Opdivo® (nivolumab)
(Intravenous)

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I. Length of Authorization Δ [1,43,47,49,50,52-54,65,68,72,73,79,81,82,89]

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

- Use in the treatment of Classical Hodgkin Lymphoma in combination with brentuximab vedotin can be authorized up to a maximum of 12 weeks of therapy (4 doses) and may NOT be renewed.
- Neoadjuvant or Perioperative Therapy of MSI-H/dMMR Gastric and Esophagogastric/Gastroesophageal Junction Cancer can be authorized for a maximum of 12 weeks of pre-operative therapy (6 doses), followed by a maximum of 36 weeks (9 doses) of postoperative therapy after surgery.
- Neoadjuvant treatment of Merkel Cell Carcinoma can be authorized up to a maximum of two (2) doses and may NOT be renewed.
- Neoadjuvant treatment of NSCLC in combination with platinum-doublet chemotherapy may be authorized for a maximum of three (3) doses and may NOT be renewed.
- Adjuvant treatment of Cutaneous Melanoma in combination with ipilimumab may be authorized for a maximum of four (4) doses and may NOT be renewed.
- 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*:
  - Biliary Tract Cancer
  - Bone Cancer
  - Cervical Cancer

- Esophageal and Esophagogastric/Gastroesophageal Junction Cancer (first-line therapy)
- Gastric Cancer (in combination with fluoropyrimidine- and platinum-containing chemotherapy)
- Kaposi Sarcoma
- Renal Cell Carcinoma (in combination with cabozantinib)
- Malignant Pleural Mesothelioma (initial therapy in combination with ipilimumab)
- Malignant Peritoneal Mesothelioma (initial therapy in combination with ipilimumab)
- Non-Small Cell Lung Cancer (in combination with ipilimumab with or without platinum-doublet chemotherapy)

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

A. Quantity Limit (max daily dose) [NDC Unit]:

- Opdivo 40 mg/4 mL single-dose vial: 2 vials per 14 days
- Opdivo 100 mg/10 mL single-dose vial: 3 vials per 14 days
- Opdivo 120 mg/12 mL single-dose vial: 3 vials per 14 days
- Opdivo 240 mg/24 mL single-dose vial: 4 vials per 14 days

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

Indication	Billable Units (BU)	Per unit time (days)
CNS Cancer, HCC, Cutaneous Melanoma, Uveal Melanoma, & MCC	120 BU	21 days
Biliary Tract Cancer, Bladder Cancer, Bone Cancer, CRC, Appendiceal Adenocarcinoma, Esophageal Cancer, GEJ Cancer, Gastric, SCCHN, HCC, cHL, Kaposi Sarcoma, RCC, MPM, MPeM, Cutaneous Melanoma, MCC, NSCLC, STS, & Cervical Cancer	240 BU	14 days
CNS Cancer, CRC, Esophageal Cancer, MPM, MPeM, Uveal Melanoma, MCC, & Cutaneous Melanoma	340 BU	14 days
CRC, cHL, & RCC	340 BU	21 days
Esophageal Cancer, GEJ Cancer, Gastric Cancer, MPM, MPeM, & NSCLC	360 BU	21 days

Bladder Cancer, Bone Cancer, CRC, Esophageal Cancer, GEJ Cancer, SCCHN, HCC, cHL, RCC, Cutaneous Melanoma, NSCLC, & STS	480 BU	28 days
Uveal Melanoma	1140 BU	14 days

III. Initial Approval Criteria [1]

Coverage is provided for the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); **AND**

Universal Criteria

- Patient has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy (e.g., cemiplimab, avelumab, pembrolizumab, atezolizumab, durvalumab, dostarlimab, nivolumab/relatlimab-rmbw, retifanlimab, etc.), unless otherwise specified ∆; **AND**

Biliary Tract Cancers (Gallbladder Cancer or Intra-/Extra-Hepatic Cholangiocarcinoma) ‡ [2,72,177e]

- Patient has tumor mutational burden-high (TMB-H) [≥ 10 mutations/megabase (mut/Mb)] disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used as subsequent treatment for progression on or after systemic treatment for unresectable, resected gross residual (R2), or metastatic disease; **AND**
- Used in combination with ipilimumab; **AND**
- Disease is refractory to standard therapies or there are no standard treatment options available

Urothelial Carcinoma (Bladder Cancer) † ‡ [1,2,30,51,62]

- Used as a single agent; **AND**
  - Used for disease that progressed during or following platinum-containing chemotherapy*; **AND**
    - Patient has one of the following diagnoses:
      - Locally advanced or metastatic urothelial carcinoma †
      - Muscle invasive bladder cancer with local recurrence or persistent disease in a preserved bladder
      - Metastatic or local bladder cancer recurrence post-cystectomy
      - Recurrent or metastatic primary carcinoma of the urethra; **AND**
        - Patient does not have recurrence of stage T3-4 disease or palpable inguinal lymph nodes
      - Metastatic upper genitourinary (GU) tract tumors ‡; **OR**
  - Used as adjuvant therapy †; **AND**

- Patient has urothelial carcinoma of the bladder, ureter, or renal pelvis; **AND**
- Patient underwent radical surgical resection; **AND**
- Patient is at high risk for disease recurrence**

**** Note:*** [10,51,60,70] – *If patient was progression free for >12 months after platinum therapy, consider re-treatment with platinum-based therapy if the patient is still platinum eligible (see below for cisplatin- or platinum-ineligible comorbidities).* ▪ *Cisplatin-ineligible comorbidities may include the following: CrCl < 60 mL/min, ECOG PS ≥ 2 or KPS ≤ 70%, hearing loss of ≥ 25 decibels (dB) at two contiguous frequencies, grade ≥ 2 peripheral neuropathy, or NYHA Heart Failure class ≥ 3. Carboplatin may be substituted for cisplatin particularly in those patients with a CrCl <60 mL/min or a PS of 2.* ▪ *Platinum-ineligible comorbidities may include the following: CrCl < 30 mL/min, ECOG PS ≥ 3, grade ≥ 2 peripheral neuropathy, or NYHA Heart Failure class > 3, etc.*
***** 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)*

Bone Cancers ‡ [2,72,177e]

- Patient has one of the following: Ewing Sarcoma, Chondrosarcoma *(excluding mesenchymal chondrosarcoma)*, Osteosarcoma, or Chordoma; **AND**
- Patient has tumor mutation burden-high (TMB-H) [≥ 10 mutations/megabase (mut/Mb)] disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
- Used in combination with ipilimumab; **AND**
- Patient has unresectable or metastatic disease that progressed following prior treatment; **AND**
- Patient has no satisfactory alternative treatment options

Adult Central Nervous System (CNS) Cancers ‡ [2,5,34,41,42]

- Used in one of the following treatment settings:
  - Used as initial treatment in patients with small asymptomatic brain metastases
  - Used for relapsed limited brain metastases with either stable systemic disease or reasonable systemic treatment options
  - Patient has recurrent limited brain metastases
  - Used for recurrent extensive brain metastases with stable systemic disease or reasonable systemic treatment options; **AND**

- Used in combination with ipilimumab for the treatment of brain metastases in patients with BRAF non-specific melanoma

Cervical Cancer ‡ [2,49,63]

- Used as subsequent therapy as a single agent; **AND**
- Patient has recurrent or metastatic disease; **AND**
- Tumor expresses PD-L1 (e.g., CPS ≥1) as determined by an FDA-approved or CLIA-compliant test❖

Colorectal Cancer (CRC) † ‡ [1,2,31,32,59,106e,107e]

- Patient is at least 12 years of age; **AND**
- Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
  - Used as subsequent therapy; **AND**
    - Used as a single agent or in combination with ipilimumab*****; **AND**
    - Patient has metastatic, unresectable, or medically inoperable disease; **AND**
    - Disease progressed following treatment with a fluoropyrimidine-, oxaliplatin-, and/or irinotecan-based chemotherapy; **OR**
  - Used as primary or initial treatment; **AND**
    - Used in combination with ipilimumab; **AND**
    - Used for isolated pelvic/anastomotic recurrence of rectal cancer; **OR**
    - Patient has T3, N Any; T1-2, N1-2; T4, N Any rectal cancer; **OR**
    - Patient has metastatic, unresectable, or medically inoperable disease

****** *Single agent nivolumab should be used in patients who are not candidates for intensive therapy*

Esophageal Cancer and Esophagogastric/Gastroesophageal Junction Cancers † ‡ Φ [1,2,44,52,56,69,133e,158e]

- Used as first-line therapy; **AND**
  - Patient has esophageal squamous cell carcinoma †; **AND**
    - Patient is not a surgical candidate or has unresectable advanced, recurrent, or metastatic disease; **AND**
      - Used in combination with ipilimumab; **OR**
      - Used in combination with fluorouracil or capecitabine AND cisplatin or oxaliplatin; **OR**
  - Patient has adenocarcinoma; **AND**
    - Patient is not a surgical candidate or has unresectable, advanced, recurrent, or metastatic disease; **AND**

        - Used in combination with oxaliplatin and either fluorouracil or capecitabine for HER2 negative disease*; **AND**
        - Patient has a Combined Positive Score (CPS) ≥5 as determined by an FDA-approved or CLIA-compliant test❖; **OR**
- Used as subsequent therapy; **AND**
    - Patient has esophageal squamous cell carcinoma †; **AND**
    - Patient is not a surgical candidate or has unresectable advanced, recurrent, or metastatic disease; **AND**
    - Used as a single agent; **AND**
    - Patient is refractory or intolerant to at least one prior fluoropyrimidine- and platinum-based regimen; **OR**
- Used as adjuvant treatment of completely resected disease †; **AND**
    - Used as a single agent in patients with residual disease following neoadjuvant chemoradiotherapy (CRT); **OR**
- Used as neoadjuvant or perioperative therapy; **AND**
    - Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
    - Patient has esophagogastric/gastroesophageal junction adenocarcinoma; **AND**
        - Used in combination with ipilimumab; **AND**
            - Used as primary treatment for patients who are medically fit for surgery with cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease; **OR**
        - Used as a single agent *(for use as perioperative therapy ONLY)*; **AND**
            - Used as postoperative management following R0 resection in patients who have received preoperative therapy with nivolumab and ipilimumab

**Note: Combination therapy with oxaliplatin and fluorouracil or capecitabine may also be used for patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖*

Gastric Cancer † ‡ Φ [1,2,53,56]

- Used as first-line therapy; **AND**
    - Patient is not a surgical candidate or has unresectable, advanced, recurrent, or metastatic disease; **AND**
    - Used in combination with oxaliplatin and either fluorouracil or capecitabine for HER2 negative disease*; **AND**
    - Patient has a Combined Positive Score (CPS) ≥5 as determined by an FDA-approved or CLIA-compliant test❖; **OR**

- Used as neoadjuvant or perioperative therapy; **AND**
  - Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
    - Used in combination with ipilimumab; **AND**
      - Used as primary treatment prior to surgery for potentially resectable locoregional disease (cT2 or higher, any N) in patients who are medically fit for surgery; **OR**
    - Used as a single agent *(for use as perioperative therapy ONLY)*; **AND**
      - Used as postoperative management following R0 resection in patients who have received preoperative therapy with nivolumab and ipilimumab

Note: Combination therapy with oxaliplatin and fluorouracil or capecitabine may also be used for patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease as determined by an FDA-approved or CLIA-compliant test❖

Squamous Cell Carcinoma of the Head and Neck (SCCHN) † ‡ [1,2,29,78]

