

Opdivo Qvantig™ (nivolumab and hyaluronidase-nvhy) (Subcutaneous)

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I. Length of Authorization ^{Δ 1}

Coverage will be provided for 6 months and may be renewed (unless otherwise specified).

- Neoadjuvant treatment of NSCLC without adjuvant treatment may be authorized for a maximum of three (3) neoadjuvant doses
- Neoadjuvant treatment followed by optional adjuvant treatment of NSCLC may be authorized for a maximum of four (4) neoadjuvant doses and thirteen (13) adjuvant doses.
- Adjuvant treatment of the following indications may be renewed up to a maximum of one (1) year of therapy*:
 - Cutaneous Melanoma (single agent)
 - Esophageal and Esophagogastric/Gastroesophageal Junction Cancer
 - Urothelial Carcinoma
- The following indications may be renewed up to a maximum of two (2) years of therapy:
 - Esophageal Squamous Cell Carcinoma
 - Esophageal and Esophagogastric/Gastroesophageal Junction Cancer
 - Gastric Cancer
 - Renal Cell Carcinoma (in combination with cabozantinib)
 - Urothelial Carcinoma (first line therapy in combination with gemcitabine and cisplatin, followed by single-agent maintenance therapy)

***Note: The maximum number of doses is dependent on the dosing frequency and duration of therapy. Refer to Section V for exact dosage.**

Dosing Frequency	Maximum length of therapy	Maximum number of doses
2 weeks	1 year	26 doses
	2 years	52 doses
3 weeks	2 years	35 doses
4 weeks	1 year	13 doses
	2 years	26 doses

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- 600 billable units every 4 weeks

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria

- Patient has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy (e.g., atezolizumab, pembrolizumab, durvalumab, avelumab, cemiplimab, dostarlimab, nivolumab/relatlimab, retifanlimab, toripalimab, tislelizumab, etc.) unless otherwise specified ^Δ (*Note: Not applicable when used as switch-therapy with intravenous nivolumab*); **AND**
- Therapy will not be used concomitantly with intravenous nivolumab; **AND**
- IV formulation of Opdivo must be used in the following:
 - Patients <80 kg; **OR**
 - Patients requiring 900 mg/15,000 units dose*; **OR**
 - Patients receiving therapy in combination with ipilimumab; **AND**

Urothelial Carcinoma (Bladder Cancer) † ^{1,2,30,51,62,92}

- Used as a single agent; **AND**
 - Used for disease that progressed during or following platinum-containing chemotherapy* OR progression with 12 months of neoadjuvant or adjuvant treatment with a platinum-containing regimen; **OR**
 - Used as adjuvant therapy in patients who are at a high risk for disease recurrence after undergoing surgical resection, **OR**
- Used in combination with cisplatin and gemcitabine; **AND**
 - Used as first line therapy in patient with unresectable or metastatic disease

**** Note:** ^{1,62}

– *High risk for disease recurrence is defined as:*

- *ypT2-ypT4a or ypN+ for patients who received neoadjuvant cisplatin (excluding prostate with stromal invasion), **OR***
- *pT3-pT4a or pN+ for patients who did not receive neoadjuvant cisplatin and are also ineligible for or refused adjuvant cisplatin therapy (excluding ureter or renal pelvis)*

Colorectal Cancer (CRC) † ‡ ^{1,2,31,32}

- Patient has microsatellite instability-high (MSI-H)/mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used as a single agent; **AND**
- Used as subsequent therapy for metastatic disease; **AND**

- Patient has disease progression following treatment with a fluoropyrimidine, oxaliplatin and irinotecan regimen

Gastric Cancer/Esophageal Cancer/Gastroesophageal Junction (GEJ) Cancer †^{1,2,44,52,56,69}

- Used as a single agent; **AND**
 - Used as adjuvant treatment of completely resected esophageal or GEJ cancer with residual pathologic disease in patients who have received neoadjuvant chemoradiotherapy (CRT).; **OR**
 - Used as subsequent therapy after prior fluoropyrimidine- and platinum-based chemotherapy; **AND**
 - Used for unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma (ESCC), **OR**
- Used in combination with fluoropyrimidine- and platinum-containing chemotherapy; **AND**
 - Used as first-line therapy; **AND**
 - Used in patients with unresectable, advanced, or metastatic esophageal squamous cell carcinoma (ESCC), **OR**
 - Used for advanced or metastatic gastric, GEJ, or esophageal adenocarcinomas

Squamous Cell Carcinoma of the Head and Neck (SCCHN) †^{1,2,29,78}

- Used as single-agent therapy; **AND**
- Patient has metastatic disease with disease progression on or after platinum-based therapy; **AND**
- Patient does not have disease of the nasopharynx

Hepatocellular Carcinoma (HCC) †^{1,2,21,86,87}

- Used as a single agent; **AND**
- Patient was previously treated with sorafenib following treatment with nivolumab/ipilimumab

Renal Cell Carcinoma (RCC) †^{1,2,25,26}

- Used as a single agent; **AND**
 - Used as first line therapy in patients with intermediate or poor risk disease following previous treatment with nivolumab and ipilimumab combination therapy; **OR**
 - Used as subsequent therapy after prior anti-angiogenic therapy, **OR**
- Used in combination with cabozantinib (Cabometyx only); **AND**
 - Used as first-line therapy for advanced disease

Cutaneous Melanoma †^{1,2,15-18,82,93}

- Used as single agent therapy; **AND**
 - Used as first-line therapy for unresectable or metastatic disease, **OR**

- Used as subsequent therapy for unresectable or metastatic disease after prior nivolumab/ipilimumab combination therapy, **OR**
- Used as adjuvant treatment and patient has stage IIB, stage IIC, stage III or metastatic disease and has undergone complete resection

Non-Small Cell Lung Cancer (NSCLC) †^{1,2,22,23,43,45,46}

- Used as single-agent therapy; **AND**
 - Used for metastatic disease; **AND**
 - Used as subsequent therapy on or after platinum-based chemotherapy (Note: Patients with EGFR or ALK genomic tumor aberrations should have disease progression on targeted therapies prior to receiving Opdivo Qvantig); **OR**
- Used in combination with platinum-doublet chemotherapy; **AND**
 - Used as neoadjuvant therapy in patients who have resectable (tumors ≥ 4 cm or node positive) disease; **OR**
 - Used as neoadjuvant therapy in resectable disease with the option of continuing to single-agent Opdivo Qvantig therapy as adjuvant treatment after surgery

