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# Drug Policy

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| **Policy:** | **201834-CC** | **Initial Effective Date: 10/20/2018** |
| **Code(s):** | **HCPCS J9325** | **Annual Review Date:** |
| **SUBJECT:** | **Imlygic® (talimogene laherparepvec )** | **Last Revised Date:** |

**Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.**

**Overview**
Imlygic is an oncolytic viral therapy indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.[1] It is a limitation of use that Imlygic has not been shown to improve overall survival or have an effect on visceral metastases.

**Disease Overview**
Oncolytic virus immunotherapy is a form of cancer therapy which uses native or genetically modified viruses to selectively enter, replicate, and lyse tumor cells.[2] Oncolytic viruses are able to be engineered to deliver therapeutic genes to cancer cells, thus, causing additional antitumor effects through cytokine secretion and induction of antitumor immune response.[3] Of note, herpes simplex virus (HSV)-1 is an attractive option for oncolytic virus therapy because it can infect a wide range of host cells and causes lysis following viral replication.[2]

Imlygic, previously referred to as T-VEC, is the first oncolytic virus immunotherapy approved in the US. It is genetically modified to attenuate HSV-1, increase selectivity for cancer cells, and secrete granulocyte macrophage colony-stimulating factor (GM-CSF). Secretion of GM-CSF is intended to enhance tumor antigen presentation to the immune system and induce systemic immune responses to the tumors.[3]

**Guidelines**
The National Comprehensive Cancer Network (NCCN) guidelines for melanoma (version 2.2018 – January 19, 2018) list Imlygic as an option for primary treatment of locally advanced (stage III) melanoma, treatment of recurrent disease, and for extracranial lesions in patients with disseminated distant metastatic disease.

**Policy Statement**
This policy involves the use of Imlygic. Prior authorization is recommended for medical benefit coverage of Imlygic. Coverage is recommended for those who meet the conditions of coverage in the **Criteria, Preferred Drug, Dosing, Initial/Extended Approval, Duration of Therapy, and Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions. **Exclusions** are listed following the recommended authorization criteria and Waste Management section.

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Because of the of the specialized skills required for evaluation and diagnosis of patients treated with Imlygic as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Imlygic to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is required, a response to therapy is required for continuation of therapy.

**Recommended Authorization Criteria**

**FDA-Approved Indications**

**1. Melanoma.**

**Criteria.** *The patient must meet ONE of the following (A OR B)*:

**A)** Initial Therapy (This includes reinitiation in patients with new lesions following a complete response). The patient meets ALL of the following (i, ii, and iii):

- **i.** The patient is an adult ≥ 18 years of age; AND
- **ii.** Imlygic will be directly injected into recurrent or unresectable cutaneous, subcutaneous, or nodal lesions; AND
- **iii.** Imlygic will be administered by or under the supervision of an oncologist, dermatologist, or surgeon.

**B)** Patinet is Currently Receiving Imlygic. The patient meets ALL of the following (i, ii, and iii):

- **i.** The patient has remaining injectable lesions for treatment; AND
- **ii.** According to the prescriber, the patient has not experienced clinically relevant disease progression (e.g., disease progression associated with a decline in performance status and/or alternative therapy was needed); AND
- **iii.** Imlygic will be administered by or under the supervision of an oncologist, dermatologist, or surgeon.

In the pivotal study evaluating Imlygic, all patients were adults with unresectable stage III (30%) or stage IV (70%) melanoma. During the initial 6 months of the trial, treatment continued despite increased size or number of lesions. Following 6 months of treatment, patients could continue Imlygic until clinically relevant disease progression (i.e., disease progression associated with a decline in performance status and/or alternative therapy was needed, according to the prescriber). Imlygic requires specialized storage conditions (-130° to -94° F). Personal protective equipment (including a gown/laboratory coat, safety glasses or face shield, and gloves) while preparing or administering, and procedures for accidental exposure to Imlygic should be followed. Healthcare providers should be prepared to manage adverse events, including immune-mediated events (e.g., glomerulonephritis, vasculitis, pneumonitis) and plasmocytoma at the injection site.

