-CSF). In clinical trials, this product boosted replication and expression of granulocyte macrophage colony-stimulating factor (GM-CSF) with responses observed in both injected and uninjected lesions. GM-CSF induces tumor-specific T-cell responses. Imlygic is FDA approved for local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery. As a limitation of use, FDA notes that it has not been shown to improve overall survival or have an effect on visceral metastases.

The phase III clinical trial for Imlygic included patients with stage IIIB to IV metastatic disease and compared the vaccine to subcutaneous recombinant GM-CSF. The primary outcome of interest was durable response rate (DRR) lasting ≥ 6 months which was significantly higher in the T-VEC arm. However, median overall survival was not significantly different. Exploratory subset analysis of the pivotal clinical trial suggests that Imlygic's response is greater in less advanced disease when measured by the primary outcome of durable response rate (Andtbacka 2015).

National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the use of Imlygic. These include the recommendation for Imlygic as the primary treatment of unresectable stage III disease in transit, local satellite recurrence, or in-transit recurrence. NCCN also recommends for nodal recurrence or distant metastatic disease, but only in certain circumstances. However, NCCN highlights the increased efficacy of Imlygic in individuals with less advanced disease. NCCN also cautions that the efficacy of Imlygic was noted in stage IIIB and IIIC disease, and was more likely to be seen in patients who were treatment naïve.

According to the package insert, Imlygic is contraindicated in immunocompromised patients and pregnant patients. Since it is a live, attenuated herpes simplex virus, it may cause life-threatening disseminated herpetic infection in patients who are immunocompromised. It should not be administered to these patients, including those with a history of primary or acquired immunodeficient states, leukemia, lymphoma, clinical manifestations of human immunodeficiency viruses, and those on immunosuppressive therapy.

Definitions and Measures

According to NCCN, "In-transit metastasis is defined as intralymphatic tumor in skin or subcutaneous tissue more than 2 cm from the primary tumor but not beyond the nearest regional lymph node basin. The presence of microsatellites, clinically evident satellites, and/or regional intransit disease is all part of the biologic continuum of regional lymphatic involvement, and these are all associated with a prognosis similar to that of patients with clinically positive nodes. This is recognized in the staging system with the designation of stage IIIC."

Melanoma: A type of cancer that begins in the melanocytes. Melanoma is also referred to as malignant melanoma and cutaneous melanoma.

Durable response rate: Rate of complete response (CR) plus partial response (PR) lasting > 6 months continuously and beginning within the first 12 months.

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.

Imlygic (talimogene laherparepvec)

Requests for Imlygic (talimogene laherparepvec) may be approved if the following criteria are met:

I. Individual has a diagnosis of unresectable melanoma; **AND**
II. Individual is using as intralesional treatment for one of the following indications:
    A. Stage III disease with clinical or satellite/in-transit metastases; **OR**
    B. Local/satellite recurrence of disease; **OR**
    C. In-transit recurrence of disease.

Requests for Imlygic (talimogene laherparepvec) may not be approvedfor the following:

I. All other indications not included above; **OR**
II. Individual is immunocompromised; **OR**
III. Individual is pregnant.

Other Melanoma Vaccines

Requests for melanoma vaccines, with the exception of talimogene laherparepvec, may not be approved.

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

J9325	Injection, talimogene laherparepvec, per 1 million plaque forming units [IMLYGIC]
J3590	Unclassified biologics [when specified as a melanoma vaccine other than IMLYGIC]

ICD-10 Diagnosis

C43.0-C43.9	Malignant melanoma of skin

Document History

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- 02/24/2023 – Annual Review: No changes. Coding Reviewed: No changes.
- 02/25/2022 – Annual Review: No changes. Coding Reviewed: No changes.
- 02/19/2021 – Annual Review: No changes. Coding Reviewed: No changes.
- 02/21/2020 – Annual Review: Wording and formatting changes for clarity; Add may not be approved criteria for immunocompromised and pregnant patients. Coding reviewed: No changes
- 05/17/2019 – Annual Review: First review of Melanoma Vaccines clinical criteria. No changes. Coding Reviewed: No changes.

References

1. Andtbacka RH, Agarwala SS, Ollila DW, et al. Cutaneous head and neck melanoma in OPTiM, a randomized phase 3 trial of talimogene laherparepvec versus granulocyte-macrophage colony-stimulating factor for the treatment of unresected stage IIIB/IIIC/IV melanoma. Head Neck. 2016; 38(12):1752-1758.
2. Andtbacka RH, Kaufman HL, Collichio F, et al. Talimogene laherparepvec improves durable response rate in patients with advanced melanoma. J Clin Oncol. 2015; 33(25):2780-2788.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 20, 2023.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.

6. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 20, 2023.
    a. Cutaneous Melanoma. V1.2023. Revised December 22, 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.