❖ If confirmed using an FDA approved assay – <http://www.fda.gov/companiondiagnostics>

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Ⓢ Orphan Drug

§ Genomic Aberration/Mutational Driver Targeted Therapies (Note: not all inclusive, refer to guidelines for appropriate use)			
EGFR exon 19 deletion or exon 21 L858R tumors	EGFR S768I, L861Q, and/or G719X mutation positive tumors	EGFR exon 20 insertion mutation positive tumors	NTRK1/2/3 gene fusion positive tumors
– Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab	– Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab	– Amivantamab	– Larotrectinib – Entrectinib – Repotrectinib
ALK rearrangement-positive tumors	ROS1 rearrangement-positive tumors	BRAF V600E-mutation positive tumors	ERBB2 (HER2) mutation positive tumors
– Alectinib – Brigatinib – Ceritinib – Crizotinib – Lorlatinib	– Ceritinib – Crizotinib – Entrectinib – Lorlatinib – Repotrectinib	– Dabrafenib ± trametinib – Encorafenib + binimetinib – Vemurafenib	– Fam-trastuzumab deruxtecan-nxki – Ado-trastuzumab emtansine
PD-L1 tumor expression $\geq 1\%$	MET exon-14 skipping mutations	RET rearrangement-positive tumors	KRAS G12C mutation positive tumors
– Pembrolizumab – Atezolizumab – Nivolumab + ipilimumab – Cemiplimab – Tremelimumab + durvalumab	– Capmatinib – Crizotinib – Tepotinib	– Selpercatinib – Cabozantinib – Pralsetinib	– Sotorasib – Adagrasib

IV. Renewal Criteria ^{Δ 1,6}

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: immune-mediated adverse reactions (e.g., pneumonitis, hepatitis, colitis, endocrinopathies, nephritis/renal dysfunction, rash/dermatitis [including Stevens-Johnson syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN)], myocarditis, pericarditis, vasculitis, solid organ transplant rejection, etc.), severe infusion-related reactions, complications of allogeneic hematopoietic stem cell transplantation (HSCT), etc.

NSCLC (neoadjuvant/adjuvant treatment)

- Patient has not exceeded a maximum of twelve (12) months (13 cycles) of therapy

^Δ Notes:

- Patients responding to therapy who relapse ≥ 6 months after discontinuation due to duration are eligible to re-initiate PD-directed therapy.
- Patients previously presenting with aggressive disease who are exhibiting stable disease on treatment as their best response (or if therapy improved performance status) may be eligible for continued therapy without interruption or discontinuation.
- 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.

V. Dosage/Administration ^{Δ 1,14,27,28}

Indication	Dose
Renal Cell Carcinoma	– 600 mg/10,000 units every 2 weeks or 1,200 mg/20,000 units every 4 weeks, until disease progression or unacceptable toxicity. – 600 mg/10,000 units every 2 weeks or 1,200 mg/20,000 units every 4 weeks administered in combination with cabozantinib 40 mg once daily without food, up to a maximum of 2 years of therapy.
Melanoma	– 600 mg/10,000 units every 2 weeks or 1,200 mg/20,000 units every 4 weeks, until disease progression or unacceptable toxicity. <i>Note: For adjuvant therapy, treat until disease recurrence or unacceptable toxicity for up to 1 year</i>
NSCLC	Neoadjuvant and adjuvant treatment

	– * 900 mg/15,000 units with platinum-doublet chemotherapy on the same day every 3 weeks for 3 cycles, then single-agent Opdivo Qvantig 1,200 mg/20,000 units every 4 weeks after surgery for up to 13 cycles. Metastatic non-small cell lung cancer – 600 mg/10,000 units every 2 weeks or 1,200 mg/20,000 units every 4 weeks, until disease progression or unacceptable toxicity.
SCCHN	– 600 mg/10,000 units every 2 weeks or 1,200 mg/20,000 units every 4 weeks, until disease progression or unacceptable toxicity.
Urothelial Carcinoma	Urothelial carcinoma – 600 mg/10,000 units every 2 weeks or 1,200 mg/20,000 units every 4 weeks, until disease progression or unacceptable toxicity. <i>Note: For adjuvant therapy, treat until disease recurrence or unacceptable toxicity for up to 1 year</i> First-line unresectable or metastatic urothelial carcinoma – * 900 mg/15,000 units every 3 weeks with cisplatin and gemcitabine on the same day for up to 6 cycles, then 600 mg/10,000 units every 2 weeks or 1,200 mg/20,000 units every 4 weeks, up to a maximum of 2 years of therapy.
Colorectal Carcinoma	– 600 mg/10,000 units every 2 weeks or 1,200 mg/20,000 units every 4 weeks, until disease progression or unacceptable toxicity.
Hepatocellular Carcinoma	– 600 mg/10,000 units every 2 weeks or 1,200 mg/20,000 units every 4 weeks, until disease progression or unacceptable toxicity.
Esophageal Squamous Cell Cancer	– 600 mg/10,000 units every 2 weeks or 1,200 mg/20,000 units every 4 weeks, until disease progression or unacceptable toxicity. OR – 600 mg/10,000 units every 2 weeks or 1,200 mg/20,000 units every 4 weeks administered in combination with fluoropyrimidine- and platinum-containing chemotherapy, up to a maximum of 2 years of therapy.
Gastric Cancer, GEJ Cancer, and Esophageal Adenocarcinoma	– 600 mg/10,000 units every 2 weeks in combination with fluoropyrimidine- and platinum-containing chemotherapy every 2 weeks, up until a maximum of 2 years of therapy. – * 900 mg/15,000 units every 3 weeks with fluoropyrimidine- and platinum-containing chemotherapy every 3 weeks, up until a maximum of 2 years of therapy. <i>Note: For adjuvant therapy in esophageal and GEJ, treat until disease recurrence or unacceptable toxicity for up to 1 year</i>
Note: – *The 900 mg/15,000 units dosing is listed in the prescribing information; however, the IV formulation of nivolumab must be used instead to prevent wastage. – Opdivo Qvantig (nivolumab and hyaluronidase-nvhy) has different dosage and administration instructions than intravenous nivolumab products. – Opdivo Qvantig is for subcutaneous use only in the abdomen or thigh. – Opdivo Qvantig is to be administered by a healthcare professional only. – Opdivo Qvantig is for subcutaneous use only administered over 3-5 minutes.	