- Patient has Very Advanced Head and Neck Cancer*; **AND**
- Patient has NON-nasopharyngeal cancer; **AND**
  - Used as a single agent; **AND**
    - Patient has unresectable, recurrent, persistent, or metastatic disease; **AND**
    - Disease has progressed on or after platinum-containing chemotherapy; **AND**
    - Patient has PD-L1 expression ≥1% as determined by an FDA-approved or CLIA-compliant test❖; **OR**
  - Used in combination with cetuximab for patients with performance status (PS) 0-1; **AND**
    - Used as first-line therapy; **AND**
    - Used for one of the following:
      - Metastatic disease at initial presentation
      - Recurrent/persistent disease with distant metastases
      - Unresectable locoregional recurrence with prior RT
      - Unresectable second primary with prior RT
      - Unresectable persistent disease with prior RT

*** Very Advanced Head and Neck Cancer includes: newly diagnosed locally advanced T4b (M0) disease, newly diagnosed unresectable regional nodal disease (typically N3), metastatic disease at initial presentation (M1), or recurrent or persistent disease.***

Hepatocellular Carcinoma (HCC) † ‡ Φ [1,2,21,86,87,38e-40e]

- Used for one of the following:

        - Patient was previously treated with sorafenib *(in combination with ipilimumab ONLY)* †
        - Patient has unresectable disease and is not a transplant candidate
        - Patient has liver-confined disease that is inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic-disease
        - Patient has metastatic disease or extensive liver tumor burden; **AND**
    - Used in combination with ipilimumab; **AND**
        - Patient has Child-Pugh Class A hepatic impairment; **AND**
        - Used as subsequent therapy for progressive disease; **OR**
    - Used as a single agent; **AND**
        - Patient has Child-Pugh Class B7 or B8 hepatic impairment

Adult Classical Hodgkin Lymphoma (cHL) † ‡ Φ [1,2,27,28,73,54,75e]

- Used as a single agent; **AND**
    - Patient has relapsed or progressive disease after autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin †; **OR**
    - Used for disease that is refractory to at least 3 prior lines of therapy including autologous HSCT †; **OR**
- Used in combination with brentuximab vedotin in patients 18 to 60 years of age; **AND**
    - Used as second-line therapy for relapsed or refractory disease; **OR**
    - Used as subsequent therapy (if not previously used) for relapsed or refractory disease; **AND**
        - Patient has a Deauville scale score of 4 or 5 following restaging with FDG-PET/CT

Pediatric Classical Hodgkin Lymphoma (cHL) ‡ [2,27,28,55]

- Patient is ≤ 18 years of age*; **AND**
- Patient has relapsed or refractory disease; **AND**
- Used in patients heavily pretreated with platinum or anthracycline-based chemotherapy or if a decrease in cardiac function was observed; **AND**
- Used as subsequent therapy (if not previously used); **AND**
- Used in combination with brentuximab vedotin

** Pediatric Hodgkin Lymphoma may be applicable to adolescent and young adult (AYA) patients up to the age of 39 years.*

Kaposi Sarcoma ‡ [2,79]

- Used in combination with ipilimumab as subsequent therapy; **AND**
- Patient has classic disease; **AND**

- Used for relapsed/refractory advanced cutaneous, oral, visceral, or nodal disease; **AND**
- Disease has progressed on or not responded to first-line therapy; **AND**
- Disease has progressed on alternate first-line therapy

Renal Cell Carcinoma (RCC) † ‡ [1,2,25,26,66e,164e]

- Used in combination with ipilimumab; **AND**
  - Patient has clear cell histology; **AND**
    - Used as first-line therapy in patients with poor or intermediate risk advanced, relapsed, or stage IV disease; **OR**
    - Used as first-line therapy in patients with favorable risk relapsed or stage IV disease; **OR**
- Used as a single agent; **AND**
  - Used as subsequent therapy in patients with advanced, relapsed, or stage IV disease and clear cell histology; **OR**
- Used in combination with cabozantinib (Cabometyx only); **AND**
  - Patient has clear cell histology; **AND**
    - Used as first-line therapy for advanced, relapsed, or stage IV disease; **OR**
  - Patient has non-clear cell histology; **AND**
    - Patient has relapsed or stage IV disease; **AND**
    - Patient does not have chromophobe RCC

Cutaneous Melanoma † ‡ Φ [1,2,15-18,82,14e,150e-152e]

- Used as first-line therapy for unresectable or metastatic* disease; **AND**
  - Patient is at least 12 years of age; **AND**
  - Used as a single agent or in combination with ipilimumab; **OR**
- Used as subsequent therapy for unresectable or metastatic* disease; **AND**
  - Patient is at least 12 years of age; **AND**
    - Used after disease progression, intolerance, and/or projected risk of progression with BRAF-targeted therapy (e.g., dabrafenib/trametinib, vemurafenib/cobimetinib, encorafenib/binimetinib, etc.); **AND**
      - Used as a single agent or in combination with ipilimumab if anti-PD-1 therapy was not previously used; **OR**
      - Used in combination with ipilimumab for disease progression on single agent anti-PD-1 therapy; **OR**
- Used as adjuvant treatment; **AND**
  - Used as a single agent; **AND**
    - Patient is at least 12 years of age; **AND**

        - Patient has stage IIB, IIC, IIIB, IIIC, or metastatic disease †; **AND**
            - Patient has undergone complete resection †; **OR**
        - Patient has oligometastatic disease and no evidence of disease (NED) following metastasis-directed therapy (i.e., stereotactic ablative therapy or complete resection) or systemic therapy followed by resection; **OR**
    - Used in combination with ipilimumab; **AND**
        - Patient has oligometastatic disease and no evidence of disease (NED) following metastasis-directed therapy (i.e., complete resection, stereotactic ablative therapy or T-VEC/intralesional therapy) or systemic therapy followed by resection

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

Uveal Melanoma ‡ [2,19,20,80]

- Patient has metastatic or unresectable disease; **AND**
- Used as first-line therapy in combination with ipilimumab

Merkel Cell Carcinoma ‡ [2,4,33,65]

- Used as neoadjuvant treatment for regional, pathologic N+ disease; **AND**
    - Used as a single agent; **OR**
- Used for M1 disseminated disease; **AND**
    - Used as a single agent; **OR**
    - Used in combination with ipilimumab; **AND**
        - Patient progressed on anti-PD-L1 or anti-PD-1 therapy OR anti-PD-L1 or anti-PD-1 therapy is contraindicated

Malignant Peritoneal Mesothelioma (MPeM) ‡ [2,64]

- Used as a single agent as subsequent therapy (if chemotherapy was administered first-line)

Malignant Pleural Mesothelioma (MPM) † ‡ Φ [1,2,37,38,47,64,81]

- Used as a single agent or in combination with ipilimumab as subsequent therapy (if chemotherapy was administered first-line); **AND**
    - Patient previously received platinum-containing chemotherapy; **OR**
- Used in combination with ipilimumab as first-line therapy; **AND**
    - Disease is medically inoperable or unresectable

Non-Small Cell Lung Cancer (NSCLC) † ‡ [1,2,11,22,23,43,45,46,43e-45e,51e-53e,56e,125e,127e,166e]

- Used as neoadjuvant therapy for resectable (tumors ≥ 4 cm or node positive) disease; **AND**

- Used in combination with platinum-doublet chemotherapy (e.g., cisplatin/carboplatin in combination with paclitaxel, pemetrexed, or gemcitabine); **OR**

- Used for recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
  - Used as first-line therapy; **AND**
    - Used for one of the following:
      - Patients with a performance status (PS) 0-1 who have tumors that are negative for actionable molecular biomarkers** and PD-L1 expression <1%
      - Patients with a PS 0-1 who are positive for one of the following molecular biomarkers: EGFR exon 20, KRAS G12C, BRAF V600E, NTRK1/2/3 gene fusions, MET exon 14 skipping, RET rearrangement, or ERBB2 (HER2)
      - PD-L1 expression-positive (PD-L1 ≥1%) tumors, as detected by an FDA or CLIA compliant test❖, that are negative for actionable molecular biomarkers**; **AND**
    - Used in combination with one of the following:
      - Ipilimumab
      - Ipilimumab and platinum-doublet chemotherapy (e.g., pemetrexed and either carboplatin or cisplatin for nonsquamous cell histology, or paclitaxel and carboplatin for squamous cell histology, etc.); **OR**
  - Used as subsequent therapy; **AND**
    - Used as a single agent; **OR**
    - Used for one of the following:
      - Patients with a PS 0-1 who are positive for one of the following molecular biomarkers and have received prior targeted therapy§: EGFR exon 19 deletion or exon 21 L858R tumors, EGFR S768I, L861Q, and/or G719X, ALK rearrangement, or ROS1 rearrangement
      - Patients with a PS 0-1 who are positive for one of the following molecular biomarkers: BRAF V600E, NTRK1/2/3 gene fusions, MET exon 14 skipping, or RET rearrangement; **AND**
        - Used in combination with one of the following:
          - Ipilimumab
          - Ipilimumab, pemetrexed, and either carboplatin or cisplatin for nonsquamous cell histology
          - Ipilimumab, paclitaxel, and carboplatin for squamous cell histology; **OR**
  - Used as continuation maintenance therapy in combination with ipilimumab; **AND**

- Patient has achieved a response or stable disease following first-line therapy with nivolumab and ipilimumab with or without chemotherapy

******* Note: Actionable molecular genomic biomarkers include EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2). If there is insufficient tissue to allow testing for all of EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.*

Soft Tissue Sarcoma ‡ [2,72,84]

- Extremity/Body Wall, Head/Neck***** or Retroperitoneal/Intra-Abdominal******
  - Used as a single agent or in combination with ipilimumab; **AND**
  - Used as subsequent therapy; **AND**
  - Patient has tumor mutational burden-high (TMB-H) [≥ 10 mutations/megabase (mut/Mb)] disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
  - Patient has no satisfactory alternative treatment options; **OR**
- Pleomorphic Rhabdomyosarcoma
  - Used as a single agent or in combination with ipilimumab; **AND**
  - Used as subsequent therapy; **AND**
  - Patient has tumor mutational burden-high (TMB-H) [≥ 10 mutations/megabase (mut/Mb)] disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**
  - Patient has no satisfactory alternative treatment options

*******Treat atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLS) extremity, abdominal wall, trunk with evidence of de-differentiation as other soft tissue sarcomas.*

********Treat well-differentiated liposarcoma (WDLS-retroperitoneum, paratesticular) with or without evidence of de-differentiation as other soft tissue sarcomas.*

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

❖ *If confirmed using an FDA approved assay – http://www.fda.gov/CompanionDiagnostics*

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

§ Genomic Aberration/Mutational Driver Targeted Therapies (Note: *not all inclusive, refer to guidelines for appropriate use*)				
Sensitizing *EGFR* mutation-positive tumors	*ALK* rearrangement-positive tumors	*ROS1* rearrangement-positive tumors	*BRAF* V600E-mutation positive tumors	*NTRK1/2/3* gene fusion positive tumors

– Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab *(exon-20 insertion)*	– Alectinib – Brigatinib – Ceritinib – Crizotinib – Lorlatinib	– Ceritinib – Crizotinib – Entrectinib – Lorlatinib	– Dabrafenib ± trametinib – Encorafenib + binimetinib – Vemurafenib	– Larotrectinib – Entrectinib
PD-L1 tumor expression ≥ 1%	*MET* exon-14 skipping mutations	*RET* rearrangement-positive tumors	*KRAS G12C* mutation positive tumors	*ERBB2 (HER2)* mutation positive tumors
– Pembrolizumab – Atezolizumab – Nivolumab + ipilimumab – Cemiplimab – Tremelimumab + durvalumab	– Capmatinib – Crizotinib – Tepotinib	– Selpercatinib – Cabozantinib – Pralsetinib	– Sotorasib – Adagrasib	– Fam-trastuzumab deruxtecan-nxki – Ado-trastuzumab emtansine

