



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 04/16/2026

Nivolumab Products

Opdivo® (nivolumab)

Opdivo Qvantig™ (nivolumab and hyaluronidase-nvhy)

HCPCS: Opdivo: J9299; Opdivo Qvantig: J9289

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. Treatment must follow the Food and Drug Administration (FDA) approved indications or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1 or 2A recommendation
 - i. Must be used with concomitant treatment according to FDA indication or NCCN Category 1 or 2A recommendation
 - b. Must be prescribed by, or in consultation with, an oncologist or hematologist
 - c. No prior failure of a programmed death receptor-1 (PD-1 or PD-L1) inhibitor
 - d. Patient is not receiving therapy for a chronic condition, such as an autoimmune disease, that requires treatment with a systemic immunosuppressant
 - e. Trial and failure, intolerance, or a contraindication to the preferred products as listed in the BCBSM/BCN utilization management medical drug list
- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity Limit: Align with FDA recommended dosing
 - b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time
 - c. Renewal Criteria:
 - i. Metastatic non-small cell lung cancer: Treatment until unacceptable toxicity or disease progression for up to a total of 24 months of therapy
 - ii. All other indication: Treatment may be continued until unacceptable toxicity or disease progression

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

Background Information:

- Opdivo is programmed death receptor-1 (PD-L1)-blocking antibody indicated for the following:
 - For adult and pediatric patients 12 years and older with unresectable or metastatic melanoma, as a single agent or in combination with ipilimumab
 - For the adjuvant treatment of adult and pediatric patients 12 years and older with completely resected Stage IIB, Stage IIC, Stage III, or Stage IV melanoma
 - Adult patients with resectable (tumors ≥ 4 cm or node positive) non-small cell lung cancer in the neoadjuvant setting, in combination with platinum-doublet chemotherapy
 - Adult patients with resectable (tumors ≥ 4 cm or node positive) non-small cell lung cancer and no known EGFR mutations or ALK rearrangements, for neoadjuvant treatment, in combination with platinum-doublet chemotherapy, followed by single-agent Opdivo as adjuvant treatment after surgery
 - Adult patients with metastatic non-small cell lung cancer expressing PD-L1 ($\geq 1\%$) as determined by an FDA-approved test, with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations, as first-line treatment in combination with ipilimumab
 - Adult patients with metastatic or recurrent non-small cell lung cancer with no EGFR or ALK genomic tumor aberrations as first-line treatment, in combination with ipilimumab and 2 cycles of platinum-doublet chemotherapy
 - Patients with metastatic non-small cell lung cancer and progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo
 - Adult patients with unresectable malignant pleural mesothelioma, as first-line treatment in combination with ipilimumab
 - Adult patients with intermediate or poor risk advanced renal cell carcinoma, as a first-line treatment in combination with ipilimumab
 - Adult patients with advanced renal cell carcinoma, as a first-line treatment in combination with cabozantinib
 - Adult patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy
 - Adult patients with classical Hodgkin lymphoma that has relapsed or progressed after:
 - Autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or
 - 3 or more lines of systemic therapy that includes autologous HSCT
 - Adult patients with recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy
 - Adjuvant treatment of adults patients with urothelial carcinoma who are at high risk of recurrence after undergoing radical resection of urothelial carcinoma

- Adult patients with unresectable or metastatic urothelial carcinoma, as first-line treatment in combination with cisplatin and gemcitabine
- Adult patients with locally advanced or metastatic urothelial carcinoma who:
 - Have disease progression during or following platinum-containing chemotherapy
 - Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
- Adult and pediatric patients 12 years of age or older with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC) in combination with ipilimumab
- Adult and pediatric patients 12 years of age and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan
- Adult patients with unresectable or metastatic hepatocellular carcinoma, as a first-line treatment in combination with ipilimumab
- Adult patients with hepatocellular carcinoma who have been previously treated with sorafenib in combination with ipilimumab
- Adult patients with completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease who have received neoadjuvant chemoradiotherapy
- Adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma as first-line treatment in combination with fluoropyrimidine- and platinum-containing chemotherapy.
- Adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma as first-line treatment in combination with ipilimumab
- Adult patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma after prior fluoropyrimidine- and platinum-based chemotherapy
- Adult patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma in combination with fluoropyrimidine- and platinum-containing chemotherapy
- Opdivo Qvantig is programmed death receptor-1 (PD-L1)-blocking antibody indicated for the following:
 - Adult patients with intermediate or poor risk advanced renal cell carcinoma, as a first-line treatment following combination treatment with intravenous nivolumab and ipilimumab
 - Adult patients with advanced renal cell carcinoma, as a first-line treatment in combination with cabozantinib
 - Adult patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy
 - Adult and pediatric patients 12 years and older who weigh 30 kg or greater with unresectable or metastatic melanoma