VI. Billing Code/Availability Information

HCPCS Code:

- J9289 – Injection, nivolumab, 2 mg and hyaluronidase-nvhy; 1 billable unit = 2 mg (*Effective 07/01/2025*)
- J9999 – Not otherwise classified, antineoplastic drugs (*Discontinue use on 07/01/2025*)
- C9399 – Unclassified drugs or biologicals (hospital outpatient use only) (*Discontinue use on 07/01/2025*)

NDC(s):

- Opdivo Qvantig single-dose vial providing 600 mg nivolumab and 10,000 units hyaluronidase per 5 mL (120 mg/ 2,000 units per mL): 00003-6120-xx

VII. References

1. Opdivo Qvantig [package insert]. Princeton, NJ; Bristol-Myers Squibb, Inc; December 2024. Accessed January 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) nivolumab. National Comprehensive Cancer Network, 2024. 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 October 2024.
3. Scherpereel A, Mazieres J, Greillier L, et al. Second- or third-line nivolumab (Nivo) versus nivo plus ipilimumab (Ipi) in malignant pleural mesothelioma (MPM) patients: Results of the IFCT-1501 MAPS2 randomized phase II trial. [Abstract]. J Clin Oncol 2017;35: Abstract LBA 8507.
4. Walocko FM, Scheier BY, Harms PW, et al. Metastatic Merkel cell carcinoma response to nivolumab. J Immunother Cancer. 2016 Nov 15; 4:79.
5. Tawbi HA-H, Forsyth PAJ, Algazi AP, et al. Efficacy and safety of nivolumab (NIVO) plus ipilimumab (IPI) in patients with melanoma (MEL) metastatic to the brain: Results of the phase II study CheckMate 204. J Clin Oncol 2017;35(15_suppl): abstr 9507.
6. Morris VK, Salem ME, Nimeiri H, et al. Nivolumab for previously treated unresectable metastatic anal cancer (NCI9673): a multicentre, single-arm, phase 2 study. Lancet Oncol. 2017 Apr;18(4):446-453. Doi: 10.1016/S1470-2045(17)30104-3. Epub 2017 Feb 18.
7. Zhao X, Ivaturi V, Gopalakrishnan M, et al. Abstract CT 101: A model-based exposure-response (E-R) assessment of a nivolumab (NIVO) 4-weekly (Q4W) dosing schedule across multiple tumor types. Cancer Res July 1, 2017 (77) (13 Supplement) CT101; DOI: 10.1158/1538-7445.AM2017-CT101.
8. Zhao X, Suryawanshi M, Hruska M, et al. Assessment of nivolumab benefit-risk profile of a 240 mg flat dose relative to a 3 mg/kg dosing regimen in patients with advanced tumors. Ann Oncol 2017; 28:2002-2008.

9. Feng Y, Xiaoning W, Bajaj G, et al. Nivolumab exposure-response analyses of efficacy and safety in previously treated squamous or nonsquamous non-small cell lung cancer. *ClinCa Res* 2017;23(18): 5394-5405.
10. Gupta S, Bellmunt J, Plimack ER, et al. Defining “platinum-ineligible” patients with metastatic urothelial cancer (mUC). *J Clin Oncol*. 2022 June 1;40(16_suppl):4577.
11. Hellmann MD, Ciuleanu TE, Pluzanski A, et al. Nivolumab plus ipilimumab in lung cancer with a high tumor mutational burden. *N Engl J Med* 2018; 378:2093-2104.
12. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. *J Oncol Pract*. 2018 Mar;14(3): e130-e136.
13. Hematology/Oncology Pharmacy Association (2019). Intravenous Cancer Drug Waste Issue Brief. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
14. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. *BMJ*. 2016 Feb 29;352: i788.
15. Weber JS, D'Angelo SP, Minor D, et al. Nivolumab versus chemotherapy in patients with advanced melanoma who progressed after anti-CTLA-4 treatment (CheckMate 037): a randomised, controlled, open-label, phase 3 trial. *Lancet Oncol*. 2015 Apr;16(4):375-84. Doi: 10.1016/S1470-2045(15)70076-8. Epub 2015 Mar 18.
16. Robert C, Long GV, Brady B, et al. Nivolumab in previously untreated melanoma without BRAF mutation. *N Engl J Med*. 2015 Jan 22;372(4):320-30. Doi: 10.1056/NEJMoa1412082. Epub 2014 Nov 16.
17. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma. *N Engl J Med*. 2015 Jul 2;373(1):23-34. Doi: 10.1056/NEJMoa1504030. Epub 2015 May 31.
18. Weber J, Mandala M, Del Vecchio M, et al. Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma. *N Engl J Med*. 2017 Nov 9;377(19):1824-1835. Doi: 10.1056/NEJMoa1709030. Epub 2017 Sep 10.
19. Algazi AP, Tsai KK, Shoushtari AN, et al. Clinical outcomes in metastatic uveal melanoma treated with PD-1 and PD-L1 antibodies. *Cancer*. 2016 Nov 15;122(21):3344-3353. Doi: 10.1002/cncr.30258. Epub 2016 Aug 17.
20. Piulats JM, Cruz-Merino LDL, Garcia MTC, et al. Phase II multicenter, single arm, open label study of nivolumab in combination with ipilimumab in untreated patients with metastatic uveal melanoma (GEM1402.NCT02626962). *J Clin Oncol* 2017; 35 Abstr 9533.
21. El-Khoueiry AB, Sangro B, Yau T, et al. Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): an open-label, non-comparative, phase ½ dose escalation and expansion trial. *Lancet*. 2017 Jun 24;389(10088):2492-2502. Doi: 10.1016/S0140-6736(17)31046-2. Epub 2017 Apr 20.
22. Brahmer J, Reckamp KL, Baas P, et al. Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer. *N Engl J Med*. 2015 Jul 9;373(2):123-35. Doi: 10.1056/NEJMoa1504627. Epub 2015 May 31.