IV. Renewal Criteria Δ 1,2,4-6,15-42,43,47,49,50,52-54,68,72,73,79,81,82,89

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion-related reactions, complications of allogeneic hematopoietic stem cell transplantation (HSCT), severe immune-mediated adverse reactions (i.e., pneumonitis, colitis, hepatitis/hepatotoxicity, endocrinopathies, nephritis/renal dysfunction, adverse skin reactions/rash, etc.), etc.; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- For the following indications, patient has not exceeded a maximum of two (2) years of therapy*:
  - Biliary Tract Cancer
  - Bone Cancer
  - Cervical Cancer
  - Esophageal and Esophagogastric/Gastroesophageal Junction Cancer (first-line therapy)
  - Gastric Cancer (in combination with fluoropyrimidine- and platinum-containing chemotherapy)
  - Kaposi Sarcoma
  - Renal Cell Carcinoma (in combination with cabozantinib)
  - Malignant Pleural Mesothelioma (initial therapy in combination with ipilimumab)
  - Malignant Peritoneal Mesothelioma (initial therapy in combination with ipilimumab)

- Non-Small Cell Lung Cancer (in combination with ipilimumab with or without platinum-doublet chemotherapy)

Urothelial Carcinoma (adjuvant therapy)*

- Patient has not exceeded a maximum of one (1) year of therapy

Esophageal and Esophagogastric/Gastroesophageal Junction Cancer (adjuvant therapy)*

- Patient has not exceeded a maximum of one (1) year of therapy

MSI-H/dMMR Gastric and Esophagogastric/Gastroesophageal Junction Cancer (neoadjuvant or perioperative therapy)

- Patient has not exceeded a maximum of 12 weeks of pre-operative therapy (6 doses), followed by a maximum of 36 weeks (9 doses) of postoperative therapy after surgery

Classical Hodgkin Lymphoma (in combination with brentuximab vedotin)

- Patient has not exceeded a maximum of 12 weeks of therapy (4 doses)

Cutaneous Melanoma (adjuvant therapy as a single agent)*

- Patient has not exceeded a maximum of one (1) year of therapy

Cutaneous Melanoma (adjuvant therapy in combination with ipilimumab)

- Patient has not exceeded a maximum of four (4) doses

Merkel Cell Carcinoma (neoadjuvant therapy)

- Patient has not exceeded a maximum of two (2) doses

Non-Small Cell Lung Cancer (neoadjuvant therapy in combination with platinum-doublet chemotherapy)

- Patient has not exceeded a maximum of three (3) doses

Non-Small Cell Lung Cancer (maintenance therapy)

- *Refer to Section III for criteria*

Δ Notes:

- Patients responding to therapy who relapse ≥ 6 months after discontinuation due to duration (i.e., receipt of 24 months of therapy) 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 [1,4-6,19,20,27,24,31-42,48-50,52-54,55,58,59,61,65,67,68,71-80-86,87,89]

Indication	Dose
Biliary Tract Cancers	Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 24 months (2 years)
Urothelial Carcinoma (Bladder Cancer)	Disease progression or second-line treatment: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity Adjuvant treatment: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease recurrence or unacceptable toxicity for up to 1 year
Bone Cancer	Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 24 months (2 years)
Adult CNS Cancers	**Metastases from Melanoma** Single agent: • Administer 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity In combination with ipilimumab: • Administer 1 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity
Colorectal Cancer (CRC)	Adult patients and for pediatric patients ≥ 12 years and ≥ 40 kg: • **Single agent:** Administer 3 mg/kg intravenously every 2 weeks, or 240 mg intravenously every 2 weeks, or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity • **In combination with ipilimumab:** Primary/initial treatment ○ Administer 3 mg/kg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity Subsequent therapy ○ Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then follow with the single agent regimen

	Pediatric patients ≥ 12 years and < 40 kg: • **Single agent:** Administer 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity • **In combination with ipilimumab:** Primary/initial treatment o Administer 3 mg/kg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity Subsequent therapy o Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then follow with the single agent regimen
Esophageal Cancer **(Squamous Cell Carcinoma)**	First-line therapy: • Administer 240 mg intravenously every 2 weeks or 360 mg intravenously every 3 weeks or 480 mg intravenously every 4 weeks (given in combination with fluoropyrimidine- and platinum-containing chemotherapy) until disease progression or unacceptable toxicity for up to 2 years • Administer 3 mg/kg intravenously every 2 weeks or 360 mg intravenously every 3 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 2 years Subsequent therapy: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity
Esophageal and Esophagogastric/ Gastroesophageal Junction Cancer **(Adjuvant Therapy)**	Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks for up to 1 year
MSI-H/dMMR Gastric and Esophagogastric/ Gastroesophageal Junction Cancer	Neoadjuvant/perioperative therapy (adenocarcinoma only): • Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) for 12 weeks, followed by surgery and then post-operative therapy *(See below)* Post-operative therapy (adenocarcinoma only): • Administer 480 mg intravenously every 4 weeks for 36 weeks (9 cycles)
Esophageal and Esophagogastric/ Gastroesophageal Junction Cancer **(Adenocarcinoma)**	First-line therapy: Administer 240 mg intravenously every 2 weeks or 360 mg intravenously every 3 weeks (given in combination with fluoropyrimidine- and platinum-containing chemotherapy) until disease progression or unacceptable toxicity for up to 2 years
Gastric Cancer	Administer 240 mg intravenously every 2 weeks or 360 mg intravenously every 3 weeks until disease progression or unacceptable toxicity for up to 2 years
SCCHN	Single agent:

	• Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity In combination with cetuximab: • Administer 240 mg intravenously every 2 weeks until disease progression or unacceptable toxicity
Hepatocellular Carcinoma (HCC)	Single agent: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity In combination with ipilimumab: • Administer 1 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity
Adult cHL	Single agent: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity In combination with brentuximab vedotin • Administer 3 mg/kg intravenously every 3 weeks for up to 12 weeks (4 cycles)
Pediatric cHL	In combination with brentuximab vedotin • Administer 3 mg/kg intravenously every 3 weeks for up to 12 weeks (4 cycles)
Kaposi Sarcoma	Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 24 months (2 years)
Renal Cell Carcinoma (RCC)	Single agent: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity In combination with ipilimumab: • Administer 3 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then follow with the single agent regimen until disease progression or unacceptable toxicity In combination with cabozantinib (Cabometyx): • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity for up to 2 years
Malignant Peritoneal Mesothelioma (MPeM)	Single agent: • Administer 3 mg/kg intravenously or 240 mg intravenously every 2 weeks until disease progression or unacceptable toxicity
Malignant Pleural Mesothelioma (MPM)	Single agent: ○ Administer 3 mg/kg intravenously or 240 mg intravenously every 2 weeks until disease progression or unacceptable toxicity In combination with ipilimumab: • Initial Therapy

	○ Administer 360 mg intravenously every 3 weeks or 3 mg/kg every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 2 years • Subsequent Therapy ○ Administer 3 mg/kg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity; **OR** ○ Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity
Cutaneous Melanoma	Adult patients and for pediatric patients ≥ 12 years and ≥ 40 kg: Single agent • Unresectable or metastatic disease: Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity • Adjuvant treatment: Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease recurrence or unacceptable toxicity for up to 1 year In combination with ipilimumab • Unresectable or metastatic disease: Administer 1 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then follow with the single agent regimen • Adjuvant treatment: Administer 1 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day) Pediatric patients ≥ 12 years and < 40 kg: Single agent • Unresectable or metastatic disease: Administer 3 mg/kg intravenously every 2 weeks or 6 mg/kg intravenously every 4 weeks until disease progression or unacceptable toxicity • Adjuvant treatment: Administer 3 mg/kg intravenously every 2 weeks or 6 mg/kg intravenously every 4 weeks until disease recurrence or unacceptable toxicity for up to 1 year In combination with ipilimumab • Unresectable or metastatic disease: Administer 1 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then follow with the single agent regimen • Adjuvant treatment: Administer 1 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day)
Uveal Melanoma	In combination with ipilimumab: • Administer 1 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity
Merkel Cell Carcinoma	Neoadjuvant treatment: • Administer 240 mg intravenously every 2 weeks (days 1 and 15) for a total of 2 doses

	M1 disseminated disease: Single agent: • Administer 240 mg intravenously every 2 weeks or 3 mg/kg intravenously every 2 weeks until disease progression or unacceptable toxicity In combination with ipilimumab: • Administer 1 mg/kg intravenously every 3 weeks for 4 doses (given in combination with ipilimumab on the same day), then follow with the single agent regimen • Administer 3 mg/kg intravenously or 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity
Non-Small Cell Lung Cancer (NSCLC)	Neoadjuvant treatment in combination with platinum-doublet chemotherapy: • Administer 360 mg intravenously with platinum-doublet chemotherapy every 3 weeks for 3 cycles. Single agent: • Administer 240 mg intravenously every 2 weeks or 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity In combination with ipilimumab: • Administer 360 mg intravenously every 3 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity for up to 2 years In combination with ipilimumab and platinum-doublet chemotherapy: • Administer 360 mg intravenously every 3 weeks (given in combination with ipilimumab every 6 weeks and histology-based platinum-doublet chemotherapy every 3 weeks for 2 cycles) until disease progression or unacceptable toxicity for up to 2 years.
Soft Tissue Sarcoma	Single agent: • Administer 480 mg intravenously every 4 weeks until disease progression or unacceptable toxicity In combination with ipilimumab: • Administer 240 mg intravenously every 2 weeks (given in combination with ipilimumab every 6 weeks) until disease progression or unacceptable toxicity
Cervical Cancer	Administer 240 mg intravenously every 2 weeks until disease progression or unacceptable toxicity for up to 2 years
Dosing should be calculated using actual body weight and not flat dosing (as applicable) based on the following: Weight ≥ 74 kg: • Standard dose 480 mg IV every 4 weeks Weight is 67 kg to 73 kg: • Use 440 mg IV every 4 weeks	

Weight is ≤ 66kg:

- Use 400 mg IV every 4 weeks

-OR-

Weight > 67 kg:

- Standard dose 240 mg IV every 2 weeks

Weight is 53 kg to 67 kg:

- Use 200 mg IV every 2 weeks

Weight is < 53kg:

- Use 160 mg IV every 2 weeks

Note: This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide. Patient-specific variables should be taken into account.

VI. Billing Code/Availability Information

HCPCS Code:

- J9299 – Injection, nivolumab, 1 mg; 1 billable unit = 1 mg

NDC(s):

- Opdivo 40 mg/4 mL single-dose vial: 00003-3772-xx
- Opdivo 100 mg/10 mL single-dose vial: 00003-3774-xx
- Opdivo 120 mg/12 mL single-dose vial: 00003-3756-xx
- Opdivo 240 mg/24 mL single-dose vial: 00003-3734-xx

VII. References (STANDARD)

1. Opdivo [package insert]. Princeton, NJ; Bristol-Myers Squibb Company; October 2023. Accessed December 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) nivolumab. National Comprehensive Cancer Network, 2023. 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 December 2023.
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 Oncol2017; 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, Chiariron-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 1/2 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 1/2 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 cohort, phase 1/2 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 3.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.
36. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Gestational Trophoblastic Neoplasia. Version 1.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.
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 1.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.
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 5.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.
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 3.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.
52. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Esophageal and Esophagogastric Junction Cancers. Version 3.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.
53. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Gastric Cancer. Version 2.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.
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, Mascarin 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 July 1, 2021. Accessed July 2021.
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 October 26, 2023. Accessed November 7, 2023. Available from https://www.uptodate.com/contents/treatment-of-metastatic-urothelial-cancer-of-the-bladder-and-urinary-tract?search=cisplatin%20ineligible&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1.
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 1.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.
64. Fennell DA, Ewings S, Ottensmeier C, et al. Nivolumab versus placebo in patients with relapsed malignant mesothelioma (CONFIRM): a multicentre, double-blind, randomised, 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 (2021). Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo as neoadjuvant treatment (tx) for resectable (1B-IIIA) non-small cell lung cancer NSCLC in the phase 3 CheckMate 816 trial. American Association for Cancer Research Annual Meeting 2021. Abstract CT003.
67. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Mesothelioma: Peritoneal. Version 1.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.
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, 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. 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. 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 tumours 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.
76. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Pediatric Aggressive Mature B-Cell Lymphomas. Version 1.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.
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, randomised, 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. PlumX Metrics

86. Yau T, Park JW, Finn RS, et al. Nivolumab versus sorafenib in advanced hepatocellular carcinoma (CheckMate 459): a randomised, 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.supp.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.