**Dosing in Melanoma.** *Dosing must meet the following*:
*Initial Dose*. $10^6$ (1 million) plaque-forming units (PFU)/mL up to a maximum of 4 mL per treatment visit
*Subsequent Doses (including reinitiation)*. $10^8$ (100 million) PFU per mL up to a maximum of 4 mL per treatment visit; the second dose is given 3 weeks after the initial dose, then all subsequent doses (including reinitiation) are given once every 2 weeks.

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In the pivotal trial, the initial dose of Imlygic was administered at $10^6$ PFU/mL (to seroconvert HSV-seronegative patients). Subsequent doses were $10^8$ PFU/mL administered 3 weeks after the first dose, then every 2 weeks. Total volume of Imlygic was up to 4.0 mL per treatment session. It may not be possible to inject all lesions at each treatment visit or over the full course of treatment. Previously injected and/or uninjected lesions may be injected at subsequent treatment visits. Continue treatment for at least 6 months unless other treatment is required or until there are no injectable lesions to treat. Imlygic may be reinitiated if new unresectable cutaneous, subcutaneous, or nodal lesions appear after a complete response.

**Initial Approval/Extended Approval.**
*Initial Approval*: 6 months
*Extended Approval*: 12 months

**Duration of therapy in Melanoma.** If tolerated, Imlygic should be administered for at least 6 months, then continued until no injectable lesions remain or clinically relevant disease progression, according to the prescriber.

Imlygic should be continued for at least 6 months, unless other treatment is required or there are no injectable lesions to treat and may also be reinitiated if new unresectable cutaneous, subcutaneous, or nodal lesions appear following a complete response. In the pivotal trial, patients were treated for at least 6 months, or until no remaining injectable lesions.

**Labs/Diagnostics.** None required.

**2. Other Cancer Indications.** Forward to the Medical Director for review on a case-by-case basis..

**Waste Management.** Determine dose volume based on lesion size. The total injection volume for each treatment visit should not exceed 4 mL for all injected lesions.

| Lesion Size (longest dimension) | Injection volume |
|---|---|
| > 5 cm | Up to 4 mL |
| > 2.5 cm to 5 cm | Up to 2 mL |
| > 1.5 cm to 2.5 cm | Up to 1 mL |
| > 0.5 cm to 1.5 cm | Up to 0.5 mL |
| ≤ 0.5 cm | Up to 0.1 mL |

**CONDITIONS NOT RECOMMENDED FOR APPROVAL**
Imlygic has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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1. **Concurrent Use with Anti-Herpetic Viral Agents.** Imlygic is a genetically modified, live, attenuated HSV-1 that is sensitive to acyclovir. Anti-herpetic viral agents (e.g., acyclovir, valacyclovir, famciclovir) may interfere with efficacy.

2. **Immoncompromised Patients.** Imlygic is contraindicated in patients who are immunocompromised, including those with a history of primary or acquired immunodeficient states, leukemia, lymphoma, acquired immunodeficiency syndrome (AIDS), or other clinical manifestations of infection with human immunodeficiency viruses, and those on immunosuppressive therapy.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

**Documentation Requirements:**

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

## REFERENCES


1. Imlygic intralesional injection [prescribing information]. Thousand Oaks, CA: BioVex/Amgen; March 2017.
2. Dharmadhikari N, Mehnert JM, Kaufman HL. Oncolytic virus immunotherapy for melanoma. *Curr Treat Options Oncol*. 2015;16(3):326.
3. Moehler M, Goepfert K, Heinrich B, et al. Oncolytic virotherapy as emerging immunotherapeutic modality: potential of parvovirus h-1. *Front Oncol*. 2014;4:92.
4. The NCCN Melanoma Clinical Practice Guidelines in Oncology (Version 2.2018 – January 19, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 4, 2018.


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## FOR MEDICAL BENEFIT COVERAGE REQUESTS:

**Prior approval is required for HCPCS Codes J9325**


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| HCPCS Code(s): | |
|---|---|
| J9325 | Injection, talimogene laherparepvec, per 1 million plaque forming units |

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