23. Borghaei H, Paz-Ares L, Horn L, et al. Nivolumab versus Docetaxel in Advanced Nonsquamous Non-Small-Cell Lung Cancer. *N Engl J Med*. 2015 Oct 22;373(17):1627-39. Doi: 10.1056/NEJMoa1507643. Epub 2015 Sep 27.
24. Antonia SJ, López-Martin JA, Bendell J, et al. Nivolumab alone and nivolumab plus ipilimumab in recurrent small-cell lung cancer (CheckMate 032): a multicentre, open-label, phase ½ trial. *Lancet Oncol*. 2016 Jul;17(7):883-895. Doi: 10.1016/S1470-2045(16)30098-5. Epub 2016 Jun 4.
25. Motzer RJ, Escudier B, McDermott DF, et al. Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2015 Nov 5;373(19):1803-13. Doi: 10.1056/NEJMoa1510665. Epub 2015 Sep 25.
26. Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2018 Apr 5;378(14):1277-1290. Doi: 10.1056/NEJMoa1712126. Epub 2018 Mar 21.
27. Armand P, Engert A, Younes A, et al. Nivolumab for Relapsed/Refractory Classic Hodgkin Lymphoma After Failure of Autologous Hematopoietic Cell Transplantation: Extended Follow-Up of the Multicohort Single-Arm Phase II CheckMate 205 Trial. *J Clin Oncol*. 2018 May 10;36(14):1428-1439. Doi: 10.1200/JCO.2017.76.0793. Epub 2018 Mar 27.
28. Ansell SM, Lesokhin AM, Borrello I, et al. PD-1 blockade with nivolumab in relapsed or refractory Hodgkin's lymphoma. *N Engl J Med*. 2015 Jan 22;372(4):311-9. Doi: 10.1056/NEJMoa1411087. Epub 2014 Dec 6.
29. Ferris RL, Blumenschein G Jr, Fayette J, et al. Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. *N Engl J Med*. 2016 Nov 10;375(19):1856-1867. Epub 2016 Oct 8.
30. 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):312-322. Doi: 10.1016/S1470-2045(17)30065-7. Epub 2017 Jan 26.
31. 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):1182-1191. Doi: 10.1016/S1470-2045(17)30422-9. Epub 2017 Jul 19.
32. Overman MJ, Lonardi S, Wong KYM, et al. Durable Clinical Benefit with Nivolumab Plus Ipilimumab in DNA Mismatch Repair-Deficient/Microsatellite Instability-High Metastatic Colorectal Cancer. *J Clin Oncol*. 2018 Mar 10;36(8):773-779. Doi: 10.1200/JCO.2017.76.9901. Epub 2018 Jan 20.
33. Topalian SL, Bhatia S, Hollebecque A, et al. non-comparative, open-label, multiple cohorts, phase ½ study to evaluate nivolumab (NIVO) in patients with virus-associated tumors (CheckMate 358): Efficacy and safety in Merkel cell carcinoma (MCC). DOI: 10.1158/1538-7445.AM2017-CT074 Published July 2017.
34. Long GV, Atkinson V, Lo S, et al. Combination nivolumab and ipilimumab or nivolumab alone in melanoma brain metastases: a multicentre randomised phase 2 study. *Lancet Oncol*. 2018 May;19(5):672-681. Doi: 10.1016/S1470-2045(18)30139-6. Epub 2018 Mar 27.
35. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Anal Carcinoma. Version 1.2024. National Comprehensive Cancer Network, 2024. 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. September 2024.

36. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Gestational Trophoblastic Neoplasia. Version 2.2024. National Comprehensive Cancer Network, 2024. 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 September 2024.
37. Scherpereel A, Mazieres J, Greillier L, et al. Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial. *Lancet Oncol*. 2019 Feb;20(2):239-253. Doi: 10.1016/S1470-2045(18)30765-4. Epub 2019 Jan 16.
38. Disselhorst MJ, Quispel-Janssen J, Lalezari F, et al. Ipilimumab and nivolumab in the treatment of recurrent malignant pleural mesothelioma (INITIATE): results of a prospective, single-arm, phase 2 trial. *Lancet Respir Med*. 2019 Mar;7(3):260-270. Doi: 10.1016/S2213-2600(18)30420-X. Epub 2019 Jan 16.
39. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Small Bowel Adenocarcinoma. Version 4.2024. National Comprehensive Cancer Network, 2024. 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 September 2024.
40. Chan TSY, Li J, Loong F, et al. PD1 blockade with low-dose nivolumab in NK/T cell lymphoma failing L-asparaginase: efficacy and safety. *Ann Hematol*. 2018 Jan;97(1):193-196. Doi: 10.1007/s00277-017-3127-2. Epub 2017 Sep 6.
41. Goldman JW, Crino L, Vokes EE, et al. Nivolumab (nivo) in patients (pts) with advanced (adv) NSCLC and central nervous system (CNS) metastases (mets). *J Clin Oncol* 34, no. 15_suppl (May 20, 2016) 9038-9038. DOI: 10.1200/JCO.2016.34.15_suppl.9038.
42. Gauvain C, Vauleon E, Chouaid C, et al. Intracerebral efficacy, and tolerance of nivolumab in non–small-cell lung cancer patients with brain metastases. *Lung Cancer*. 2018 Feb; 116:62-66. Doi: 10.1016/j.lungcan.2017.12.008.
43. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Non-Small Cell Lung Cancer. Version 11.2024. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed October 2024.

