Imlygic™ (talimogene laherparepvec)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- Imlygic 10^6 (1 million) PFU per mL: 4 mL one time only
- Imlygic 10^8 (100 million) PFU per mL: 4 mL three weeks after initial treatment followed by 4 mL every two weeks thereafter

B. Max Units (per dose and over time) [Medical Benefit]:

Initial treatment:	4 billable units
Second treatment:	400 billable units occurring 3 weeks after initial treatment
All subsequent treatments:	400 billable units occurring 2 weeks after previous treatment

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is 18 years of age or older; **AND**
- Patient is not pregnant; **AND**
- Patient is not immunocompromised; **AND**
- Imlygic must be administered intralesionally; **AND**

Cutaneous Melanoma †

- Patient has stage IIIB to stage IV disease; **AND**
- Patient has one of the following:
  - Unresectable, distant metastatic disease (excluding visceral metastatic disease [stage IVM1b]); **OR**
  - Unresectable or incomplete resection of nodal recurrence: **OR**
  - Used as first or second line therapy; **AND**
    - Unresectable stage III with clinical satellite or in-transit metastases; **OR**
    - Local/satellite and/or in-transit unresectable recurrence; **OR**

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s)

IV. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: herpetic infection, injection site complications (necrosis, ulceration, cellulitis and systemic bacterial infection), immune-mediated events, plasmacytoma at injection site, obstructive airway disorder, etc.; **AND**
- Patient continues to have injectable lesions to treat; **AND**
- Tumor response with stabilization of disease or decrease in size of tumor or tumor spread

V. Dosage/Administration

Indication	Dose
Melanoma	**Initial Treatment** • Imlygic 10^6 (1 million) PFU per mL • Inject largest lesion(s) first • Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated
	Second Treatment • Imlygic 10^8 (100 million) PFU per mL • 3 weeks after initial treatment • Inject any new lesion(s) (lesions that have developed since initial treatment) first. • Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated.
	All subsequent Treatments (including reinitiation) • Imlygic 10^8 (100 million) PFU per mL • 2 weeks after previous treatment • Inject any new lesion(s) (lesions that have developed since previous treatment) first. • Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated.
The total injection volume for each treatment visit should not exceed 4 mL for all injected lesions combined. 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 lesion(s) may be injected at subsequent treatment visits.	

Lesion size (longest dimension)	Intralesional 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

- Store and transport at −90°C to −70°C (−130°F to −94°F), thaw immediately prior to administration.
- Protect from light, store in the carton until use.

VI. Billing Code/Availability Information

Jcode:

- J9325 - Injection, talimogene laherparepvec, per 1 million plaque forming units

NDC(s):

- Imlygic 10^6 (1 million) PFU per mL is light green, single-use vial (NDC 55513-0078-01)
- Imlygic 10^8 (100 million) PFU per mL is royal blue, single-use vial (NDC 55513-0079-01)

VII. References

1. Imlygic [package insert]. Thousand Oaks, CA; Amgen Inc; December 2018. Accessed May 2019.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for talimogene laherparepvec. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed May 2019.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Cutaneous Melanoma, Version 2.2019. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed May 2019.
4. Magellan Health, Magellan Rx Management. Imlygic Clinical Literature Review Analysis. Last updated May 2019. Accessed May 2019.
5. Andtbacka RH, Kaufman HL, Collichio F, et al. Talimogene Laherparepvec Improves Durable Response Rate in Patients With Advanced Melanoma. J Clin Oncol. 2015 Sep 1;33(25):2780-8.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C43.0	Malignant melanoma of lip
C43.10	Malignant melanoma of unspecified eyelid, including canthus

ICD-10	ICD-10 Description
C43.11	Malignant melanoma of right eyelid, including canthus
C43.12	Malignant melanoma of left eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified
C80.0	Disseminated malignant neoplasm, unspecified
C80.1	Malignant (primary) neoplasm, unspecified
Z85.820	Personal history of malignant melanoma of skin

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Appendix 3 - CLINICAL LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate; DRR = durable response rate

Cutaneous Melanoma

Primary treatment							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Talimogene laherparepvec (T-VEC)	1 preferred (for stage III disease or local satellite/ in-transit recurrence)	Yes (unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery)	Phase 3 (OPTiM), randomized, open-label	Granulocyte macrophage colony-stimulating factor (GM-CSF)	DRR (ORR ≥ 6 months)	All lines of therapy	• T-VEC resulted in a higher DRR (P < .001) and longer median OS (P = .051), particularly in untreated patients or those with stage IIIB, IIIC, or IVM1a disease.
Bacillus Calmette-Guerin (BCG)	2B						
Interferon	2B						
Interleukin-2	2B						