- Adult and pediatric patients 12 years and older who weigh 30 kg or greater with unresectable or metastatic melanoma following combination treatment with intravenous nivolumab and ipilimumab
- For the adjuvant treatment of adult and pediatric patients 12 years and older who weigh 30 kg or greater with completely resected stage IIB, stage IIC, stage III, or stage IV melanoma
- Adult patients with resectable (tumors $\geq$ 4 cm or node positive) non-small cell lung cancer in the neoadjuvant setting, in combination with platinum-doublet chemotherapy
- Adult patients with resectable (tumors $\geq$ 4 cm or node positive) non-small cell lung cancer and no known EGFR mutations or ALK rearrangements, for neoadjuvant treatment, in combination with platinum-doublet chemotherapy, followed by Opdivo Qvantig monotherapy as adjuvant treatment after surgery
- Adult patients with metastatic non-small cell lung cancer and progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo Qvantig
- Adult patients with recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy
- As adjuvant treatment of adult patients with urothelial carcinoma who are at high risk of recurrence after undergoing radical resection of urothelial carcinoma
- Adult patients with unresectable or metastatic urothelial carcinoma, as first-line treatment in combination with cisplatin and gemcitabine
- Adult patients with locally advanced or metastatic urothelial carcinoma who:
 - Have disease progression during or following platinum-containing chemotherapy
 - Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
- Adult and pediatric patients 12 years and older who weigh 30 kg or greater with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC), following combination treatment with intravenous nivolumab and ipilimumab
- Adult and pediatric patients 12 years and older who weigh 30 kg or greater with MSI-H or dMMR metastatic CRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan
- Adult patients with unresectable or metastatic HCC, as a first-line treatment following combination treatment with intravenous nivolumab and ipilimumab
- Adult patients with hepatocellular carcinoma previously treated with sorafenib and following combination treatment with intravenous nivolumab and ipilimumab
- Adult patients with completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease, who have received neoadjuvant chemoradiotherapy
- Adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma as first-line treatment in combination with fluoropyrimidine- and platinum-containing chemotherapy

- Adult patients with unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma after prior fluoropyrimidine and platinum-based chemotherapy
- Adult patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma in combination with fluoropyrimidine- and platinum-containing chemotherapy
- Limitations of Use: Opdivo Qvantig is not indicated in combination with ipilimumab
- The National Comprehensive Cancer Network (NCCN) guidelines category 1 and 2A recommendations are based on uniform NCCN consensus that the recommendations are appropriate. Treatment regimens have been studied and shown to be efficacious when administered as listed in the guidelines. Category 2B and 3 recommendations do not have a high level of evidence to support use and also do not have a uniform consensus from the NCCN panel that the recommendations are appropriate.
- There are no studies to support use of Opdivo or Opdivo Qvantig following failure. NCCN treatment guidelines also do not recommend use of Opdivo or other PD-L1 checkpoint inhibitors following a previous failure.
- Opdivo and Opdivo Qvantig have not been studied in patients on chronic immunosuppressant therapy and therefore, should not be used in patients on chronic immunosuppressants.
- Opdivo and Opdivo Qvantig have not been studied in patients with an ECOG performance status of greater than 2 and therefore, should not be used in patients with an ECOG score greater than 2.

References:

1. Opdivo [prescribing information]. Princeton, NJ: Bristol-Myers Squibb; June 2025.
2. Opdivo Qvantig [prescribing information]. Princeton, NJ: Bristol Myers Squibb Company; November 2025.
3. Sharma P, Retz M, Siefker-Radtke A, et al. Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial. *Lancet Oncol*. 2017 Mar; 18 (3): 312-22.
4. Overman MJ, McDermott R, Leach JL, et al. Nivolumab in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142): an open-label, multicentre, phase 2 study. *Lancet Oncol*. 2017 Sep; 18 (9): 1182 - 91.
5. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined nivolumab and ipilimumab or monotherapy in untreated melanoma. *NEJM*. 2015 Jul 2; 373 (1): 23 - 34.
6. Ferris RL, Blumenschein Jr G, Fayette J, et al. Nivolumab for recurrent squamous-cell carcinoma of the head and neck. *NEJM*. 2016 Nov 10; 375 (19): 1856 – 67.
7. Yau T, Kang Y, Kim T, et al. Efficacy and safety of nivolumab plus ipilimumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib: the CheckMate 040 randomized clinical trial. *JAMA Oncol*. 2020; 6 (11): e204564.
8. Weber J, Mandala M, Del Vecchio M, et al. Adjuvant nivolumab versus ipilimumab in resected stage III or IV melanoma (CheckMate 238). *NEJM*. 2017; 377: 1824 - 35.
9. Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus ipilimumab versus sunitinib in advanced renal-cell carcinoma. *NEJM*. 2018; 378: 1277 – 90.
10. Overman MJ, Lonardi S, Wonk KYM, et al. Durable clinical benefit with nivolumab plus ipilimumab in DNA mismatch repair-deficient/microsatellite instability-high metastatic colorectal cancer. *J Clinical Oncol*. 2018; 36 (8): 773 – 9.
11. National Comprehensive Cancer Network. Cutaneous melanoma (Version 1.2026). 2026 Feb 17. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed on February 19, 2026.
12. National Comprehensive Cancer Network. Non-small cell lung cancer (Version 3.2026). 2025 Dec 24. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed on February 19, 2026.