44. Kato K, Cho BC, Takahashi M, et al. Nivolumab versus chemotherapy in patients with advanced esophageal squamous cell carcinoma refractory or intolerant to previous chemotherapy (ATTRACTION-3): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol*. 2019;20(11):1506-1517. Doi:10.1016/S1470-2045(19)30626-6.
45. Hellmann MD, Paz-Ares L, Bernabe Caro R, et al. Nivolumab plus Ipilimumab in Advanced Non-Small-Cell Lung Cancer. *N Engl J Med*. 2019;381(21):2020-2031. Doi:10.1056/NEJMoa1910231.
46. Reck M, Ciuleanu T-E, Dols MC, et al. Nivolumab (NIVO) + ipilimumab (IPI) + 2 cycles of platinum-doublet chemotherapy (chemo) vs 4 cycles chemo as first-line (1L) treatment (tx) for stage IV/recurrent non-small cell lung cancer (NSCLC): CheckMate 9LA [abstract]. *J Clin Oncol* 2020;38: Abstract 9501-9501.
47. Zalcman G, Peters S, Mansfield AS, et al. Checkmate 743: A phase 3, randomized, open-label trial of nivolumab (nivo) plus ipilimumab (ipi) vs pemetrexed plus cisplatin or carboplatin as first-line therapy in unresectable pleural mesothelioma. *Journal of Clinical Oncology* 2017 35:15_suppl, TPS8581-TPS8581
48. Azad NS, Gray RJ, Overman MJ, et al. Nivolumab Is Effective in Mismatch Repair-Deficient Noncolorectal Cancers: Results from Arm Z1D-A Subprotocol of the NCI-MATCH (EAY131) Study. *J Clin Oncol*. 2020 Jan 20;38(3):214-222.
49. Naumann RW, Hollebecque A, Meyer T, et al. Safety and Efficacy of Nivolumab Monotherapy in Recurrent or Metastatic Cervical, Vaginal, or Vulvar Carcinoma: Results from the Phase I/II CheckMate 358 Trial. *J Clin Oncol*. 2019 Nov 1;37(31):2825-2834.
50. Choueiri TK, Powles T, Burotto M, et al. 696O_PR Nivolumab + cabozantinib vs sunitinib in first-line treatment for advanced renal cell carcinoma: First results from the randomized phase III CheckMate 9ER trial. Volume 31, SUPPLEMENT 4, S1159, September 01, 2020.
51. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Bladder Cancer. Version 4.2024. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
52. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Esophageal and Esophagogastric Junction Cancers. Version 4.2024. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
53. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Gastric Cancer. Version 4.2024. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.

54. Herrera AF, Moskowitz AJ, Bartlett NL, et al. Interim results of brentuximab vedotin in combination with nivolumab in patients with relapsed or refractor Hodgkin lymphoma. *Blood*. 2018 Mar 15;131 (11):1183-1194.
55. Cole PD, Mauz-Körholz C, Mascarín M, et al. HL-032: Nivolumab and Brentuximab Vedotin (BV)–Based, Response-Adapted Treatment in Children, Adolescents, and Young Adults (CAYA) With Standard-Risk Relapsed/Refractory Classical Hodgkin Lymphoma (R/R cHL): Primary Analysis of the Standard-Risk Cohort of the Phase 2 CheckMate 744 Study. *Clinical Lymphoma Myeloma and Leukemia*. Volume 20, Supplement 1, September 2020, Pages S245-S246.
56. Moehler M, Shitara K, Garrido M, et al. Nivolumab (nivo) plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced gastric cancer/gastroesophageal junction cancer (GC/GEJC)/esophageal adenocarcinoma (EAC): First results of the CheckMate 649 study. [abstract]. Presented at the Oral Presentation presented at the ESMO 2020 Annual Meeting; September 19-21, 2020; Virtual Meeting.
57. Kelly RJ, Ajani JA, Kuzdzal J, et al. Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer. *N Engl J Med*. 2021 Apr 1;384(13):1191-1203. Doi: 10.1056/NEJMoa2032125.
58. Nivolumab. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. <http://micromedex.com/>. Updated January 8, 2024. Accessed January 2024.
59. Lenz HJ, Lonardi S, Zagonel V, et al. Nivolumab (NIVO) + low-dose ipilimumab (IPI) as first-line (1L) therapy in microsatellite instability-high/DNA mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Clinical update [abstract]. *Journal of Clinical Oncology* 2019; 37:3521-3521.
60. Bellmunt, J. (2023). Treatment of metastatic urothelial cancer of the bladder and urinary tract. In Lerner SP, Shah S (Eds.), *UptoDate*. Last updated Jul 17, 2024. Accessed September 11, 2024. Available from <https://www.uptodate.com/contents/treatment-of-metastatic-urothelial-cancer-of-the-bladder-and-urinary-tract>.
61. Ready NE, Ott PA, Hellmann MD, et al. Nivolumab Monotherapy and Nivolumab Plus Ipilimumab in Recurrent Small Cell Lung Cancer: Results from the CheckMate 032 Randomized Cohort. *J Thorac Oncol*. 2020 Mar;15(3):426-435. Doi: 10.1016/j.jtho.2019.10.004.
62. Bajorin DF, Witjes JA, Gschwend JE, et al. Adjuvant Nivolumab versus Placebo in Muscle-Invasive Urothelial Carcinoma. *N Engl J Med*. 2021 Jun 3;384(22):2102-2114. Doi: 10.1056/NEJMoa2034442.
63. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Cervical Cancer. Version 3.2024. National Comprehensive Cancer Network, 2024. 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 September 2024.