VIII. References (ENHANCED)

1e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Central Nervous System Cancers. Version 1.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.
2e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Colon Cancer. Version 4.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.
3e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Melanoma: Cutaneous. Version 3.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.
4e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Head and Neck Cancers. Version 2.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.

5e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hepatocellular Carcinoma. Version 2.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.

6e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Hodgkin Lymphoma. Version 1.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.

7e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Kidney Cancer. Version 1.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.

8e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Mesothelioma: Pleural. Version 1.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.

9e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Merkel Cell Carcinoma. Version 1.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.

10e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Rectal Cancer. Version 6.2023. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®.

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11e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Small Cell Lung Cancer. Version 2.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.

12e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) T-Cell Lymphomas. Version 1.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.

13e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Melanoma: Uveal. Version 1.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.

14e. Robert C, Schachter J, Long GV, et al. Pembrolizumab versus Ipilimumab in Advanced Melanoma. N Engl J Med. 2015 Jun 25;372(26):2521-32. Doi: 10.1056/NEJMoa1503093.

15e. Ascierto PA, Long GV, Robert C, et al. Survival Outcomes in Patients With Previously Untreated BRAF Wild-Type Advanced Melanoma Treated With Nivolumab Therapy: Three-Year Follow-up of a Randomized Phase 3 Trial [published correction appears in JAMA Oncol. 2019 Feb 1;5(2):271]. JAMA Oncol. 2019;5(2):187–194. Doi:10.1001/jamaoncol.2018.4514.

16e. Wolchok JD, Chiarion-Sileni V, Gonzalez R, et al. Overall Survival with Combined Nivolumab and Ipilimumab in Advanced Melanoma [published correction appears in N Engl J Med. 2018 Nov 29;379(22):2185]. N Engl J Med. 2017;377(14):1345–1356. Doi:10.1056/NEJMoa1709684.

17e. Regan MM, Werner L, Rao S, et al. Treatment-Free Survival: A Novel Outcome Measure of the Effects of Immune Checkpoint Inhibition-A Pooled Analysis of Patients With Advanced Melanoma. J Clin Oncol. 2019;37(35):3350-3358. Doi:10.1200/JCO.19.00345.

18e. Ribas A, Puzanov I, Dummer R, et al. Pembrolizumab versus investigator-choice chemotherapy for ipilimumab-refractory melanoma (KEYNOTE-002): a randomised, controlled, phase 2 trial. Lancet Oncol. 2015 Aug;16(8):908-18. Doi: 10.1016/S1470-2045(15)00083-2.

19e. Hamid O, Puzanov I, Dummer R, et al. Final analysis of a randomised trial comparing pembrolizumab versus investigator-choice chemotherapy for ipilimumab-refractory advanced melanoma. Eur J Cancer. 2017 Nov;86:37-45. Doi: 10.1016/j.ejca.2017.07.022.

20e. Hodi FS, O'Day SJ, McDermott DF, et al. Improved survival with ipilimumab in patients with metastatic melanoma [published correction appears in N Engl J Med. 2010 Sep 23;363(13):1290]. N Engl J Med. 2010;363(8):711–723. Doi:10.1056/NEJMoa1003466.

21e. Larkin J, Minor D, D'Angelo S, et al. Overall Survival in Patients With Advanced Melanoma Who Received Nivolumab Versus Investigator's Choice Chemotherapy in CheckMate 037: A Randomized, Controlled, Open-Label Phase III Trial. J Clin Oncol. 2018;36(4):383–390. Doi:10.1200/JCO.2016.71.8023.

22e. Hersh EM, O'Day SJ, Ribas A, et al. A phase 2 clinical trial of nab-paclitaxel in previously treated and chemotherapy-naive patients with metastatic melanoma. Cancer. 2010 Jan 1;116(1):155-63.

23e. Kottschade LA, Suman VJ, Amatruda T 3rd, et al. A phase II trial of nab-paclitaxel (ABI-007) and carboplatin in patients with unresectable stage IV melanoma: a North Central Cancer Treatment Group Study, N057E(1). Cancer. 2011 Apr 15;117(8):1704-10.

24e. Agarwala SS, et al. Randomized phase III study of paclitaxel plus carboplatin with or without sorafenib as second-line treatment in patients with advanced melanoma. Journal of Clinical Oncology 2007 25:18_suppl, 8510-8510.

25e. Rao RD, et al. Combination of paclitaxel and carboplatin as second-line therapy for patients with metastatic melanoma. Cancer. 2006 Jan 15;106(2):375-82.

26e. Middleton MR, et al. Randomized phase III study of temozolomide versus dacarbazine in the treatment of patients with advanced metastatic malignant melanoma. J Clin Oncol. 2000 Jan;18(1):158-66.

27e. Einzig AI, et al. A phase II study of taxol in patients with malignant melanoma. Invest New Drugs. 1991 Feb;9(1):59-64.

28e. Robert C, Ribas A, Schachter J, et al. Pembrolizumab versus ipilimumab in advanced melanoma (KEYNOTE-006): post-hoc 5-year results from an open-label, multicentre, randomised, controlled, phase 3 study. Lancet Oncol 2019; 20:1239.

29e. Eggermont AMM, Blank CU, Mandala M, et al. Adjuvant Pembrolizumab versus Placebo in Resected Stage III Melanoma. N Engl J Med. 2018 May 10;378(19):1789-1801. doi: 10.1056/NEJMoa1802357.

30e. Eggermont AM, Chiarion-Sileni V, Grob JJ, et al. Prolonged Survival in Stage III Melanoma with Ipilimumab Adjuvant Therapy [published correction appears in N Engl J

Med. 2018 Nov 29;379(22):2185]. N Engl J Med. 2016;375(19):1845–1855. doi:10.1056/NEJMoa1611299.

31e. Kottschade LA, McWilliams RR, Markovic SN, et al. The use of pembrolizumab for the treatment of metastatic uveal melanoma. Melanoma Res. 2016 Jun;26(3):300-3. doi: 10.1097/CMR.0000000000000242.

32e. Zimmer L, Vaubel J, Mohr P, et al. Phase II DeCOG-study of ipilimumab in pretreated and treatment-naïve patients with metastatic uveal melanoma. PLoS One. 2015;10(3):e0118564. Published 2015 Mar 11. doi:10.1371/journal.pone.0118564.

33e. Piulats Rodriguez JM, Ochoa de Olza M, Codes M, et al. Phase II study evaluating ipilimumab as a single agent in the first-line treatment of adult patients (Pts) with metastatic uveal melanoma (MUM): The GEM-1 trial. J Clin Oncol 2014; 32S:ASCO #9033.

34e. Luke JJ, Callahan MK, Postow MA, et al. Clinical activity of ipilimumab for metastatic uveal melanoma: a retrospective review of the Dana-Farber Cancer Institute, Massachusetts General Hospital, Memorial Sloan-Kettering Cancer Center, and University Hospital of Lausanne experience. Cancer. 2013;119(20):3687–3695. doi:10.1002/cncr.28282.

35e. Zhu AX, Finn RS, Edeline J, et al. Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib (KEYNOTE-224): a non-randomised, open-label phase 2 trial. Lancet Oncol. 2018 Jul;19(7):940-952. doi: 10.1016/S1470-2045(18)30351-6.

36e. Crocenzi TS, El-Khoueiry AB, Yau T, et al. Nivolumab (nivo) in sorafenib (sor)-naive and -experienced pts with advanced hepatocellular carcinoma (HCC): CheckMate 040 study. J Clin Oncol 35, 2017 (suppl; abstr 4013).

37e. Qin S, Bai Y, Lim HY, et al. Randomized, multicenter, open-label study of oxaliplatin plus fluorouracil/leucovorin versus doxorubicin as palliative chemotherapy in patients with advanced hepatocellular carcinoma from Asia. J Clin Oncol. 2013 Oct 1;31(28):3501-8. doi: 10.1200/JCO.2012.44.5643.

38e. Bruix J, Qin S, Merle P, et al. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2017 Jan 7;389(10064):56-66.

39e. Abou-Alfa GK, Meyer T, Cheng AL, et al. Cabozantinib in Patients with Advanced and Progressing Hepatocellular Carcinoma. N Engl J Med. 2018 Jul 5;379(1):54-63.

40e. Zhu AX, Park JO, Ryoo BY, et al. Ramucirumab versus placebo as second-line treatment in patients with advanced hepatocellular carcinoma following first-line therapy with sorafenib (REACH): a randomised, double-blind, multicentre, phase 3 trial. Lancet Oncol. 2015 Jul;16(7):859-70.

41e. Zhu AX, Kang YK, Yen CJ, et al. Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased α-fetoprotein concentrations (REACH-2): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2019 Feb;20(2):282-296.

42e. Yau T, et al. Nivolumab (NIVO) + ipilimumab (IPI) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040 (abstract). J Clin Oncol 37, 2019 (suppl; abstr 4012). Abstract available inglibrary.asco.org/record/173194/abstract (Accessed on April 24, 2020).

43e. Paz-Ares L, et al. Pembrolizumab plus Chemotherapy for Squamous Non–Small-Cell Lung Cancer. N Engl J Med 2018; 379:2040-2051.

44e. Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus Chemotherapy for PD-L1–Positive Non–Small-Cell Lung Cancer. N Engl J Med 2016; 375:1823-1833.

45e. Gandhi L, et al. Pembrolizumab plus Chemotherapy in Metastatic Non–Small-Cell Lung Cancer. N Engl J Med 2018; 378:2078-2092.

46e. Planchard D, Smit EF, Groen HJM, et al. Dabrafenib plus trametinib in patients with previously untreated BRAFV600E-mutant metastatic non-small-cell lung cancer: an open-label, phase 2 trial. Lancet Oncol. 2017 Oct;18(10):1307-1316. doi: 10.1016/S1470-2045(17)30679-4.

47e. Planchard D, Kim TM, Mazieres J, et al. Dabrafenib in patients with BRAF(V600E)-positive advanced non-small-cell lung cancer: a single-arm, multicentre, open-label, phase 2 trial. Lancet Oncol. 2016 May;17(5):642-50. doi: 10.1016/S1470-2045(16)00077-2.

48e. Gautschi O, Milia J, Cabarrou B, et al. Targeted Therapy for Patients with BRAF-Mutant Lung Cancer: Results from the European EURAF Cohort. J Thorac Oncol. 2015 Oct;10(10):1451-7. doi: 10.1097/JTO.0000000000000625.

49e. Drilon A, Laetsch TW, Kummar S, et al. Efficacy of Larotrectinib in TRK Fusion-Positive Cancers in Adults and Children. N Engl J Med. 2018;378(8):731–739. doi:10.1056/NEJMoa1714448.

50e. Doebele R, Paz-Ares L, Farago AF, et al. Entrectinib in NTRK-fusion positive (NTRK-FP) non-small cell lung cancer (NSCLC): Integrated analysis of patients enrolled in three trials (STARTRK-2, STARTRK-1 and ALKA-372-001)[abstract]. AACR Annual Meeting. Atlanta, GA:Abstract CT131.

51e. Carbone DP, Reck M, Paz-Ares L, et al. First-Line Nivolumab in Stage IV or Recurrent Non-Small-Cell Lung Cancer. N Engl J Med. 2017;376(25):2415–2426. doi:10.1056/NEJMoa1613493.

52e. West H, McCleod M, Hussein M, et al. Atezolizumab in combination with carboplatin plus nab-paclitaxel chemotherapy compared with chemotherapy alone as first-line treatment for metastatic non-squamous non-small-cell lung cancer (IMpower130): a multicentre, randomised, open-label, phase 3 trial. Lancet Oncol. 2019;20(7):924–937. doi:10.1016/S1470-2045(19)30167-6.

53e. Socinski MA, Jotte RM, Cappuzzo F, et. al. Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC. N Engl J Med 2018; 378:2288-2301. DOI: 10.1056/NEJMoa1716948.

54e. Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. Lancet. 2016 Apr 9;387(10027):1540-1550. doi: 10.1016/S0140-6736(15)01281-7.

55e. Barlesi F, Park K, Ciardiello F, et al. Primary analysis from OAK, a randomized phase III study comparing atezolizumab with docetaxel in 2L/3L NSCLC. Ann of Oncol 2016 Oct;27(suppl_6):LBA44_PR.

56e. Mok TS, Wu Y-L, Ahn M-J, et al. Osimertinib or Platinum-Pemetrexed in EGFR T790M-Positive Lung Cancer. N Engl J Med. 2017;376(7):629–640. doi:10.1056/NEJMoa1612674.

57e. Solomon BJ, Besse B, Bauer TM, et al. Lorlatinib in patients with ALK-positive non-small-cell lung cancer: results from a global phase 2 study [published correction appears in Lancet Oncol. 2019 Jan;20(1):e10]. Lancet Oncol. 2018;19(12):1654–1667. doi:10.1016/S1470-2045(18)30649-1.

58e. Ou SH, Ahn JS, De Petris L, et al. Alectinib in Crizotinib-Refractory ALK-Rearranged Non-Small-Cell Lung Cancer: A Phase II Global Study. J Clin Oncol. 2016;34(7):661–668. doi:10.1200/jco.2015.63.9443.

59e. Huber RM, Hansen KH, Paz-Ares Rodríguez L, et al. Brigatinib in Crizotinib-Refractory ALK+ NSCLC: 2-Year Follow-up on Systemic and Intracranial Outcomes in the Phase 2 ALTA Trial. J Thorac Oncol. 2020;15(3):404–415. doi:10.1016/j.jtho.2019.11.004.

60e. Shaw AT, Kim TM, Crinò L, et al. Ceritinib versus chemotherapy in patients with ALK-rearranged non-small-cell lung cancer previously given chemotherapy and crizotinib (ASCEND-5): a randomised, controlled, open-label, phase 3 trial. Lancet Oncol. 2017;18(7):874–886. doi:10.1016/S1470-2045(17)30339-X.

61e. Rini BI, Plimack ER, Stus V, et al. Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. N Engl J Med. 2019;380(12):1116–1127. doi:10.1056/NEJMoa1816714.

62e. Sternberg CN, Davis ID, Mardiak J, et al. Pazopanib in locally advanced or metastatic renal cell carcinoma: results of a randomized phase III trial. J Clin Oncol. 2010 Feb 20;28(6):1061-8.

63e. Sternberg CN, Hawkins RE, Wagstaff J, et al. A randomised, double-blind phase III study of pazopanib in patients with advanced and/or metastatic renal cell carcinoma: final overall survival results and safety update. Eur J Cancer. 2013 Apr;49(6):1287-96.

64e. Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. N Engl J Med. 2007 Jan 11;356(2):115-24.

65e. Choueiri TK, Halabi S, Sanford BL, et al. Cabozantinib Versus Sunitinib As Initial Targeted Therapy for Patients With Metastatic Renal Cell Carcinoma of Poor or Intermediate Risk: The Alliance A031203 CABOSUN Trial. J Clin Oncol. 2016;35(6):591–597.

66e. Hammers HJ, Plimack ER, Infante JR, et al. Safety and Efficacy of Nivolumab in Combination With Ipilimumab in Metastatic Renal Cell Carcinoma: The CheckMate 016 Study. J Clin Oncol. 2017;35(34):3851–3858. doi:10.1200/JCO.2016.72.1985.

67e. Choueiri TK, Escudier B, Powles T, et al. Cabozantinib versus Everolimus in Advanced Renal-Cell Carcinoma. N Engl J Med. 2015;373(19):1814–1823. doi:10.1056/NEJMoa1510016.

68e. Koshkin VS, Barata PC, Zhang T, et al. Clinical activity of nivolumab in patients with non-clear cell renal cell carcinoma. J Immunother Cancer. 2018;6(1):9. Published 2018 Jan 29. doi:10.1186/s40425-018-0319-9.

69e. Armstrong AJ, Halabi S, Eisen T, et al. Everolimus versus sunitinib for patients with metastatic non-clear cell renal cell carcinoma (ASPEN): a multicentre, open-label, randomised phase 2 trial. Lancet Oncol. 2016;17(3):378–388. doi:10.1016/S1470-2045(15)00515-X.

70e. Campbell MT, Bilen MA, Shah AY, et al. Cabozantinib for the treatment of patients with metastatic non-clear cell renal cell carcinoma: A retrospective analysis. Eur J Cancer. 2018;104:188–194. doi:10.1016/j.ejca.2018.08.014.

71e. Blank CU, Bono P, Larkin JMG, et al. Safety and efficacy of everolimus in patients with non-clear cell renal cell carcinoma refractory to VEGF-targeted therapy: Subgroup analysis of REACT [abstract]. J Clin Oncol 2012; 30 (5_suppl):Abstract 402.

72e. Chen R, Zinzani PL, Fanale MA, et al. Phase II Study of the Efficacy and Safety of Pembrolizumab for Relapsed/Refractory Classic Hodgkin Lymphoma. J Clin Oncol. 2017;35(19):2125–2132. doi:10.1200/JCO.2016.72.1316.

73e. Chen R, Zinzani PL, Lee HJ, et al. Pembrolizumab in relapsed or refractory Hodgkin lymphoma: 2-year follow-up of KEYNOTE-087. Blood. 2019;134(14):1144–1153. doi:10.1182/blood.2019000324.

74e. Armand P, Shipp MA, Ribrag V, et al. Programmed Death-1 Blockade With Pembrolizumab in Patients With Classical Hodgkin Lymphoma After Brentuximab Vedotin Failure. J Clin Oncol. 2016;34(31):3733–3739. doi:10.1200/JCO.2016.67.3467.

75e. 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;17(9):1283–1294. doi:10.1016/S1470-2045(16)30167-X.

76e. Moskowitz AJ, Hamlin PA Jr, Perales MA, et al. Phase II study of bendamustine in relapsed and refractory Hodgkin lymphoma. J Clin Oncol. 2013;31(4):456–460. doi:10.1200/JCO.2012.45.3308.

77e. Gopal AK, Press OW, Shustov AR, et al. Efficacy and safety of gemcitabine, carboplatin, dexamethasone, and rituximab in patients with relapsed/refractory lymphoma: a prospective multi-center phase II study by the Puget Sound Oncology Consortium. Leuk Lymphoma. 2010;51(8):1523–1529. doi:10.3109/10428194.2010.491137.

78e. Rodriguez MA, Cabanillas FC, Hagemeister FB, et al. A phase II trial of mesna/ifosfamide, mitoxantrone and etoposide for refractory lymphomas. Ann Oncol. 1995 Jul;6(6):609-11.

79e. Colwill R, Crump M, Couture F, et al. Mini-BEAM as salvage therapy for relapsed or refractory Hodgkin's disease before intensive therapy and autologous bone marrow transplantation. J Clin Oncol. 1995 Feb;13(2):396-402.

80e. Martín A, Fernández-Jiménez MC, et al. Long-term follow-up in patients treated with Mini-BEAM as salvage therapy for relapsed or refractory Hodgkin's disease. Br J Haematol. 2001 Apr;113(1):161-71.

81e. Herrera AF, Moskowitz AJ, Bartlett NL, et al. Interim results of brentuximab vedotin in combination with nivolumab in patients with relapsed or refractory Hodgkin lymphoma. Blood. 2018;131(11):1183–1194. doi:10.1182/blood-2017-10-811224.

82e. Chen RW, Palmer J, Martin, et al. Results of a Phase II Trial of Brentuximab Vedotin As First Line Salvage Therapy in Relapsed/Refractory HL Prior to AHCT [abstract]. Blood 2014;124:Abstract 501.

83e. O'Connor OA, Lue JK, Sawas A, et al. Brentuximab vedotin plus bendamustine in relapsed or refractory Hodgkin's lymphoma: an international, multicentre, single-arm, phase 1-2 trial. Lancet Oncol 2018; 19:257.

84e. Cohen EEW, Soulières D, Le Tourneau C, et al. Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study. Lancet. 2019 Jan 12;393(10167):156-167.

85e. Cohen EE, Harrington KJ, Le Tourneau C, et al. LBA45_PR - Pembrolizumab (pembro) vs standard of care (SOC) for recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC): Phase 3 KEYNOTE-040. Ann Oncol. 2017;28(suppl_5):605-649. doi:10.1093/annonc/mdx440.

86e. Chow LQM, Haddad R, Gupta S, et al. Antitumor Activity of Pembrolizumab in Biomarker-Unselected Patients With Recurrent and/or Metastatic Head and Neck Squamous Cell Carcinoma: Results From the Phase Ib KEYNOTE-012 Expansion Cohort. J Clin Oncol. 2016;34(32):3838–3845. doi:10.1200/JCO.2016.68.1478.

87e. Bellmunt J, de Wit R, Vaughn DJ, et al. Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma. N Engl J Med. 2017;376(11):1015–1026. doi:10.1056/NEJMoa1613683.

88e. Apolo AB, Infante JR, Balmanoukian A, et al. Avelumab, an Anti-Programmed Death-Ligand 1 Antibody, In Patients With Refractory Metastatic Urothelial Carcinoma: Results From a Multicenter, Phase Ib Study. J Clin Oncol. 2017;35(19):2117–2124. doi:10.1200/JCO.2016.71.6795.

89e. Patel MR, Ellerton J, Infante JR, et al. Avelumab in metastatic urothelial carcinoma after platinum failure (JAVELIN Solid Tumor): pooled results from two expansion cohorts of an open-label, phase 1 trial. Lancet Oncol. 2018 Jan;19(1):51-64.

90e. Rosenberg JE, Hoffman-Censits J, Powles T, et al. Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: a single-arm, multicentre, phase 2 trial. Lancet. 2016;387(10031):1909–1920. doi:10.1016/S0140-6736(16)00561-4.

91e. Powles T, Durán I, van der Heijden MS, et al. Atezolizumab versus chemotherapy in patients with platinum-treated locally advanced or metastatic urothelial carcinoma (IMvigor211): a multicentre, open-label, phase 3 randomised controlled trial. Lancet. 2018 Feb 24;391(10122):748-757. doi: 10.1016/S0140-6736(17)33297-X.

92e. Massard C, Gordon MS, Sharma S, et al. Safety and Efficacy of Durvalumab (MEDI4736), an Anti-Programmed Cell Death Ligand-1 Immune Checkpoint Inhibitor, in Patients With Advanced Urothelial Bladder Cancer. J Clin Oncol. 2016;34(26):3119–3125. doi:10.1200/JCO.2016.67.9761.

93e. Siefker-Radtke AO, Necchi A, Park SH, et al. First results from the primary analysis population of the phase 2 study of erdafitinib (ERDA; JNJ-42756493) in patients (pts) with metastatic or unresectable urothelial carcinoma (mUC) and FGFR alterations (FGFRalt). J Clin Oncol 2018;36(15_suppl):4503.

94e. Chung HC, Piha-Paul SA, Lopez-Martin J, et al. Pembrolizumab After Two or More Lines of Previous Therapy in Patients With Recurrent or Metastatic SCLC: Results From the KEYNOTE-028 and KEYNOTE-158 Studies. J Thorac Oncol. 2020;15(4):618–627. doi:10.1016/j.jtho.2019.12.109.

95e. Chung HC, Lopez-Martin JA, Kao S C-H, et al. Phase 2 study of pembrolizumab in advanced small-cell lung cancer (SCLC): KEYNOTE-158. J Clin Oncol 2018; 36S: ASCO# 8506.

96e. Ott PA, Elez E, Hiret S, et al. Pembrolizumab in Patients With Extensive-Stage Small-Cell Lung Cancer: Results From the Phase Ib KEYNOTE-028 Study. J Clin Oncol 2017; 35:3823.

97e. Reck M, Vicente D, Ciuleanu T, et al. LBA5: Efficacy and safety of nivolumab (nivo) monotherapy versus chemotherapy (chemo) in recurrent small cell lung cancer (SCLC): Results from CheckMate 331 [abstract]. Ann Oncol 2018;29:43.

98e. von Pawel J, Schiller JH, Shepherd FA, et al. Topotecan versus cyclophosphamide, doxorubicin, and vincristine for the treatment of recurrent small-cell lung cancer. J Clin Oncol. 1999 Feb;17(2):658-67.

99e. O'Brien ME, Ciuleanu TE, Tsekov H, et al. Phase III trial comparing supportive care alone with supportive care with oral topotecan in patients with relapsed small-cell lung cancer. J Clin Oncol. 2006 Dec 1;24(34):5441-7.

100e. Yamamoto N, Tsurutani J, Yoshimura N, et al. Phase II study of weekly paclitaxel for relapsed and refractory small cell lung cancer. Anticancer Res. 2006 Jan-Feb;26(1B):777-81.

101e. Smit EF, Fokkema E, Biesma B, Groen HJ, Snoek W, Postmus PE. A phase II study of paclitaxel in heavily pretreated patients with small-cell lung cancer. Br J Cancer. 1998;77(2):347–351. doi:10.1038/bjc.1998.54.

102e. Smyth JF, Smith IE, Sessa C, et al. Activity of docetaxel (Taxotere) in small cell lung cancer. The Early Clinical Trials Group of the EORTC. Eur J Cancer. 1994;30A(8):1058-60.

103e. Masuda N, Fukuoka M, Kusunoki Y, et al. CPT-11: a new derivative of camptothecin for the treatment of refractory or relapsed small-cell lung cancer. J Clin Oncol. 1992 Aug;10(8):1225-9.

104e. Pietanza MC, Kadota K, Huberman K, et al. Phase II trial of temozolomide in patients with relapsed sensitive or refractory small cell lung cancer, with assessment of methylguanine-DNA methyltransferase as a potential biomarker. Clin Cancer Res. 2012 Feb 15;18(4):1138-45. doi: 10.1158/1078-0432.CCR-11-2059.

105e. 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.

106e. Le DT, Uram JN, Wang H, et al. PD-1 Blockade in Tumors with Mismatch-Repair Deficiency. N Engl J Med. 2015;372(26):2509–2520. doi:10.1056/NEJMoa1500596.

107e. Le DT, Kim TW, Van Cutsem E, et al. Phase II Open-Label Study of Pembrolizumab in Treatment-Refractory, Microsatellite Instability-High/Mismatch Repair-Deficient Metastatic Colorectal Cancer: KEYNOTE-164. J Clin Oncol 2020; 38:11.

108e. Nghiem PT, Bhatia S, Lipson EJ, et al. PD-1 Blockade with Pembrolizumab in Advanced Merkel-Cell Carcinoma. N Engl J Med. 2016;374(26):2542–2552. doi:10.1056/NEJMoa1603702.

109e. D'Angelo SP, Russell J, Lebbé C, et al. Efficacy and Safety of First-line Avelumab Treatment in Patients With Stage IV Metastatic Merkel Cell Carcinoma: A Preplanned Interim Analysis of a Clinical Trial. JAMA Oncol. 2018;4(9):e180077. doi:10.1001/jamaoncol.2018.0077.

110e. Kaufman HL, Russell JS, Hamid O, et al. Updated efficacy of avelumab in patients with previously treated metastatic Merkel cell carcinoma after ≥1 year of follow-up: JAVELIN Merkel 200, a phase 2 clinical trial. J Immunother Cancer. 2018;6(1):7. Published 2018 Jan 19. doi:10.1186/s40425-017-0310-x.

111e. Kluger HM, Chiang V, Mahajan A, et al. Long-Term Survival of Patients With Melanoma With Active Brain Metastases Treated With Pembrolizumab on a Phase II Trial. J Clin Oncol. 2019;37(1):52–60. doi:10.1200/JCO.18.00204.

112e. Margolin K, Ernstoff MS, Hamid O, et al. Ipilimumab in patients with melanoma and brain metastases: an open-label, phase 2 trial. Lancet Oncol. 2012 May;13(5):459-65. doi: 10.1016/S1470-2045(12)70090-6.

113e. Goldberg SB, Gettinger SN, Mahajan A, et al. Pembrolizumab for patients with melanoma or non-small-cell lung cancer and untreated brain metastases: early analysis of a non-randomised, open-label, phase 2 trial. Lancet Oncol. 2016;17(7):976–983. doi:10.1016/S1470-2045(16)30053-5.

114e. Ott PA, Piha-Paul SA, Munster P, et al. Safety and antitumor activity of the anti-PD-1 antibody pembrolizumab in patients with recurrent carcinoma of the anal canal. Ann Oncol. 2017;28(5):1036–1041. doi:10.1093/annonc/mdx029.

115e. Ghorani E, Kaur B, Fisher RA, et al. Pembrolizumab is effective for drug-resistant gestational trophoblastic neoplasia. Lancet 2017; 390:2343.

116e. Alley EW, Lopez J, Santoro A, et al. Clinical safety and activity of pembrolizumab in patients with malignant pleural mesothelioma (KEYNOTE-028): preliminary results from a non-randomised, open-label, phase 1b trial. Lancet Oncol. 2017 May;18(5):623-630.

117e. Alley EW, Lopez J, Santoro A, et al. Long-Term Overall Survival for Patients with Malignant Pleural Mesothelioma on Pembrolizumab Enrolled in KEYNOTE-028. J Thorac Oncol. 2017 Jan;12(1):S294.

118e. Metaxas Y, Rivalland G, Mauti LA, et al. Pembrolizumab as Palliative Immunotherapy in Malignant Pleural Mesothelioma. J Thorac Oncol. 2018 Nov;13(11):1784-1791.

119e. Jassem J, Ramlau R, Santoro A, et al, "Phase III Trial of Pemetrexed Plus Best Supportive Care Compared With Best Supportive Care in Previously Treated Patients With Advanced Malignant Pleural Mesothelioma," J Clin Oncol, 2008, 26(10):1698-704. [PubMed 18375898]

120e. Zucali PA, Simonelli M, Michetti G, et al. Second-line chemotherapy in malignant pleural mesothelioma: results of a retrospective multicenter survey. Lung Cancer. 2012 Mar;75(3):360-7.

121e. Quispel-Janssen J, van der Noort V, de Vries JF, et al. Programmed Death 1 Blockade With Nivolumab in Patients With Recurrent Malignant Pleural Mesothelioma. J Thorac Oncol. 2018 Oct;13(10):1569-1576.

122e. Popat S, Curioni-Fontecedro A, Polydoropoulou V, et al. A multicentre randomized phase III trial comparing pembrolizumab (P) versus single-agent chemotherapy (CT) for advanced pretreated malignant pleural mesothelioma (MPM): Results from the European Thoracic Oncology Platform (ETOP 9-15) PROMISE-meso trial. Ann Oncol 2019; 30S: ESMO #LBA91_PR.

123e. Chung HC, Ros W, Derlord JP, et al. Efficacy and Safety of Pembrolizumab in Previously Treated Advanced Cervical Cancer: Results From the Phase II KEYNOTE-158 Study. J Clin Oncol. 2019;37(17):1470-1478.

124e. Kwong YL, Chan TSY, Tan D, et al. PD1 blockade with pembrolizumab is highly effective in relapsed or refractory NK/T-cell lymphoma failing l-asparaginase. Blood 2017; 129:2437.

125e. Rittmeyer A, Barlesi F, Waterkamp D, et al. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label,

multicentre randomised controlled trial [published correction appears in Lancet. 2017 Apr 8;389(10077):e5]. Lancet. 2017;389(10066):255-265. doi:10.1016/S0140-6736(16)32517-X.

126e. Gauvain C, Vauléon E, Chouaid C, et al. Intracerebral efficacy and tolerance of nivolumab in non-small-cell lung cancer patients with brain metastases [published correction appears in Lung Cancer. 2019 Oct;136:159]. Lung Cancer. 2018;116:62-66. doi:10.1016/j.lungcan.2017.12.008.

127e. Rizvi NA, Mazières J, Planchard D, et al. Activity and safety of nivolumab, an anti-PD-1 immune checkpoint inhibitor, for patients with advanced, refractory squamous non-small-cell lung cancer (CheckMate 063): a phase 2, single-arm trial. Lancet Oncol. 2015;16(3):257-265. doi:10.1016/S1470-2045(15)70054-9.

128e. Herbst RS, Giaccone G, de Marinis F, et al. Atezolizumab for First-Line Treatment of PD-L1-Selected Patients with NSCLC. N Engl J Med. 2020 Oct 1;383(14):1328-1339. doi: 10.1056/NEJMoa1917346.

129e. Assersohn L, Brown G, Cunningham D, et al. Phase II study of irinotecan and 5-fluorouracil/leucovorin in patients with primary refractory or relapsed advanced oesophageal and gastric carcinoma. Ann Oncol. 2004;15(1):64-69. doi:10.1093/annonc/mdh007.

130e. Cole PD, Mauz-Körholz C, Mascarin, M, et al. 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. Journal of Clinical Oncology 2020;38:8013.

131e. Cole PD, McCarten KM, Pei Q, et al. Brentuximab vedotin with gemcitabine for paediatric and young adult patients with relapsed or refractory Hodgkin's lymphoma (AHOD1221): a Children's Oncology Group, multicentre single-arm, phase 1-2 trial. Lancet Oncol. 2018 Sep;19(9):1229-1238. doi: 10.1016/S1470-2045(18)30426-1.

132e. Kelly R, Ajani J, Kuzdzal J, et al. Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer (EC/GEJC) following neoadjuvant chemoradiation therapy (CRT): First results of the CheckMate 577 study. [abstract]. Presented at the Oral Presentation presented at the ESMO 2020 Annual Meeting; September 19-21, 2020; Virtual Meeting.

133e. Kato K, Sun JM, Shah M.A., et al. Pembrolizumab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced esophageal cancer: The phase 3 KEYNOTE-590 study. [abstract]. Presented at the Oral Presentation presented at the ESMO 2020 Annual Meeting; September 19-21, 2020; Virtual Meeting.

134e. Kojima T, Shah MA, Muro K, et al. Randomized Phase III KEYNOTE-181 Study of Pembrolizumab Versus Chemotherapy in Advanced Esophageal Cancer. J Clin Oncol. 2020 Dec 10;38(35):4138-4148. doi: 10.1200/JCO.20.01888.

135e. Andre T, Shiu KK, Kim TW, et al. Pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: The phase 3 KEYNOTE-177 Study. J Clin Oncol. 2020;38(18_suppl):LBA4-LBA4.

136e. 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 Thorac Oncol 2016;11:S238-S239.

137e. Zalcman G, Mazieres J, Margery J, et al. Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial. Lancet. 2016 Apr 2;387(10026):1405-1414. doi: 10.1016/S0140-6736(15)01238-6. Epub 2015 Dec 21.

138e. Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. J Clin Oncol. 2003 Jul 15;21(14):2636-44. doi: 10.1200/JCO.2003.11.136.

139e. Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. N Engl J Med. 2021 Apr 8;384(14):1289-1300. doi: 10.1056/NEJMoa2035716.

140e. Yau T, Park JW, Finn RS, et al. LBA38_PR - CheckMate 459: A randomized, multi-center phase III study of nivolumab (NIVO) vs sorafenib (SOR) as first-line (1L) treatment in patients (pts) with advanced hepatocellular carcinoma (aHCC). Ann of Oncol 2019 Oct;30(suppl_5):v874-v875.

141e. Powles T, Rosenberg JE, Sonpavde GP, et al. Enfortumab Vedotin in Previously Treated Advanced Urothelial Carcinoma. N Engl J Med. 2021 Mar 25;384(12):1125-1135. doi: 10.1056/NEJMoa2035807. Epub 2021 Feb 12.

142e. Balar AV, McGregor BA, Rosenberg JE, et al. EV-201 Cohort 2: Enfortumab vedotin in cisplatin-ineligible patients with locally advanced or metastatic urothelial cancer who received prior PD-1/PD-L1 inhibitors. DOI: 10.1200/JCO.2021.39.6_suppl.394 Journal of Clinical Oncology 39, no. 6_suppl (February 20, 2021) 394-394.

143e. Sternberg CN, de Mulder PH, Schornagel JH, et al. Randomized phase III trial of high-dose-intensity methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) chemotherapy and recombinant human granulocyte colony-stimulating factor versus classic MVAC in advanced urothelial tract tumors: European Organization for Research and Treatment of Cancer Protocol no. 30924. J Clin Oncol. 2001 May 15;19(10):2638-46. doi: 10.1200/JCO.2001.19.10.2638.

144e. von der Maase H, Hansen SW, Roberts JT, et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. J Clin Oncol. 2000 Sep;18(17):3068-77. doi: 10.1200/JCO.2000.18.17.3068.

145e. Zalcman G, Mazieres J, Greillier L, et al. Second/third-line nivolumab vs nivo plus ipilimumab in malignant pleural mesothelioma: Long-term results of IFCT-1501 MAPS2

phase IIR trial with a focus on hyperprogression (HPD). Ann of Oncol 2016 Oct;30(suppl_5):v747.

146e. Sosman JA. (2021). Immunotherapy of advanced melanoma with immune checkpoint inhibition. In Atkins MB & Shah S (Eds.), UpToDate. Availttps://www.uptodate.com/contents/immunotherapy-of-advanced-melanoma-with-immune-checkpoint-inhibition?search=melanoma%20treatment&topicRef=85841&source=see_link#H1774428 41.

147e. Motzer RJ, Hutson TE, Glen H, et al. Lenvatinib, everolimus, and the combination in patients with metastatic renal cell carcinoma: a randomised, phase 2, open-label, multicentre trial. Lancet Oncol. 2015 Nov;16(15):1473-1482. doi: 10.1016/S1470-2045(15)00290-9. Epub 2015 Oct 22. Erratum in: Lancet Oncol. 2016 Jul;17 (7):e270. Erratum in: Lancet Oncol. 2018 Oct;19(10):e509.

148e. Sezer A, Kilickap S, Gümüş M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. Lancet. 2021 Feb 13;397(10274):592-604. doi: 10.1016/S0140-6736(21)00228-2.

149e. Tawbi HA, Forsyth PA, Algazi A, et al. Combined Nivolumab and Ipilimumab in Melanoma Metastatic to the Brain. N Engl J Med. 2018;379(8):722-730. doi:10.1056/NEJMoa1805453.

150e. Spigel DR, Vicente D, Ciuleanu TE, et al. Second-line nivolumab in relapsed small-cell lung cancer: CheckMate 331☆. Ann Oncol. 2021 May;32(5):631-641. doi: 10.1016/j.annonc.2021.01.071. Epub 2021 Feb 1.

151e. Wolchok JD, Chiarion-Sileni V, Gonzalez R, et al. CheckMate 067: 6.5-year outcomes in patients (pts) with advanced melanoma. J Clin Oncol 2021; 39;15S.

152e. Pires da Silva I, Ahmed T, Reijers ILM, et al. Ipilimumab alone or ipilimumab plus anti-PD-1 therapy in patients with metastatic melanoma resistant to anti-PD-(L)1 monotherapy: a multicentre, retrospective, cohort study. Lancet Oncol. 2021 Jun;22(6):836-847. doi: 10.1016/S1470-2045(21)00097-8.

153e. Chung HC, Ros W, Delord JP, et al. Efficacy and Safety of Pembrolizumab in Previously Treated Advanced Cervical Cancer: Results From the Phase II KEYNOTE-158 Study. J Clin Oncol. 2019 Jun 10;37(17):1470-1478. doi: 10.1200/JCO.18.01265. Epub 2019 Apr 3.

154e. Janjigian YY, Shitara K, Moehler M, et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. Lancet. 2021;398(10294):27-40. doi:10.1016/S0140-6736(21)00797-2.

155e. Olson D, Luke J, Poklepovic A, et al. Significant antitumor activity for low-dose ipilimumab (IPI) with pembrolizumab (PEMBRO) immediately following progression on

PD1 Ab in melanoma (MEL) in a phase II trial. Journal of Clinical Oncology 2020 38:15_suppl, 10004-10004.

156e. Berton D, Banerjee S, Curigliano G, et al. Antitumor activity of dostarlimab in patients with mismatch repair-deficient/microsatellite instability–high tumors: A combined analysis of two cohorts in the GARNET study. Journal of Clinical Oncology. Volume 39, Issue 15_suppl. doi/abs/10.1200/JCO.2021.39.15_suppl.2564.

157e. Baas P, Scherpereel A, Nowak AK, et al. First-line nivolumab plus ipilimumab in unresectable malignant pleural mesothelioma (CheckMate 743): a multicentre, randomised, open-label, phase 3 trial. Lancet. 2021 Jan 30;397(10272):375-386. doi: 10.1016/S0140-6736(20)32714-8. Epub 2021 Jan 21. Erratum in: Lancet. 2021 Feb 20;397(10275):670.

158e. Kato K, Shah MA, Enzinger P, et al. KEYNOTE-590: Phase III study of first-line chemotherapy with or without pembrolizumab for advanced esophageal cancer. Future Oncol. 2019 Apr;15(10):1057-1066. doi: 10.2217/fon-2018-0609.

159e. Motzer RJ, Penkov K, Haanen J, et al. Avelumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. N Engl J Med. 2019 Mar 21;380(12):1103-1115. doi: 10.1056/NEJMoa1816047. Epub 2019 Feb 16.

160e. Tawbi HA, Schadendorf D, Lipson EJ, et al. Relatlimab and Nivolumab versus Nivolumab in Untreated Advanced Melanoma. N Engl J Med. 2022 Jan 6;386(1):24-34. doi: 10.1056/NEJMoa2109970.

161e. Vanderwalde AM, Moon J, Kendra K et al. S1616: Ipilimumab plus nivolumab versus ipilimumab alone in patients with metastatic or unresectable melanoma that did not respond to anti-PD-1 therapy In: Proceedings of the 113th Annual Meeting of the American Association for Cancer Research; 2021 April 8-13; New Orleans LA. Philadelphia (PA): AACR; 2022. Abstract CT013. https://www.abstractsonline.com/pp8/#!/10517/presentation/20155 (Accessed on June 10, 2022).

162e. 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.

163e. Raghav KPS, Overman MJ, Liu S, et al. A phase II trial of atezolizumab and bevacizumab in patients with relapsed/refractory and unresectable malignant peritoneal mesothelioma. Journal of Clinical Oncology 2020 38:15_suppl, 9013-9013.

164e. Lee CH, Voss MH, Carlo MI, et al. Phase II Trial of Cabozantinib Plus Nivolumab in Patients With Non-Clear-Cell Renal Cell Carcinoma and Genomic Correlates. J Clin Oncol. 2022 Jul 20;40(21):2333-2341.

165e. Atkins MB, Lee SJ, Chmielowski B, et al. DREAMseq (Doublet, Randomized Evaluation in Advanced Melanoma Sequencing): A phase III trial—ECOG-ACRIN EA6134. J Clin Oncol. 2021 Dec 20;39(36_suppl):356154-356-154.

166e. Mok TS, Wu Y-L, Ahn M-J, et al. Osimertinib or Platinum-Pemetrexed in EGFR T790M-Positive Lung Cancer. N Engl J Med. 2017 Feb 16;376(7):629-640.

167e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Pediatric Central Nervous System Cancers. Version 2.2023. National Comprehensive Cancer Network, 2023. 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 December 2023.

168e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Uterine Neoplasms. Version 1.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.

169e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Vulvar Cancer. Version 2.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.

170e. André T, Lonardi S, Wong KYM, et al. Nivolumab plus low-dose ipilimumab in previously treated patients with microsatellite instability-high/mismatch repair-deficient metastatic colorectal cancer: 4-year follow-up from CheckMate 142. Ann Oncol. 2022 Oct;33(10):1052-1060.

171e. Johnson ML, Cho BC, Luft A, et al; POSEIDON investigators. Durvalumab With or Without Tremelimumab in Combination With Chemotherapy as First-Line Therapy for Metastatic Non-Small-Cell Lung Cancer: The Phase III POSEIDON Study. J Clin Oncol. 2022 Nov 3:JCo2200975. doi: 10.1200/JCO.22.00975.

172e. Gogishvili M, Melkadze T, Makharadze T, et al. LBA51 EMPOWER-Lung 3: Cemiplimab in combination with platinum doublet chemotherapy for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC). Annals of Oncology, ISSN: 0923-7534, Vol: 32, SUPPLEMENT 5, S1328, SEPTEMBER 01, 2021. DOI10.1016/j.annonc.2021.08.2130.

173e. Delyon J, Biard L, Renaud M, et al. PD-1 blockade with pembrolizumab in classic or endemic Kaposi's sarcoma: a multicentre, single-arm, phase 2 study. Lancet Oncol. 2022 Apr;23(4):491-500. doi: 10.1016/S1470-2045(22)00097-3.

174e. 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). Ann Oncol. 2022 Jul;33(7):720-727. doi: 10.1016/j.annonc.2022.03.012.

175e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Kaposi Sarcoma. Version 1.2024. National Comprehensive Cancer Network, 2023. 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 December 2023.

176e. Rao S, Guren MG, Khan K, et al. Anal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2021 Sep;32(9):1087-1100. doi: 10.1016/j.annonc.2021.06.015.

177e. Marabelle A, Fakih M, Lopez J, et al. Association of Tumor Mutational Burden with Outcomes in Patients with Select Advanced Solid Tumors Treated with Pembrolizumab in KEYNOTE-158. Ann Oncol. 2019;30(suppl_5):v475-v532. doi: 10.1093/annonc/mdz253.

178e. Polizzotto MN, Uldrick TS, Wyvill KM, et al. Pomalidomide for Symptomatic Kaposi's Sarcoma in People With and Without HIV Infection: A Phase I/II Study. J Clin Oncol. 2016 Dec;34(34):4125-4131.

179e. Marabelle A, Cassier PA, Fakih M, et al. Pembrolizumab for previously treated advanced anal squamous cell carcinoma: results from the non-randomised, multicohort, multicentre, phase 2 KEYNOTE-158 study. Lancet Gastroenterol Hepatol. 2022 May;7(5):446-454.

180e. André T, Tougeron D, Piessen G, et al. Neoadjuvant Nivolumab Plus Ipilimumab and Adjuvant Nivolumab in Localized Deficient Mismatch Repair/Microsatellite Instability-High Gastric or Esophagogastric Junction Adenocarcinoma: The GERCOR NEONIPIGA Phase II Study. J Clin Oncol. 2023 Jan 10;41(2):255-265.

181e. Ludford K, Ho WJ, Thomas JV, et al. Neoadjuvant Pembrolizumab in Localized Microsatellite Instability High/Deficient Mismatch Repair Solid Tumors. J Clin Oncol. 2023 Apr 20;41(12):2181-2190.

182e. Pietrantonio F, Raimondi A, Lonardi S, et al. INFINITY: A multicentre, single-arm, multi-cohort, phase II trial of tremelimumab and durvalumab as neoadjuvant treatment of patients with microsatellite instability-high (MSI) resectable gastric or gastroesophageal junction adenocarcinoma (GAC/GEJAC). Journal of Clinical Oncology 2023;41:358-358.

183e. Magellan Rx Management. Opdivo Clinical Literature Review Analysis. Last updated December 2023. Accessed December 2023.

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
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
C18.1	Malignant neoplasm of appendix
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
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.0	Liver cell carcinoma
C22.1	Intrahepatic bile duct carcinoma
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C23	Malignant neoplasm of gallbladder
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
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
C40.00	Malignant neoplasm of scapula and long bones of unspecified upper limb
C40.01	Malignant neoplasm of scapula and long bones of right upper limb
C40.02	Malignant neoplasm of scapula and long bones of left upper limb
C40.10	Malignant neoplasm of short bones of unspecified upper limb
C40.11	Malignant neoplasm of short bones of right upper limb
C40.12	Malignant neoplasm of short bones of left upper limb
C40.20	Malignant neoplasm of long bones of unspecified lower limb
C40.21	Malignant neoplasm of long bones of right lower limb
C40.22	Malignant neoplasm of long bones of left lower limb
C40.30	Malignant neoplasm of short bones of unspecified lower limb
C40.31	Malignant neoplasm of short bones of right lower limb
C40.32	Malignant neoplasm of short bones of left lower limb
C40.80	Malignant neoplasm of overlapping sites of bone and articular cartilage of unspecified limb
C40.81	Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb
C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb
C40.90	Malignant neoplasm of unspecified bones and articular cartilage of unspecified limb
C40.91	Malignant neoplasm of unspecified bones and articular cartilage of right limb
C40.92	Malignant neoplasm of unspecified bones and articular cartilage of left limb
C41.0	Malignant neoplasm of bones of skull and face
C41.1	Malignant neoplasm of mandible
C41.2	Malignant neoplasm of vertebral column
C41.3	Malignant neoplasm of ribs, sternum and clavicle
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C41.9	Malignant neoplasm of bone and articular cartilage, unspecified
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
C45.0	Mesothelioma of pleura
C45.1	Mesothelioma of peritoneum
C4A.0	Merkel cell carcinoma of lip
C4A.10	Merkel cell carcinoma of eyelid, including canthus
C4A.111	Merkel cell carcinoma of right upper eyelid, including canthus
C4A.112	Merkel cell carcinoma of right lower eyelid, including canthus
C4A.121	Merkel cell carcinoma of left upper eyelid, including canthus
C4A.122	Merkel cell carcinoma of left lower eyelid, including canthus
C4A.20	Merkel cell carcinoma of unspecified ear and external auricular canal
C4A.21	Merkel cell carcinoma of right ear and external auricular canal
C4A.22	Merkel cell carcinoma of left ear and external auricular canal
C4A.30	Merkel cell carcinoma of unspecified part of face
C4A.31	Merkel cell carcinoma of nose
C4A.39	Merkel cell carcinoma of other parts of face

C4A.4	Merkel cell carcinoma of scalp and neck
C4A.51	Merkel cell carcinoma of anal skin
C4A.52	Merkel cell carcinoma of skin of breast
C4A.59	Merkel cell carcinoma of other part of trunk
C4A.60	Merkel cell carcinoma of unspecified upper limb, including shoulder
C4A.61	Merkel cell carcinoma of right upper limb, including shoulder
C4A.62	Merkel cell carcinoma of left upper limb, including shoulder
C4A.70	Merkel cell carcinoma of unspecified lower limb, including hip
C4A.71	Merkel cell carcinoma of right lower limb, including hip
C4A.72	Merkel cell carcinoma of left lower limb, including hip
C4A.8	Merkel cell carcinoma of overlapping sites
C4A.9	Merkel cell carcinoma, unspecified
C46.0	Kaposi's sarcoma of skin
C46.1	Kaposi's sarcoma of soft tissue
C46.2	Kaposi's sarcoma of palate
C46.3	Kaposi's sarcoma of lymph nodes
C46.4	Kaposi's sarcoma of gastrointestinal sites
C46.50	Kaposi's sarcoma of unspecified lung
C46.51	Kaposi's sarcoma of right lung
C46.52	Kaposi's sarcoma of left lung
C46.7	Kaposi's sarcoma of other sites
C46.9	Kaposi's sarcoma, unspecified
C47.0	Malignant neoplasm of peripheral nerves of head, face and neck
C47.10	Malignant neoplasm of peripheral nerves of unspecified upper limb, including shoulder
C47.11	Malignant neoplasm of peripheral nerves of right upper limb, including shoulder
C47.12	Malignant neoplasm of peripheral nerves of left upper limb, including shoulder
C47.20	Malignant neoplasm of peripheral nerves of unspecified lower limb, including hip
C47.21	Malignant neoplasm of peripheral nerves of right lower limb, including hip
C47.22	Malignant neoplasm of peripheral nerves of left lower limb, including hip
C47.3	Malignant neoplasm of peripheral nerves of thorax
C47.4	Malignant neoplasm of peripheral nerves of abdomen
C47.5	Malignant neoplasm of peripheral nerves of pelvis
C47.6	Malignant neoplasm of peripheral nerves of trunk, unspecified
C47.8	Malignant neoplasm of overlapping sites of peripheral nerves and autonomic nervous system
C47.9	Malignant neoplasm of peripheral nerves and autonomic nervous system, unspecified
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum

C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including shoulder
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.6	Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C53.0	Malignant neoplasm of endocervix
C53.1	Malignant neoplasm of exocervix
C53.8	Malignant neoplasm of overlapping sites of cervix uteri
C53.9	Malignant neoplasm of cervix uteri, unspecified
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
C69.30	Malignant neoplasm of unspecified choroid
C69.31	Malignant neoplasm of right choroid
C69.32	Malignant neoplasm of left choroid
C69.40	Malignant neoplasm of unspecified ciliary body
C69.41	Malignant neoplasm of right ciliary body
C69.42	Malignant neoplasm of left ciliary body
C69.60	Malignant neoplasm of unspecified orbit
C69.61	Malignant neoplasm of right orbit
C69.62	Malignant neoplasm of left orbit
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
C79.31	Secondary malignant neoplasm of brain
C7A.1	Malignant poorly differentiated neuroendocrine tumors
C7B.1	Secondary Merkel cell carcinoma
C81.10	Nodular sclerosis Hodgkin lymphoma, unspecified site
C81.11	Nodular sclerosis Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.12	Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes
C81.13	Nodular sclerosis Hodgkin lymphoma, intra-abdominal lymph nodes
C81.14	Nodular sclerosis Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.15	Nodular sclerosis Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.16	Nodular sclerosis Hodgkin lymphoma, intrapelvic lymph nodes
C81.17	Nodular sclerosis Hodgkin lymphoma, spleen
C81.18	Nodular sclerosis Hodgkin lymphoma, lymph nodes of multiple sites
C81.19	Nodular sclerosis Hodgkin lymphoma, extranodal and solid organ sites
C81.20	Mixed cellularity Hodgkin lymphoma, unspecified site
C81.21	Mixed cellularity Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.22	Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes

C81.23	Mixed cellularity Hodgkin lymphoma, intra-abdominal lymph nodes
C81.24	Mixed cellularity Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.25	Mixed cellularity Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.26	Mixed cellularity Hodgkin lymphoma, intrapelvic lymph nodes
C81.27	Mixed cellularity Hodgkin lymphoma, spleen
C81.28	Mixed cellularity Hodgkin lymphoma, lymph nodes of multiple sites
C81.29	Mixed cellularity Hodgkin lymphoma, extranodal and solid organ sites
C81.30	Lymphocyte depleted Hodgkin lymphoma, unspecified site
C81.31	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.32	Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes
C81.33	Lymphocyte depleted Hodgkin lymphoma, intra-abdominal lymph nodes
C81.34	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.35	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.36	Lymphocyte depleted Hodgkin lymphoma, intrapelvic lymph nodes
C81.37	Lymphocyte depleted Hodgkin lymphoma, spleen
C81.38	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of multiple sites
C81.39	Lymphocyte depleted Hodgkin lymphoma, extranodal and solid organ sites
C81.40	Lymphocyte-rich Hodgkin lymphoma, unspecified site
C81.41	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.42	Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes
C81.43	Lymphocyte-rich Hodgkin lymphoma, intra-abdominal lymph nodes
C81.44	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.45	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.46	Lymphocyte-rich Hodgkin lymphoma, intrapelvic lymph nodes
C81.47	Lymphocyte-rich Hodgkin lymphoma, spleen
C81.48	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of multiple sites
C81.49	Lymphocyte-rich Hodgkin lymphoma, extranodal and solid organ sites
C81.70	Other Hodgkin lymphoma unspecified site
C81.71	Other Hodgkin lymphoma lymph nodes of head, face, and neck
C81.72	Other Hodgkin lymphoma intrathoracic lymph nodes
C81.73	Other Hodgkin lymphoma intra-abdominal lymph nodes
C81.74	Other Hodgkin lymphoma lymph nodes of axilla and upper limb
C81.75	Other Hodgkin lymphoma lymph nodes of inguinal region and lower limb
C81.76	Other Hodgkin lymphoma intrapelvic lymph nodes
C81.77	Other Hodgkin lymphoma spleen

C81.78	Other Hodgkin lymphoma lymph nodes of multiple sites
C81.79	Other Hodgkin lymphoma extranodal and solid organ sites
C81.90	Hodgkin lymphoma, unspecified site
C81.91	Hodgkin lymphoma, unspecified lymph nodes of head, face, and neck
C81.92	Hodgkin lymphoma, unspecified intrathoracic lymph nodes
C81.93	Hodgkin lymphoma, unspecified intra-abdominal lymph nodes
C81.94	Hodgkin lymphoma, unspecified lymph nodes of axilla and upper limb
C81.95	Hodgkin lymphoma, unspecified lymph nodes of inguinal region and lower limb
C81.96	Hodgkin lymphoma, unspecified intrapelvic lymph nodes
C81.97	Hodgkin lymphoma, unspecified spleen
C81.98	Hodgkin lymphoma, unspecified lymph nodes of multiple sites
C81.99	Hodgkin lymphoma, unspecified extranodal and solid organ sites
D09.0	Carcinoma in situ of bladder
D19.1	Benign neoplasm of mesothelial tissue of peritoneum
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
Z85.71	Personal history of Hodgkin lymphoma
Z85.820	Personal history of malignant melanoma of skin
Z85.821	Personal history of Merkel cell carcinoma
Z85.830	Personal history of malignant neoplasm of bone
Z85.831	Personal history of malignant neoplasm of soft tissue

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)
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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC