

Medical Policy:

Opdualag (nivolumab and relatlimab-rmbw) intravenous infusion

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.355	March 4, 2025	May 12, 2022

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The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as “EmblemHealth”), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions:

Opdualag, a combination of a programmed death receptor-1 (PD-1) blocking antibody and a lymphocyte activation gene-3 (LAG-3) blocking antibody, is indicated for the treatment of unresectable or metastatic melanoma in patients ≥ 12 years of age

Length of Authorization:

Coverage will be provided for 12 months

Dosing Limits [Medical Benefit]:

- Approve 480 mg of nivolumab and 160 mg of relatlimab administered by intravenous infusion no more frequently than once every 4 weeks.
 - 160 billable units (480 mg nivolumab/160 mg relatlimab) every 28 days

Guideline:

Initial Criteria

1. **Melanoma.** Approve if the patients meet the following criteria (A, B, C, **AND** D):
 - A. Patient is \geq 12 years of age; **AND**
 - B. Patient weighs \geq 40kg; **AND**
 - C. Patient has unresectable or metastatic disease; **AND**
 - D. Prescribed by or in consultation with an Oncologist; **AND**
 - E. Patient has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy (e.g., cemiplimab, avelumab, pembrolizumab, atezolizumab, durvalumab, dostarlimab, retifanlimab, nivolumab, toripalimab, etc.), unless otherwise specified ^Δ; **AND**
 - i. Used as first-line therapy; **OR**
 - ii. Used as subsequent therapy for disease progression if single-agent anti-PD-1 therapy or combination checkpoint blockade was not previously used; **OR**
 - iii. Used as re-induction therapy in patients with prior combination anti-PD-1/LAG-3 therapy that resulted in disease control (i.e., complete response, partial response, or stable disease) with no residual toxicity, but with disease progression or relapse $>$ 3 months after treatment discontinuation

**Metastatic disease includes stage III unresectable/borderline resectable disease with clinically positive node(s) or clinical satellite/in-transit metastases, as well as unresectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease.*

^Δ Notes:

- Patients who complete adjuvant therapy and progress \geq 6 months after discontinuation are eligible to re-initiate PD-directed therapy for metastatic disease.
- Patients whose tumors, upon re-biopsy, demonstrate a change in actionable mutation (e.g., MSS initial biopsy; MSI-H subsequent biopsy) may be eligible to re-initiate PD-directed therapy and will be evaluated on a case-by-case basis

Renewal Criteria

1. Member is responding positively to therapy, as determined by the prescriber; **AND**
2. Member has not experienced unacceptable toxicity from the drug

Dosing/Administration:

The recommended dose in patients \geq 12 years of age and weighing \geq 40 kg is 480 mg of nivolumab and 160 mg of relatlimab administered by intravenous (IV) infusion once every 4 weeks until disease progression or unacceptable adverse events.

Applicable Procedure Codes

Code	Description
J9298	Injection, nivolumab and relatlimab-rmbw, 3 mg/1 mg; 1 billable unit = 3 mg nivolumab/1 mg relatlimab

Applicable NDC Codes

Code	Description
00003-7125-11	80 mg relatlimab and 240 mg nivolumab 20 mL (single-dose vial)

ICD-10 Diagnoses

Code	Description
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C43	Malignant melanoma of skin
C43.0	Malignant melanoma of lip
C43.1	Malignant melanoma of eyelid, including canthus
C43.10	Malignant melanoma of unspecified eyelid, including canthus
C43.11	Malignant melanoma of right eyelid, including canthus
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.12	Malignant melanoma of left eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.2	Malignant melanoma of ear and external auricular canal
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
C43.3	Malignant melanoma of other and unspecified parts of face
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
C43.5	Malignant melanoma of trunk
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.6	Malignant melanoma of upper limb, including shoulder
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
C43.7	Malignant melanoma of lower limb, including hip
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
C21	Malignant neoplasm of anus and anal canal
C21.0	Malignant neoplasm of anus, unspecified
C21.1	Malignant neoplasm of anal canal
C51	Malignant neoplasm of vulva
C51.0	Malignant neoplasm of labium majus
C51.1	Malignant neoplasm of labium minus
C51.2	Malignant neoplasm of clitoris
C51.9	Malignant neoplasm of vulva, unspecified
C52	Malignant neoplasm of vagina
C57	Malignant neoplasm of other and unspecified female genital organs
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C57.9	Malignant neoplasm of female genital organ, unspecified

C60	Malignant neoplasm of penis
C60.0	Malignant neoplasm of prepuce
C60.1	Malignant neoplasm of glans penis
C60.8	Malignant neoplasm of overlapping sites of penis
C60.9	Malignant neoplasm of penis, unspecified
C63	Malignant neoplasm of other and unspecified male genital organs
C63.0	Malignant neoplasm of epididymis
C63.00	Malignant neoplasm of unspecified epididymis
C63.01	Malignant neoplasm of right epididymis
C63.02	Malignant neoplasm of left epididymis
C63.1	Malignant neoplasm of spermatic cord
C63.10	Malignant neoplasm of unspecified spermatic cord
C63.11	Malignant neoplasm of right spermatic cord
C63.12	Malignant neoplasm of left spermatic cord
C63.2	Malignant neoplasm of scrotum
C63.7	Malignant neoplasm of other specified male genital organs
C63.8	Malignant neoplasm of overlapping sites of male genital organs
C63.9	Malignant neoplasm of male genital organ, unspecified
Z51.12	Encounter for antineoplastic immunotherapy

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	3/04/2025	Annual Review: Initial Criteria: Melanoma: Added: "Patient has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy (e.g., cemiplimab, avelumab, pembrolizumab, atezolizumab, durvalumab, dostarlimab, retifanlimab, nivolumab, toripalimab, etc.), unless otherwise specified ^Δ ; AND Used as first-line therapy; OR nUsed as subsequent therapy for disease progression if single-agent anti-PD-1 therapy or combination checkpoint blockade was not previously used; OR Used as re-induction therapy in patients with prior combination anti-PD-1/LAG-3 therapy that resulted in disease control (i.e., complete response, partial response, or stable disease) with no residual toxicity, but with disease progression or relapse >3 months after treatment discontinuation *Metastatic disease includes stage III unresectable/borderline resectable disease with clinically positive node(s) or clinical satellite/in-transit metastases, as well as unresectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease. ^Δ Notes: • Patients who complete adjuvant therapy and progress ≥ 6 months after discontinuation are eligible to re-initiate PD-directed therapy for metastatic disease. • Patients whose tumors, upon re-biopsy, demonstrate a change in actionable mutation (e.g., MSS initial biopsy; MSI-H subsequent biopsy) may be eligible to re-initiate PD-directed therapy and will be evaluated on a case-by-case basis"
EmblemHealth & ConnectiCare	1/29/2024	Annual Review: Removed J9999
EmblemHealth & ConnectiCare	5/24/2023	Annual Review: removed code:C9399, added code J9298
EmblemHealth & ConnectiCare	5/12/2022	New Policy

References

1. Opdualag (nivolumab/relatlimab) [packaging insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022. Accessed April 14, 2022.
2. Opdualag. IBM Micromedex [database online]. Princeton, NJ: Bristol-Myers Squibb Company; March 2022. Available at: <https://www.micromedexsolutions.com>. Updated April 11, 2022. Accessed April 14, 2022.