64. Fennell DA, Ewings S, Ottensmeier C, et al. Nivolumab versus placebo in patients with relapsed malignant mesothelioma (CONFIRM): a multicentre, double-blind, 13mmune13zed, phase 3 trial. *Lancet Oncol* 2021; 22:1530.
65. Topalian SL, Bhatia S, Amin A, et al. Neoadjuvant Nivolumab for Patients with Resectable Merkel Cell Carcinoma in the CheckMate 358 Trial. *J Clin Oncol*. 2020;38(22):2476-2487. Doi:10.1200/JCO.20.00201.
66. Forde PM, Spicer J, Lu S et al. Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. *N Engl J Med*. 2022 May 26;386(21):1973-1985. doi: 10.1056/NEJMoa2202170. Epub 2022 Apr 11. PMID: 35403841; PMCID: PMC9844511.
67. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Mesothelioma: Peritoneal. Version 1.2024. National Comprehensive Cancer Network, 2024. 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 September 2024.
68. Scherpereel A, Mazieres J, Greillier L, et al; French Cooperative Thoracic Intergroup. Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, 13mmune13zed, non-comparative, phase 2 trial. *Lancet Oncol*. 2019 Feb;20(2):239-253. Doi: 10.1016/S1470-2045(18)30765-4. Epub 2019 Jan 16. Erratum in: *Lancet Oncol*. 2019 Mar;20(3): e132.
69. Doki Y, Ajani JA, Kato K, et al. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma. *N Engl J Med*. 2022 Feb 3;386(5):449-462. Doi: 10.1056/NEJMoa2111380.
70. De Santis M, Bellmunt J, Mead G, et al. Randomized phase II/III trial assessing gemcitabine/carboplatin and methotrexate/carboplatin/vinblastine in patients with advanced urothelial cancer “unfit” for cisplatin-based chemotherapy: phase II—results of EORTC study 30986. *J Clin Oncol*. 2009 Nov 20;27(33):5634-9. Doi: 10.1200/JCO.2008.21.4924. Epub 2009 Sep 28.
71. Bouffet E, Larouche V, Campbell BB, et al. Immune Checkpoint Inhibition for Hypermutant Glioblastoma Multiforme Resulting from Germline Biallelic Mismatch Repair Deficiency. *J Clin Oncol*. 2016 Jul 1;34(19):2206-11.
72. Schenker M, Burotto M, Richardet M, et al. CheckMate 848: A randomized, open-label, phase 2 study of nivolumab in combination with ipilimumab or nivolumab monotherapy in patients with advanced or metastatic solid tumors of high tumor mutational burden. Oral Presentation presented at the American Association for Cancer Research (AACR) 2022 Annual Meeting; April 8-13, 2022; New Orleans, LA.
73. Mei MG, Lee HJ, Palmer J, et al. Response-adapted anti-PD-1-based salvage therapy for Hodgkin lymphoma with nivolumab alone or in combination with ICE. *Blood*. 2022 Jun 23;139(25):3605-3616. Doi: 10.1182/blood.2022015423.
74. Zinzani P, Santoro A, Gritti G, et al. Nivolumab Combined with Brentuximab Vedotin for Relapsed/Refractory Primary Mediastinal Large B-Cell Lymphoma: Efficacy and Safety from the Phase II CheckMate 436 Study. *J Clin Oncol*. 2019 Nov 20;37(33):3081-3089. Doi: 10.1200/JCO.19.01492. Epub 2019 Aug 9.

75. Davis K, Fox E, Merchant M, et al. Nivolumab in children and young adults with relapsed or refractory solid tumors or lymphoma (ADVL1412): a multicentre, open-label, single-arm, phase 1–2 trial. *The Lancet*. Volume 21, issue 4, p541-550, April 01, 2020, [https://doi.org/10.1016/S1470-2045\(20\)30023-1](https://doi.org/10.1016/S1470-2045(20)30023-1).
76. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Pediatric Aggressive Mature B-Cell Lymphomas. Version 2.2024. National Comprehensive Cancer Network, 2024. 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 September 2024.
77. Younes A, Santoro A, Shipp M, et al. Nivolumab for classical Hodgkin's lymphoma after failure of both autologous stem-cell transplantation and brentuximab vedotin: a multicentre, multicohort, single-arm phase 2 trial. *Lancet Oncol*. 2016 Sep;17(9):1283-94. Doi: 10.1016/S1470-2045(16)30167-X.
78. Chung C, Li J, Steuer C, et al. Phase II Multi-institutional Clinical Trial Result of Concurrent Cetuximab and Nivolumab in Recurrent and/or Metastatic Head and Neck Squamous Cell Carcinoma. *Clin Cancer Res*. 2022 Jun 1;28(11):2329-2338. Doi: 10.1158/1078-0432.CCR-21-3849.
79. Zer A, Icht O, Yosef L, et al. Phase II single-arm study of nivolumab and ipilimumab (Nivo/Ipi) in previously treated classical Kaposi sarcoma (cKS). *Annals of Oncology*. Volume 33, Issue 7, July 2022, Pages 720-727. <https://doi.org/10.1016/j.annonc.2022.03.012>.
80. Pelster MS, Gruschkus SK, Bassett R, et al. Nivolumab and Ipilimumab in Metastatic Uveal Melanoma: Results from a Single-Arm Phase II Study. *J Clin Oncol*. 2021 Feb 20;39(6):599-607. Doi: 10.1200/JCO.20.00605.
81. Baas P, Scherpereel A, Nowak AK, et al. First-line nivolumab plus ipilimumab in unresectable malignant pleural mesothelioma (CheckMate 743): a multicentre, 14mmune14zed, open-label, phase 3 trial. *Lancet*. 2021 Jan 30;397(10272):375-386. Doi: 10.1016/S0140-6736(20)32714-8.
82. Blank CU, Rozeman EA, Fanchi LF, et al. Neoadjuvant versus adjuvant ipilimumab plus nivolumab in macroscopic stage III melanoma. *Nat Med*. 2018 Nov;24(11):1655-1661. Doi: 10.1038/s41591-018-0198-0.
83. Glutsch V, Kneitz, Gesierich A, et al. Activity of ipilimumab plus nivolumab in avelumab-refractory Merkel cell carcinoma. *Cancer Immunology, Immunotherapy* volume 70, pages2087–2093 (2021)
84. Wagner M, Othus M, Patel S, et al. Multicenter phase II trial (SWOG S1609, cohort 51) of ipilimumab and nivolumab in metastatic or unresectable angiosarcoma: a substudy of dual anti-CTLA-4 and anti-PD-1 blockade in rare tumors (DART). *J Immunother Cancer*. 2021 Aug;9(8): e002990. Doi: 10.1136/jitc-2021-002990.
85. Kim S, Wuthrick E, Blakaj D, et al. Combined nivolumab and ipilimumab with or without stereotactic body radiation therapy for advanced Merkel cell carcinoma: a randomized, open

label, phase 2 trial. The Lancet. Published: September 11, 2022. Doi:
[https://doi.org/10.1016/S0140-6736\(22\)01659-2](https://doi.org/10.1016/S0140-6736(22)01659-2). PlumX Metrics

