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

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 ≥ 12 years of age; **AND**
   B. Patient weighs ≥ 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 ≥ 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 ≥ 12 years of age and weighing ≥ 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

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.