13. National Comprehensive Cancer Network. Mesothelioma: pleural (Version 2.2026). 2025 Oct 3. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mpm.pdf. Accessed on February 19, 2026.
14. National Comprehensive Cancer Network. Kidney cancer (Version 1.2026). 2025 July 24. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed on February 20, 2026.
15. National Comprehensive Cancer Network. Hodgkin lymphoma (Version 1.2026). 2025 Oct 22. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed on February 20, 2026.
16. National Comprehensive Cancer Network. Head and neck cancers (Version 1.2026). 2025 Dec 8. Available at: https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed on February 20, 2026.
17. National Comprehensive Cancer Network. Bladder cancer (Version 3.2025). 2025 Dec 19. https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed on February 20, 2026.
18. National Comprehensive Cancer Network. Hepatocellular carcinoma (Version 2.2025). 2025 Oct 22. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf. Accessed on February 20, 2026.
19. National Comprehensive Cancer Network. Esophageal and esophagogastric junction cancers (Version 2.2026). 2026 Jan 21. Available at: https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed on February 20, 2026.
20. National Comprehensive Cancer Network. Colon cancer (Version 5.2025). 2025 Oct 30. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed on February 20, 2026.
21. National Comprehensive Cancer Network. Gastric cancer (Version 2.2026). 2026 Jan 21. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed on February 20, 2026.

Policy History		
#	Date	Change Description
3.3	Effective Date: 04/16/2026	Annual review of criteria was performed, no changes were made.
3.2	Effective Date: 08/20/2025	UM medical management system update to BCBS, BCN, BCNA, and MAPPO for Opdivo Qvantig
3.1	Effective Date: 05/27/2025 P&T Date: 04/10/2025	Updated to include the trial and failure of preferred products statement and updated the renewal criteria to only allow for only 24 months of therapy for non-small cell lung cancer
3.0	Effective Date: 02/13/2025	Updated to include Opdivo Qvantig
2.9	Effective Date: 04/11/2024	Updated to remove the ECOG requirement
2.8	Effective Date: 04/06/2023	Updated approval length to allow for no less than a 60 day approval duration
2.7	Effective Date: 04/14/2022	Updated approval length to allow for FDA recommended dosing or up to 6 months at a time
2.6	Effective Date: 04/08/2021	Updated to remove the renewal authorization period and only allow for a 6 months approval at a time.
2.5	Effective Date: 12/01/2020	UM medical management system update for BCBS for Opdivo
2.4	Effective Date: 04/16/2020	Annual review of criteria was performed, no changes were made.
2.3	Effective Date: 05/09/2019	Updated criteria: NCCN 1 and 2A and FDA approved indication
2.2	Effective Date: 11/01/2018	Expanded indications: SCLC and CRC

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

2.1	Effective Date: 08/09/2018	Expanded indications: melanoma and renal cell carcinoma
2.0	Effective Date: 05/03/2018	Expanded indications: colorectal cancer and hepatocellular carcinoma
1.9	Effective Date: 02/12/2018	UM medical management system update for BCNA and MAPPO for Opdivo
1.8	Effective Date: 11/09/2017	FDA labeling update for cHL
1.7	Effective Date: 08/10/2017	Expanded indication: Urothelial carcinoma
1.6	Effective Date: 05/04/2017	Expanded indication: SCCHN Updated RCC to include non-clear cell Updated dosing for: melanoma, NSCLC, and RCC
1.5	Effective Date: 11/10/2016	Expanded indication: cHL
1.4	Effective Date: 08/11/2016	Expanded indication: as monotherapy or combination therapy with Yervoy in BRAF V600 mutation
1.3	Effective Date: 05/05/2016	Expanded indications: as monotherapy in unresectable or metastatic melanoma in wild-type BRAF V600 and renal cell carcinoma
1.2	Effective Date: 02/11/2016	Expanded indications: unresectable or metastatic melanoma in wild-type BRAF V600 and non-squamous NSCLC
1.1	Effective Date: 08/13/2015	Expanded indication: squamous NSCLC
1.0	Effective Date: 05/07/2015	New policy UM medical management system update for BCN for Opdivo

* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.