86. Yau T, Park JW, Finn RS, et al. Nivolumab versus sorafenib in advanced hepatocellular carcinoma (CheckMate 459): a 15mmune15zed, multicentre, open-label, phase 3 trial. Lancet Oncol. 2022 Jan;23(1):77-90.
87. Kudo M, Matilla A, Santoro A, et al. CheckMate 040 cohort 5: A phase I/II study of nivolumab in patients with advanced hepatocellular carcinoma and Child-Pugh B cirrhosis. J Hepatol. 2021 Sep;75(3):600-609.
88. Long GV, Del Vecchio M, Weber J, et al. (2023). Adjuvant therapy with nivolumab versus placebo in patients with resected stage IIB/C melanoma (CheckMate 76K). SKIN The Journal of Cutaneous Medicine, 7(2), s163. <https://doi.org/10.25251/skin.7.suppl.163>.
89. Advani RH, Moskowitz AJ, Bartlett NL, et al. Brentuximab vedotin in combination with nivolumab in relapsed or refractory Hodgkin lymphoma: 3-year study results. Blood. 2021 Aug 12;138(6):427-438. Doi: 10.1182/blood.2020009178.
90. Dagogo-Jack I, Madison RW, Lennerz JK, et al. Molecular characterization of mesothelioma: Impact of histologic type and site of origin on molecular landscape. JCO Precis Oncol 2022;6: e2100422.
91. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Colon Cancer. Version 5.2024. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed August 2024.
92. van der Heijden, MS, Sonpavde G, Powles T, et al; CheckMate 901 Trial Investigators. Nivolumab plus Gemcitabine-Cisplatin in Advanced Urothelial Carcinoma. N Engl J Med. 2023 Nov 9;389(19):1778-1789. doi: 10.1056/NEJMoa2309863. Epub 2023 Oct 22. PMID: 37870949.
93. Amaria R, Reddy S, Tawbi H, et al. Neoadjuvant Immune Checkpoint Blockade in High-Risk Resectable Melanoma. Nat Med. 2018 Nov; 24(11): 1649–1654. Published online 2018 Oct 8. Doi: 10.1038/s41591-018-0197-1
94. Ma, D, Ding X, Shi P, et al Combined targeted therapy and immunotherapy in anaplastic thyroid carcinoma with distant metastasis: A case report
95. Kollipara R, Schneider K, Radovich M, et al. Exceptional response with immunotherapy in a patient with anaplastic thyroid cancer. Oncologist 2017; 22:1149-1151.
96. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Thyroid Carcinoma. Version 4.2024. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
97. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Vaginal Cancer. Version 2.2025. National Comprehensive Cancer Network,

2024. 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 September 2024.

98. Reijers ILM, Menzies AM, van Akkooi ACJ, et al. Personalized response-directed surgery and adjuvant therapy after neoadjuvant ipilimumab and nivolumab in high-risk stage III melanoma: the PRADO trial. *Nat Med* 2022; 28:1178-1188.
99. Versluis JM, Menzies AM, Sikorska K, et al. Survival update of neoadjuvant ipilimumab plus nivolumab in macroscopic stage III melanoma in the OpACIN and OpACINneo trials. *Ann Oncol* 2023; 34:420-430.
100. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Melanoma: Cutaneous Version 2.2024. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
101. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab + Ipilimumab followed by Nivolumab: Colon Cancer Chemotherapy Order Template, COL68. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed August 2024.
102. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab + Ipilimumab followed by Nivolumab: Rectal Cancer Chemotherapy Order Template, REC80. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed August 2024.
103. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for mFOLFOX6 (Continuous Infusion Fluorouracil/Leucovorin/OXALIplatin) + Nivolumab: Gastric Cancer Chemotherapy Order Template, GAS95. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
104. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for CapeOX (Capecitabine/OXALIplatin) + Nivolumab: Gastric Cancer Chemotherapy Order Template, GAS96. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.

105. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab + Ipilimumab followed by nivolumab: Ampullary Adenocarcinoma Chemotherapy Order Template, AMP22. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed July 2024
106. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab: Mesothelioma: Peritoneal Chemotherapy Order Template, MPEM10. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
107. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab + Ipilimumab followed by Nivolumab: Central Nervous System Cancers Chemotherapy Order Template, CNS61. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
108. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab: Central Nervous System Cancers Chemotherapy Order Template, CNS63. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
109. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab + Ipilimumab: Non-Small Cell Lung Cancer Chemotherapy Order Template, NSC97. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
110. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab: T-Cell Lymphomas Chemotherapy Order Template, TCL39. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
111. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab: Small Cell Lung Cancer Chemotherapy Order Template, SCL24. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.

112. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab: Endometrial Carcinoma Chemotherapy Order Template, UTE34. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
113. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab: Cervical Cancer Chemotherapy Order Template, CRV35. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
114. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab: Vulvar Cancer Chemotherapy Order Template, VUL17. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
115. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Nivolumab: Vaginal Cancer Chemotherapy Order Template, VAG34. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
116. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Brentuximab vedotin + Nivolumab: Hodgkin Lymphoma Chemotherapy Order Template, HDL53. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.
117. Herrera AF, LeBlanc ML, Castellino SM, et al. SWOG S1826, a randomized study of nivolumab(N)-AVD versus brentuximab vedotin (BV)-AVD in advanced stage (AS) classic Hodgkin lymphoma (HL). Journal of Clinical Oncology 2023;41: LBA4-LBA4.
118. Bröckelmann PJ, Buhen I, Meissner J et al. Nivolumab and Doxorubicin, Vinblastine, and Dacarbazine in Early-Stage Unfavorable Hodgkin Lymphoma: Final Analysis of the Randomized German Hodgkin Study Group Phase II NIVAHL Trial. J Clin Oncol. 2023 Feb 20;41(6):1193-1199. doi: 10.1200/JCO.22.02355. Epub 2022 Dec 12. PMID: 36508302.
119. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for AVD (DOXOrubicin/VinBLASStine/Dacarbazine) + Nivolumab: Hodgkin

Lymphoma Chemotherapy Order Template, HDL75. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed September 2024.

120. Cascone T, Awad MM, Spicer JD, et al. Perioperative Nivolumab in Resectable Lung Cancer. N Engl J Med. 2024 May 16;390(19):1756-1769. doi: 10.1056/NEJMoa2311926. PMID: 38749033.

121. Opdivo [package insert]. Princeton, NJ; Bristol-Myers Squibb Company; October 2024. Accessed October 2024.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C00.0	Malignant neoplasm of external upper lip
C00.1	Malignant neoplasm of external lower lip
C00.2	Malignant neoplasm of external lip, unspecified
C00.3	Malignant neoplasm of upper lip, inner aspect
C00.4	Malignant neoplasm of lower lip, inner aspect
C00.5	Malignant neoplasm of lip, unspecified, inner aspect
C00.6	Malignant neoplasm of commissure of lip, unspecified
C00.8	Malignant neoplasm of overlapping sites of lip
C00.9	Malignant neoplasm of lip, unspecified
C01	Malignant neoplasm of base of tongue
C02.0	Malignant neoplasm of dorsal surface of tongue
C02.1	Malignant neoplasm of border of tongue
C02.2	Malignant neoplasm of ventral surface of tongue
C02.3	Malignant neoplasm of anterior two-thirds of tongue, part unspecified
C02.4	Malignant neoplasm of lingual tonsil
C02.8	Malignant neoplasm of overlapping sites of tongue
C02.9	Malignant neoplasm of tongue, unspecified
C03.0	Malignant neoplasm of upper gum
C03.1	Malignant neoplasm of lower gum
C03.9	Malignant neoplasm of gum, unspecified
C04.0	Malignant neoplasm of anterior floor of mouth
C04.1	Malignant neoplasm of lateral floor of mouth
C04.8	Malignant neoplasm of overlapping sites of floor of mouth
C04.9	Malignant neoplasm of floor of mouth, unspecified

C05.0	Malignant neoplasm of hard palate
C05.1	Malignant neoplasm of soft palate
C05.8	Malignant neoplasm of overlapping sites of palate
C05.9	Malignant neoplasm of palate, unspecified
C06.0	Malignant neoplasm of cheek mucosa
C06.2	Malignant neoplasm of retromolar area
C06.80	Malignant neoplasm of overlapping sites of unspecified parts of mouth
C06.89	Malignant neoplasm of overlapping sites of other parts of mouth
C06.9	Malignant neoplasm of mouth, unspecified
C09.0	Malignant neoplasm of tonsillar fossa
C09.1	Malignant neoplasm of tonsillar pillar (anterior) (posterior)
C09.8	Malignant neoplasm of overlapping sites of tonsil
C09.9	Malignant neoplasm of tonsil, unspecified
C10.0	Malignant neoplasm of vallecula
C10.1	Malignant neoplasm of anterior surface of epiglottis
C10.2	Malignant neoplasm of lateral wall of oropharynx
C10.3	Malignant neoplasm of posterior wall of oropharynx
C10.4	Malignant neoplasm of branchial cleft
C10.8	Malignant neoplasm of overlapping sites of oropharynx
C10.9	Malignant neoplasm of oropharynx, unspecified
C11.0	Malignant neoplasm of superior wall of nasopharynx
C11.1	Malignant neoplasm of posterior wall of nasopharynx
C11.2	Malignant neoplasm of lateral wall of nasopharynx
C11.3	Malignant neoplasm of anterior wall of nasopharynx
C11.8	Malignant neoplasm of overlapping sites of nasopharynx
C11.9	Malignant neoplasm of nasopharynx, unspecified
C12	Malignant neoplasm of pyriform sinus
C13.0	Malignant neoplasm of postcricoid region
C13.1	Malignant neoplasm of aryepiglottic fold, hypopharyngeal aspect
C13.2	Malignant neoplasm of posterior wall of hypopharynx
C13.8	Malignant neoplasm of overlapping sites of hypopharynx
C13.9	Malignant neoplasm of hypopharynx, unspecified
C14.0	Malignant neoplasm of pharynx, unspecified
C14.2	Malignant neoplasm of Waldeyer's ring
C14.8	Malignant neoplasm of overlapping sites of lip, oral cavity, and pharynx

C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C15.9	Malignant neoplasm of esophagus, unspecified
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified
C18.0	Malignant neoplasm of cecum
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C22.0	Liver cell carcinoma
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C30.0	Malignant neoplasm of nasal cavity
C31.0	Malignant neoplasm of maxillary sinus
C31.1	Malignant neoplasm of ethmoidal sinus
C32.0	Malignant neoplasm of glottis
C32.1	Malignant neoplasm of supraglottis
C32.2	Malignant neoplasm of subglottis
C32.3	Malignant neoplasm of laryngeal cartilage

C32.8	Malignant neoplasm of overlapping sites of larynx
C32.9	Malignant neoplasm of larynx, unspecified
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus, or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus, or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus, or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus, or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus, or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C43.0	Malignant melanoma of lip
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower 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
C44.00	Unspecified malignant neoplasm of skin of lip
C44.02	Squamous cell carcinoma of skin of lip
C44.09	Other specified malignant neoplasm of skin of lip
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C66.1	Malignant neoplasm of right ureter
C66.2	Malignant neoplasm of left ureter
C66.9	Malignant neoplasm of unspecified ureter
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
C67.9	Malignant neoplasm of bladder, unspecified
C68.0	Malignant neoplasm of urethra
C76.0	Malignant neoplasm of head, face, and neck
C77.0	Secondary and unspecified malignant neoplasm of lymph nodes of head, face, and neck
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung

C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
D09.0	Carcinoma in situ of bladder
D37.01	Neoplasm of uncertain behavior of lip
D37.02	Neoplasm of uncertain behavior of tongue
D37.05	Neoplasm of uncertain behavior of pharynx
D37.09	Neoplasm of uncertain behavior of other specified sites of the oral cavity
D37.1	Neoplasm of uncertain behavior of stomach
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
D38.0	Neoplasm of uncertain behavior of larynx
D38.5	Neoplasm of uncertain behavior of other respiratory organs
D38.6	Neoplasm of uncertain behavior of respiratory organ, unspecified
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ
Z85.01	Personal history of malignant neoplasm of esophagus
Z85.028	Personal history of other malignant neoplasm of stomach
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.51	Personal history of malignant neoplasm of bladder
Z85.59	Personal history of malignant neoplasm of other urinary tract organ

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
6	MN, WI, IL	National Government Services, Inc. (NGS)
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 GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
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