STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Opdualag (nivolumab and relatlimab-rmbw)
PAM-057

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	10/01/2022
Revision Number:	2	**Last Rev Date:**	07/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	07/18/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	07/21/2023

Overview

Medication:[1]	nivolumab and relatlimab-rmbw
Brand Name:	Opdualag®
Pharmacologic Category:	Antineoplastic; programmed death receptor-1 (PD-1) blocking antibody and lymphocyte activation gene-3 (LAG-3) blocking antibody
FDA-Approved Indication(s):	Treatment of unresectable or metastatic melanoma in: • Adult patients • Pediatric patients 12 years of age and older who weight at least 40 kg
How Supplied:	20 mL single-dose vial containing 240 mg of nivolumab and 80 mg of relatlimab
Dosage and Administration:	40 mL (480 mg nivolumab and 160 mg relatlimab) administered intravenously (IV) every 4 weeks until disease progression or unacceptable toxicity
Benefit Category:	Medical

Descriptive Narrative

Survival rates for people with melanoma depend on the stage of the disease at the time of diagnosis, so early diagnosis is crucial to improve patient outcome and save lives. Although most melanomas are detected by patients themselves, clinician detection is associated with thinner, more curable tumors. Most patients with thin, invasive melanoma (Breslow thickness ≤1 mm) can expect prolonged disease-free survival and likely cure following treatment.[2]

Surgery remains the primary treatment modality for cutaneous melanoma, with the goals of both durable local control and cure in patients without occult regional nodal or distant metastasis. For patients with nodal involvement or metastasis, systemic therapy is typically required.

In the United States, melanoma is the fifth most common cancer in men and women, and its incidence increases with age. It is rare in individuals younger than 20 years of age, with an estimated annual incidence rate of nine per million in those aged 15 to 19 years old (and is even rarer in younger children).[3] The American Cancer Society estimates that there will be 1,380 new cases of melanoma of the skin and 100 deaths in the state of Iowa in 2024.[4]

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[5]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines® for Melanoma: Cutaneous (Version 2.2024 – April 3, 2024)[6]

NCCN Guidelines® Recommendation(s) for nivolumab and relatlimab-rmbw (Opdualag®)
(1) Systemic therapy for metastatic or unresectable disease A. Systemic therapy for metastatic or unresectable disease i. First-line therapy: Nivolumab and relatlimab-rmbw (Category 1, preferred [a, b]) ii. Second-line or subsequent therapy [c]: Nivolumab and relatlimab-rmbw (Category 2A, preferred [a, b]) (2) Systemic therapy considerations: recommendations for patients who progress on systemic therapy A. BRAF V600 mutation present: for patients who progress on immunotherapy, options include the following (if not already received): Nivolumab and relatlimab-rmbw (Category 2A) B. For patients who progress following BRAF/MEK inhibitor combination therapy, consider the following options (if not previously received): Nivolumab and relatlimab-rmbw (Category 2A) C. BRAF V600 mutation NOT present: For patients with progression on anti-PD-1 monotherapy, consider the following options (if not already received): Nivolumab and relatlimab-rmbw (Category 2A) [a] Testing for tumor PD-L1 should not guide clinical decision-making. The utility of this biomarker requires further investigation. [b] The combination nivolumab and relatlimab-rmbw is associated with higher PFS but more frequent and more severe toxicity than nivolumab alone. Nivolumab and relatlimab-rmbw showed a 9%–12% objective response rate in patients with PD-1/PD-L1 refractory disease. [c] For patients who experience progression of melanoma during or shortly after adjuvant or first-line therapy, consider second-line agents if not used first line and if from a different class. For patients who progressed on single-agent anti-PD-1 checkpoint immunotherapy, anti-PD-1/ipilimumab or nivolumab and relatlimab combination immunotherapy, or BRAF/MEK inhibitor combination therapy are reasonable treatment options. Ipilimumab monotherapy may also be considered, though it is less effective than combination therapy. For patients who experience disease control (CR, PR, or SD) and have no residual toxicity, but subsequently experience disease progression/relapse >3 months after treatment discontinuation, reinduction with the same agent or same class of agents may be considered.

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Criteria

Prior authorization is required.

Opdualag® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of unresectable or metastatic melanoma; **AND**
2. Member meets **ALL** of the following:
    a. 12 years of age or older; **AND**
    b. Body weight is at least 40 kg; **AND**
3. Member does **NOT** have active brain metastases or leptomeningeal metastases; **AND**
4. Prescribed by, or in consultation with, an oncologist; **AND**
5. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 40 mL (480 mg nivolumab and 160 mg relatlimab) administered intravenously once every 4 weeks; **OR**
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Opdualag® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist; **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 40 mL (480 mg nivolumab and 160 mg relatlimab) administered intravenously once every 4 weeks; **OR**
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits	40 mL (480 mg nivolumab & 160 mg relatlimab) every 4 weeks until disease progression or unacceptable toxicity	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9298	Injection, nivolumab and relatlimab-rmbw, 3 mg/1 mg

ICD-10	Description
C43	Malignant melanoma of skin [excludes melanoma in situ (D03–D03.9), malignant melanoma of skin of genital organs (C51–C52; C60–C60.9; C63–C63.9), Merkel cell carcinoma (C4A–C4A.9), and sites other than skin (code to malignant neoplasm of the site)]

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/ Pkg
00003-7125-11 (240 mg nivolumab and 80 mg relatlimab per 20 mL single-dose vial)	Bristol-Myers Squibb Company (00003)	3 mg/1 mg	1	EA	80

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Opdualag® prescribing information (03/2024). Bristol-Myers Squibb Company: Princeton, NJ. Available online at www.opdivohcp.com/efficacy/melanoma/opdualag. Accessed May 24, 2024.

[2] Swetter S, Geller AC. Melanoma: Clinical features and diagnosis. Corona R, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 8, 2024.

[3] Hawryluk EB, Pappo AS, et al. Melanoma in children. Corona R, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 8, 2024.

[4] Cancer Statistics Center – State of Iowa. American Cancer Society. Available online at cancerstatisticscenter.cancer.org/#!/state/Iowa. Accessed June 8, 2024.

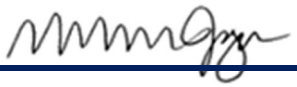
[5] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 11, 2023.

[6] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Melanoma: Cutaneous (v. 2.2024 – April 3, 2024). Accessed June 8, 2024. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
07/19/2024	CAC	Annual review. Updated melanoma statistics for Iowa for 2024. Reviewed and updated NCCN Guidelines®. Added dosing information into criteria. Updated references.	2
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
07/21/2023	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee