Medical Policy:
KEYTRUDA® (pembrolizumab) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.89	June 20, 2023	

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

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

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

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

Length of Authorization

- Adrenal Gland Tumors, Anal Carcinoma, Bladder Cancer/Urothelial Carcinoma, Cervical Cancer, cHL, CNS Cancer, Cutaneous Melanoma (in combination with ipilimumab), cSCC, Endometrial Carcinoma, Esophageal/GEJ Cancer, Gastric Cancer, HCC, MCC, MSIH/dMMR Cancer, NSCLC (first-line or subsequent therapy), PMBCL, Primary Cutaneous Lymphomas, RCC (first-line or subsequent therapy), SCCHN, SCLC, Thymic Carcinoma, TMB-H Cancer, TNBC (recurrent unresectable or metastatic disease), Uveal Melanoma, and Vulvar Cancer can be authorized up to a maximum of twenty-four (24) months of therapy.
- Adjuvant therapy in Cutaneous Melanoma, NSCLC, and RCC can be authorized up to a maximum of twelve (12) months of therapy.

- Neoadjuvant therapy in TNBC can be authorized up to a maximum of twenty-four (24) weeks of therapy.
- Adjuvant therapy in TNBC can be authorized up to a maximum of twenty-seven (27) weeks of therapy.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

Indication	Billable Units (BU)	Per Unit time (days)
Adrenal Gland Tumors, Bladder/Urothelial, Cervical, cHL, Pediatric CNS Cancers, cSCC, Cutaneous Melanoma, Endometrial Carcinoma, Esophageal, GEJ, Gastric, Gestational Trophoblastic Neoplasia, HCC, MCC, MSIH/dMMR, NSCLC, PMBCL, RCC, SCCHN, Soft Tissue Sarcoma, Thymic, TMB-H Cancer, TNBC, & Vulvar	200 BU	21 days
Adult CNS Cancer & SCLC	1150 BU	14 days
Anal Carcinoma, Primary Cutaneous Lymphomas, Extranodal NK/T-Cell Lymphomas, & Uveal Melanoma	250 BU	21 days

Guideline

I. Initial Approval Criteria

Coverage is provided in the following conditions:

1. Patient must be 18 years of age or older (unless otherwise specified); **AND**
2. Patient has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy (e.g., avelumab, nivolumab, atezolizumab, durvalumab, etc.) unless otherwise specified; **AND**

Melanoma †

1. Patient has unresectable or metastatic disease; **OR**
2. Keytruda is being used as Adjuvant treatment of patients 12 years and older with Stage IIB, IIC, or III melanoma following complete resection.

Gastric Cancer †

1. Patient meets one of the following (i or ii):
   i. Patient meets **ALL** of the following (a, b, and c):
      a. Patient's tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 1; **AND**
      b. Patient has tried at least two previous chemotherapy regimens; **AND**
      Note: Examples of chemotherapy regimens are fluoropyrimidine (fluorouracil or capecitabine) and

oxaliplatin, fluoropyrimidine and cisplatin, paclitaxel with cisplatin or carboplatin, docetaxel with cisplatin.

c. If the patient's tumor is human epidermal growth factor receptor 2 (HER2) or HER2/neu positive, targeted therapy with trastuzumab has been tried; **OR**

ii. Patient meets **ALL** of the following (a, b, and c):
   a. Patient has locally advanced unresectable or metastatic disease; **AND**
   b. Tumor is human epidermal growth factor receptor 2 (HER2) or HER2/neu positive; **AND**
   c. Medication is used in combination with trastuzumab, cisplatin or oxaliplatin, and fluorouracil or capecitabine

Merkel Cell Carcinoma †

1. Keytruda is approved for both Adult and pediatric patients; **AND**
2. Patient has recurrent, locally advanced, or metastatic Merkel cell carcinoma (MCC).

Non-Small Cell Lung Cancer (NSCLC) †

A. Patient has recurrent, advanced, or metastatic disease; **AND**
B. Patient meets **ONE** of the following (i, ii, or iii):
   i. Patient meets **BOTH** of the following (a and b):
      a. Keytruda is used as first-line or continuation maintenance therapy; **AND**
      Note: This is regardless of PD-L1 status.
      b. The tumor is negative for actionable mutations; **OR**
      Note: Examples of actionable mutations include sensitizing epidermal growth factor receptor (EGFR) mutation, anaplastic lymphoma kinase (ALK) fusions, NTRK gene fusion-positive, ROS1, BRAF V600E, MET 14 skipping mutation, RET rearrangement.
   ii. Patient meets **BOTH** of the following (a and b):
      a. Keytruda is used as first-line or subsequent therapy; **AND**
      Note: This is regardless of the PD-L1 status.
      b. The tumor is positive for one of the following mutations [(1), (2), (3), (4), (5), or (6)]:
         (1) Epidermal growth factor receptor (EGFR) exon 20 mutation; **OR**
         (2) KRAS G12C mutation; **OR**
         (3) BRAF V600E mutation; **OR**
         (4) NTRK1/2/3 gene fusion; **OR**
         (5) MET exon 14 skipping mutation; **OR**
         (6) RET rearrangement; **OR**
   iii. Keytruda is used as subsequent therapy and the patient meets **ONE** of the following (a, b, or c):
      a. Patient meets **BOTH** of the following [(1) and (2)]:
         (1) The tumor is epidermal growth factor receptor (EGFR) S768I, L861Q, and/or G719X mutation positive; **AND**
         (2) The patient has received targeted drug therapy for the specific mutation; **OR**
         Note: Examples of targeted drug therapy include Gilotrif (afatinib tablet), Tagrisso (osimertinib tablet), erlotinib, Iressa (gefitinib tablet), or Vizimpro (dacomitinib tablet).
      b. Patient meets **BOTH** of the following [(1) and (2)]:
         (1) The tumor is ROS1 rearrangement positive; **AND**
         (2) The patient has received targeted drug therapy for the specific mutation; **OR**
         Note: Examples of targeted drug therapy include Xalkori (crizotinib capsule), Rozlytrek (entrectinib capsule), or Zykadia (ceritinib tablet).
      c. Patient meets **ALL** of the following [(1), (2), and (3)]:

(1) Patient has tried systemic therapy; **AND**

Note: Examples of systemic chemotherapy include cisplatin, carboplatin, Alimta (pemetrexed intravenous infusion), Abraxane (paclitaxel albumin-bound intravenous infusion), gemcitabine, paclitaxel.

(2) Patient has not progressed on prior therapy with a programmed death-1 (PD-1)/PD-ligand 1 (PD-L1) inhibitor; **AND**

Note: This includes previous therapy with either one of Keytruda, Opdivo (nivolumab intravenous infusion), or Tecentriq (atezolizumab intravenous infusion).

(3) If tumor is positive for an actionable mutation, the patient has received targeted drug therapy for the specific mutation; **AND**

Note: Examples of actionable mutations include sensitizing epidermal growth factor receptor (EGFR) mutation, anaplastic lymphoma kinase (ALK) fusions, NTRK gene fusion positive, ROS1, BRAF V600E, MET exon 14 skipping mutation, RET rearrangement.

***Every effort needs to be made to establish the genetic alteration status. A blood assay may be used if a tissue assay is not feasible.*

Esophageal Cancer and Esophagogastric Junction Cancer

A. Patient meets **ONE** of the following (i or ii):
   i. According to the prescriber, the patient is not a surgical candidate; **OR**
   ii. Patient has unresectable, recurrent, or metastatic disease; **AND**

B. Patient meets **ONE** of the following (i, ii, iii, or iv):
   i. Patient meets ALL of the following (a, b, and c):
      a. Patient's tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 10; **AND**
      b. The medication is used first-line; **AND**
      c. The medication is used in combination with chemotherapy; **OR**

      Note: Examples of chemotherapy include cisplatin plus fluorouracil or capecitabine; and oxaliplatin plus fluorouracil or capecitabine.
   ii. Patient meets ALL of the following (a, b, and c):
      a. Patient has squamous cell carcinoma; **AND**
      b. Patient's tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 10; **AND**
      c. Patient has tried at least one previous chemotherapy regimen; **OR**

      Note: Examples of chemotherapy regimens are fluoropyrimidine (fluorouracil or capecitabine) and oxaliplatin, fluoropyrimidine and cisplatin, paclitaxel with cisplatin or carboplatin, docetaxel with cisplatin.
   iii. Patient meets **BOTH** of the following (a and b):
      a. Tumor is human epidermal growth factor receptor 2 (HER2) or HER2/neu positive; **AND**
      b. Medication is used in combination with trastuzumab, cisplatin or oxaliplatin, and fluorouracil or capecitabine; **OR**
   iv. Patient meets ALL of the following (a, b, and c):
      a. Patient's tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 1; **AND**
      b. Patient has tried at least two previous chemotherapy regimens; **AND**

      Note: Examples of chemotherapy regimens are fluoropyrimidine (fluorouracil or capecitabine) and oxaliplatin, fluoropyrimidine and cisplatin, paclitaxel with cisplatin or carboplatin, docetaxel with cisplatin.

C. If the patient's tumor is human epidermal growth factor receptor 2 (HER2) or HER2/neu

positive, targeted therapy with trastuzumab has been tried

Squamous Cell Carcinoma of the Head and Neck (SCCHN) †

A. Patient has recurrent, unresectable, or metastatic disease; **AND**
B. Patient meets **ONE** of the following (i or ii):
   i. If the medication is used for first-line treatment, patient must meet **ONE** of the following (a or b):
      a. Keytruda is used in combination with chemotherapy; **OR**
      Note: Examples of chemotherapy are cisplatin, carboplatin, fluorouracil, gemcitabine.
      b Keytruda is used as a single agent if the tumors are PD-L1-positive (combined positive score ≥ 1), as determined by an approved test.
   ii. For subsequent therapy, patient has tried at least one platinum-containing chemotherapy regimen; AND

Note: Examples of platinum-contain chemotherapy regimens are: cisplatin or carboplatin with Erbitux (cetuximab intravenous infusion), gemcitabine, or 5-fluorouracil (5-FU).

Classical Hodgkin Lymphoma (cHL) †

1. Adult patients
   a. Patient has relapsed or refractory disease
2. Pediatric patients
   a. Patient has a refractory disease; **OR**
   b. Patient has cHL that has relapsed after 2 or more lines of therapy.

Primary Mediastinal Large B-Cell Lymphoma (PMBCL) †

1. Used as single agent; **AND**
2. Patient has relapsed or refractory disease; **AND**
3. Patient must be at least 2 years old; **AND**
4. Used after two or more prior lines of therapy

Bladder Cancer/Urothelial Carcinoma ‡ †

A. Patient meets **ONE** of the following conditions (i, ii, or iii):
   i. Patient has tried at least one platinum-based chemotherapy; **OR**
   Note: Cisplatin and carboplatin are platinum-based chemotherapies.
   ii. According to the prescriber, patient is not eligible for platinum-based chemotherapy (i.e., with cisplatin and carboplatin); **OR**
   Note: This is regardless of PD-L1 status.
   iii. Patient meets both of the following (a and b):
      a. Patient has non-muscle invasive bladder cancer; **AND**
      b. Patient has tried Bacillus Calmette-Guerin (BCG) or intravesical chemotherapy; **AND**
      Note: Examples of agents used as intravesical chemotherapy include mitomycin and gemcitabine.

Cervical Cancer †

1. Patient has recurrent or metastatic disease; **AND**
2. Tumor expresses PD-L1 (CPS ≥1%) as determined by an FDA-approved test; **AND**

3. Disease progressed on or after chemotherapy

Microsatellite Instability-High (MSI-H) Cancer †

1. Patient must be at least 2 years old; **AND**
2. One of the following conditions applies (i, ii, iii, iv, v, vi, vii, or viii):
   i. Patient has advanced or metastatic ampullary cancer; **OR**
   ii. Patient has unresectable or metastatic colon or rectal cancer; **OR**
   iii. Patient has unresectable or metastatic gallbladder cancer (including intra- and extra-hepatic cholangiocarcinoma); **OR**
   iv. Patient has unresectable or metastatic head and neck squamous cell carcinoma; **OR**
   v. Patient has persistent or recurrent ovarian/fallopian tube/primary peritoneal carcinoma; **OR**
   vi. Patient has locally advanced or metastatic pancreatic adenocarcinoma; **OR**
   vii. Patient has advanced or metastatic small bowel carcinoma; **OR**
   viii. Patient meets **BOTH** of the following (a and b):
      a. Patient has tried at least one prior systemic therapy for an MSI-H or dMMR solid tumor; **AND**
      b. Patient has unresectable or metastatic disease

Hepatocellular Carcinoma (HCC) †

1. Patient has tried at least one tyrosine kinase inhibitor

Note: Examples of tyrosine kinase inhibitors include Nexavar (sorafenib tablets), Lenvima (lenvatinib capsules).

Renal Cell Carcinoma (RCC) †

A. Patient meets ONE of the following (i, ii, or iii):
   i. Approve if the patient meets ALL of the following (a, b, and c):
      a. The tumor has clear cell histology; **AND**
      b. Patient has relapsed or metastatic disease; **AND**
      c. The medication is used in combination with Inlyta (axitinib tablets) or Lenvima (lenvatinib capsules); **OR**
   ii. Approve for 1 year if the patient meets **ALL** of the following (a, b, and c):
      a. The tumor has non-clear cell histology; **AND**
      b. Patient has relapsed or metastatic disease; **AND**
      c. The medication is used as single-agent therapy; **OR**
   iii. Approve for up to 1 year (total) if patient meets ALL of the following (a, b, c, and d):
      a. Keytruda is used as adjuvant therapy; **AND**
      b. The tumor has clear cell histology; **AND**
      c. Patient has advanced disease; **AND**
      d. The medication is used as single-agent therapy

Endometrial Carcinoma

A. The medication is used in combination with Lenvima (lenvatinib capsules); **AND**
B. Patient has progressed on at least one prior systemic therapy; **AND**

Note: Examples of systemic therapy are carboplatin, paclitaxel, docetaxel, cisplatin, doxorubicin, ifosfamide, everolimus, letrozole.

C. Patient is not a candidate for curative surgery or radiation

Tumor Mutational Burden-High Cancer †

1. Patient has unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors, as determined by an FDA-approved test; **AND**

2. Patient has progressed following prior treatment or have no satisfactory alternative treatment options; **AND**

3. Pediatric patients do not have a diagnosis of TMB-H central nervous system cancer; **AND**

Cutaneous Squamous Cell Carcinoma (cSCC)†

1. Patient has recurrent or metastatic disease; **AND**
2. Patient is not a candidate for surgical or radiation therapy

Triple-Negative Breast Cancer

A. Disease is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); **AND**
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria.

B. Disease is not tumor mutational burden-high (≥ 10 mutations/megabase); **AND**
Note: If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.

C. Patient has triple-negative breast cancer (i.e., estrogen receptor-negative, progesterone receptor-negative, human epidermal growth factor receptor 2 [HER2]-negative); **AND**

D. Patient meets **ONE** of the following (i or ii):
   i. Patient meets **ALL** of the following (a, b, and c):
      a. Patient has recurrent unresectable (local or regional) or metastatic disease; **AND**
      b. The medication is used in combination with chemotherapy; **AND**
      c. Patient's tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 10; **OR**
   ii. Patient has high-risk, early-stage disease

❖ *As confirmed using an immunotherapy assay such as the PD-L1 IHC 22C3 pharmDx*.

† FDA Approved Indication(s); ‡ Compendia Approved Indication(s)

Genomic Aberration Targeted Therapies (*not all inclusive*) §
Sensitizing EGFR mutation-positive tumors – Erlotinib – Afatinib – Gefitinib – Osimertinib
ALK rearrangement-positive tumors – Crizotinib – Ceritinib – Brigatinib – Alectinib
ROS1 rearrangement-positive tumors – Crizotinib – Ceritinib

BRAF V600E-mutation positive tumors – Dabrafenib/Trametinib
PD-L1 expression-positive tumors (≥50%) – Pembrolizumab

II. Renewal Criteria

Coverage can be renewed based upon the following criteria:

1. Patient continues to meet criteria identified above; **AND**
2. Tumor response with stabilization of disease or decrease in size of tumor or tumor spread; **AND**
3. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include severe infusion reactions, immune-mediated adverse reactions (e.g., pneumonitis, hepatitis, colitis, endocrinopathies, nephritis and renal dysfunction, skin, etc.); **AND**
4. For the follow indications, patient has not exceeded a maximum of twenty-four (24) months of therapy:

- Cervical Cancer
- Classical Hodgkin Lymphoma (cHL)
- CNS Cancer
- Cutaneous Melanoma
- Cutaneous Squamous Cell Carcinoma
- Endometrial Carcinoma
- Esophageal Cancer
- Gastric/GEJ Adenocarcinoma
- Hepatocellular Carcinoma (HCC)
- Merkel Cell Carcinoma
- MSI-H Cancer (including the following cancers: colorectal, pancreatic, bone, gastric/gastroesophageal, ovarian, uterine, penile, testicular, hepatobiliary and other solid tumors)
- Non-Small Cell Lung Cancer (NSCLC)
- Primary Cutaneous Lymphomas
- Primary Mediastinal Large B-Cell Lymphoma (PMBCL)
- Renal Cell Carcinoma
- Squamous Cell Carcinoma of the Head and Neck (SCCHN)
- Tumor Mutational Burden-High Cancer
- Triple Negative Breast Cancer
- Urothelial Carcinoma/Bladder

Melanoma (metastatic or unresectable disease) ‡

Used for re-treatment of patients who experienced disease control, but subsequently have disease progression/relapse > 3 months after treatment discontinuation

Limitations/Exclusions

Keytruda is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.

Applicable Procedure Codes

Code	Description
J9271	Injection, pembrolizumab, 1 mg; 1 billable unit = 1 mg

Applicable NDCs

Code	Description
00006-3026-XX	Keytruda 100 mg/4 mL single use vial

ICD-10 Diagnoses

Code	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
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

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
C10.3	Malignant neoplasm of posterior wall of oropharynx
C11.0	Malignant neoplasm of superior wall of nasopharynx
C11.1	Malignant neoplasm of posterior wall of nasopharynx
C11.2	Malignant neoplasm of lateral wall of nasopharynx
C11.3	Malignant neoplasm of anterior wall of nasopharynx
C11.8	Malignant neoplasm of overlapping sites of nasopharynx
C11.9	Malignant neoplasm of nasopharynx, unspecified
C12	Malignant neoplasm of pyriform sinus
C13.0	Malignant neoplasm of postcricoid region
C13.1	Malignant neoplasm of aryepiglottic fold, hypopharyngeal aspect
C13.2	Malignant neoplasm of posterior wall of hypopharynx
C13.8	Malignant neoplasm of overlapping sites of hypopharynx
C13.9	Malignant neoplasm of hypopharynx, unspecified
C14.0	Malignant neoplasm of pharynx, unspecified
C14.2	Malignant neoplasm of Waldeyer's ring
C14.8	Malignant neoplasm of overlapping sites of lip, oral cavity and pharynx
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C15.9	Malignant neoplasm of esophagus, unspecified
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified
C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.8	Malignant neoplasm of overlapping sites of small intestine
C17.9	Malignant neoplasm of small intestine, 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
C21.0	Malignant neoplasm of anus, unspecified
C21.1	Malignant neoplasm of anal canal
C21.2	Malignant neoplasm of cloacogenic zone
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.1	Intrahepatic bile duct carcinoma
C23	Malignant neoplasm of gallbladder
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.1	Malignant neoplasm of ampulla of Vater
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
C25.0	Malignant neoplasm of head of pancreas
C25.1	Malignant neoplasm of body of the pancreas
C25.2	Malignant neoplasm of tail of pancreas
C25.3	Malignant neoplasm of pancreatic duct
C25.7	Malignant neoplasm of other parts of pancreas
C25.8	Malignant neoplasm of overlapping sites of pancreas
C25.9	Malignant neoplasm of pancreas, 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
C38.4	Malignant neoplasm of pleura
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
C43.10	Malignant melanoma of unspecified eyelid, including canthus
C43.11	Malignant melanoma of right eyelid, including canthus
C43.12	Malignant melanoma of left 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
C44.92	Squamous cell carcinoma of skin, unspecified
C45.0	Mesothelioma of pleura
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
C4A.0	Merkel cell carcinoma of lip
C4A.10	Merkel cell carcinoma of eyelid, including canthus
C4A.11	Merkel cell carcinoma of right eyelid, including canthus
C4A.12	Merkel cell carcinoma of left 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
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
C54.0	Malignant neoplasm of isthmus uteri

C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.10	Malignant neoplasm of unspecified broad ligament
C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.20	Malignant neoplasm of unspecified round ligament
C57.21	Malignant neoplasm of right round ligament
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium
C57.4	Malignant neoplasm of uterine adnexa, unspecified
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C57.9	Malignant neoplasm of female genital organ, unspecified
C60.0	Malignant neoplasm of prepuce
C60.1	Malignant neoplasm of glans penis
C60.2	Malignant neoplasm of body of penis
C60.8	Malignant neoplasm of overlapping sites of penis
C60.9	Malignant neoplasm of penis, unspecified
C61	Malignant neoplasm of prostate
C62.00	Malignant neoplasm of unspecified undescended testis
C62.01	Malignant neoplasm of undescended right testis
C62.02	Malignant neoplasm of undescended left testis
C62.10	Malignant neoplasm of unspecified descended testis
C62.11	Malignant neoplasm of descended right testis
C62.12	Malignant neoplasm of descended left testis
C62.90	Malignant neoplasm of unspecified testis, unspecified whether descended or undescended
C62.91	Malignant neoplasm of right testis, unspecified whether descended or undescended
C62.92	Malignant neoplasm of left testis, unspecified whether descended or undescended
C63.7	Malignant neoplasm of other specified male genital organs
C63.8	Malignant neoplasm of overlapping sites of male genital organs
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
C69.90	Malignant neoplasm of unspecified site of unspecified eye
C69.91	Malignant neoplasm of unspecified site of right eye
C69.92	Malignant neoplasm of unspecified site of left eye
C74.00	Malignant neoplasm of cortex of unspecified adrenal gland
C74.01	Malignant neoplasm of cortex of right adrenal gland
C74.02	Malignant neoplasm of cortex of left adrenal gland
C74.90	Malignant neoplasm of unspecified part of unspecified adrenal gland
C74.91	Malignant neoplasm of unspecified part of right adrenal gland
C74.92	Malignant neoplasm of unspecified part of left adrenal gland
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
C78.89	Secondary malignant neoplasm of other digestive organs
C79.31	Secondary malignant neoplasm of brain
C7B.00	Secondary carcinoid tumors unspecified site
C7B.01	Secondary carcinoid tumors of distant lymph nodes
C7B.02	Secondary carcinoid tumors of liver
C7B.03	Secondary carcinoid tumors of bone
C7B.04	Secondary carcinoid tumors of peritoneum
C7B.1	Secondary Merkel cell carcinoma

C7B.8	Other secondary neuroendocrine tumors
C79.89	Secondary malignant neoplasm of other specified sites
C79.9	Secondary malignant neoplasm of unspecified site
C80.0	Disseminated malignant neoplasm, unspecified
C80.1	Malignant (primary) neoplasm, unspecified
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, 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
C84.90	Mature T/NK-cell lymphomas, unspecified site
C84.91	Mature T/NK-cell lymphomas, lymph nodes of head, face, and neck
C84.92	Mature T/NK-cell lymphomas, intrathoracic lymph nodes
C84.93	Mature T/NK-cell lymphomas, intra-abdominal lymph nodes
C84.94	Mature T/NK-cell lymphomas, lymph nodes of axilla and upper limb
C84.95	Mature T/NK-cell lymphomas, lymph nodes of inguinal region and lower limb
C84.96	Mature T/NK-cell lymphomas, intrapelvic lymph nodes
C84.97	Mature T/NK-cell lymphomas, spleen
C84.98	Mature T/NK-cell lymphomas, lymph nodes of multiple sites
C84.99	Mature T/NK-cell lymphomas, extranodal and solid organ sites
C84.Z0	Other mature T/NK-cell lymphomas, Unspecified site
C84.Z1	Other mature T/NK-cell lymphomas, lymph nodes of head, face, and neck
C84.Z2	Other mature T/NK-cell lymphomas, intrathoracic lymph nodes
C84.Z3	Other mature T/NK-cell lymphomas, intra-abdominal lymph nodes
C84.Z4	Other mature T/NK-cell lymphomas, lymph nodes of axilla and upper limb
C84.Z5	Other mature T/NK-cell lymphomas, lymph nodes of inguinal region and lower limb
C84.Z6	Other mature T/NK-cell lymphomas, intrapelvic lymph nodes
C84.Z7	Other mature T/NK-cell lymphomas, spleen
C84.Z8	Other mature T/NK-cell lymphomas, lymph nodes of multiple sites
C84.Z9	Other mature T/NK-cell lymphomas, extranodal and solid organ sites
C85.20	Mediastinal (thymic) large B-cell lymphoma, unspecified site
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face and neck
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb

C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites
C86.0	Other specified types of T/NK-cell lymphoma
D09.0	Carcinoma in situ of bladder
D37.01	Neoplasm of uncertain behavior of lip
D37.02	Neoplasm of uncertain behavior of tongue
D37.05	Neoplasm of uncertain behavior of pharynx
D37.09	Neoplasm of uncertain behavior of other specified sites of the oral cavity
D37.1	Neoplasm of uncertain behavior of stomach
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
D38.0	Neoplasm of uncertain behavior of larynx
D38.5	Neoplasm of uncertain behavior of other respiratory organs
D38.6	Neoplasm of uncertain behavior of respiratory organ, unspecified
Z80.49	Family history of malignant neoplasm of other genital organs
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
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.07	Personal history of malignant neoplasm of pancreas
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.21	Personal history of malignant neoplasm of larynx
Z85.22	Personal history of malignant neoplasm of nasal cavities, middle ear, and accessory sinuses
Z85.43	Personal history of malignant neoplasm of ovary
Z85.47	Personal history of malignant neoplasm of testis
Z85.49	Personal history of malignant neoplasm of other male genital organs
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
Z85.810	Personal history of malignant neoplasm of tongue
Z85.818	Personal history of malignant neoplasm of other sites of lip, oral cavity and pharynx
Z85.819	Personal history of malignant neoplasm of unspecified site of lip, oral cavity and pharynx
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
Z85.858	Personal history of malignant neoplasm of other endocrine glands
Z85.59	Personal history of malignant neoplasm of other urinary tract organ
C22.0	Liver cell carcinoma
C22	Malignant neoplasm of liver and intrahepatic bile ducts
Z85.05	Personal history of malignant neoplasm of liver

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	6/20/2023	Annual Review: Melanoma: Initial Criteria: Removed "Used as a single agent; **AND** a. Used as re-treatment therapy; **OR** b. Patient has unresectable or metastatic Uveal Melanoma: OR c. Patient has melanoma with involvement of lymph node(s) " Added "Adjuvant treatment of patients 12 years and older with Stage IIB, IIC, or III melanoma following complete resection." Gastric Cancer: Initial Criteria: Removed "1. Used as a single agent: AND a. Patient has gastric or gastro-esophageal junction adenocarcinoma; AND b. Patient has recurrent locally advanced or metastatic disease; AND c. Tumor expresses PD-L1 (CPS ≥1%) as determined by an FDA-approved test; AND d. Patient progressed on or after at least two prior systemic treatments which must have included a fluoropyrimidine and platinum-containing regimen; AND e. Patients with HER2 positive disease must have previously failed on HER2 directed therapy; OR" Added: "1. Patient meets one of the following (i or ii): i. Patient meets ALL of the following (a, b, and c): a. Patient's tumor expression for programmed death-ligand 1 (PD-L1) as determined by an approved test has a combined positive score (CPS) ≥ 1; AND b. Patient has tried at least two previous chemotherapy regimens; AND Note: Examples of chemotherapy regimens are fluoropyrimidine (fluorouracil or capecitabine) and oxaliplatin, fluoropyrimidine and cisplatin, paclitaxel with cisplatin or carboplatin, docetaxel with cisplatin. c. If the patient's tumor is human epidermal growth factor receptor 2 (HER2) or HER2/neu positive, targeted therapy with trastuzumab has been tried; OR ii. Patient meets ALL of the following (a, b, and c): a. Patient has locally advanced unresectable or metastatic disease; AND b. Tumor is human epidermal growth factor receptor 2 (HER2) or HER2/neu positive; AND

		c. Medication is used in combination with trastuzumab, cisplatin or oxaliplatin, and fluorouracil or capecitabine" Merkel Cell Carcinoma: Initial Criteria: Removed "1. Used as a single agent; AND Patient has disseminated metastatic disease" Added: "1. Keytruda is approved for both Adult and pediatric patients; AND 2. Patient has recurrent, locally advanced, or metastatic Merkel cell carcinoma (MCC)." NSCLC: Initial Criteria: removed "1.Tumor has high PD-L1 expression [(Tumor Proportion Score (TPS) ≥50%)] as determined by an FDA-approved test; AND a. Used as a single agent for metastatic or disseminated recurrent disease; AND i. Used as first-line therapy for genomic tumor aberration (e.g., EGFR, ALK, ROS1, and BRAF) negative or unknown; OR 2. Tumor expresses PD-L1 (TPS ≥1%) as determined by an FDA-approved test; AND a. Used as a single agent for metastatic disease; AND i. Disease must have progressed during or following cytotoxic therapy; AND ii. Patients with genomic tumor aberrations must have progressed following systemic therapy for those aberrations (e.g., EGFR, ALK, etc.); OR 3.Used in combination with one of the following regimens for metastatic or disseminated recurrent disease: a. In combination with pemetrexed and either carboplatin or cisplatin for nonsquamous cell histology; OR b. In combination with carboplatin and paclitaxel for squamous cell histology; AND i. Used as first-line therapy for genomic tumor aberration (e.g., EGFR, ALK, ROS1 and BRAF) negative or unknown**, and PD-L1 expression <50% or unknown; OR ii. Used as first-line therapy for BRAF V600E-mutation positive tumors; OR iii. Used as subsequent therapy for genomic tumor aberration (e.g., EGFR, BRAF V600E, ALK, and ROS1) positive and prior targeted therapy§; OR iv. Used as subsequent therapy if PD-L1 expression-positive (≥50%) and genomic tumor aberration (e.g., EGFR, ALK, ROS1 and BRAF) negative or unknown**; OR

		4. Used as continuation maintenance therapy; AND a. Patient has a performance status of 0-2; AND b. Patient achieved tumor response or stable disease following initial therapy; AND i. Used in combination with pemetrexed; AND Pembrolizumab was given first-line in combination with pemetrexed and either carboplatin or cisplatin for disease of non-squamous cell histology; OR ii. Used as a single agent; AND Pembrolizumab was given first-line in combination with carboplatin and paclitaxel for disease of squamous cell histology" Added "A. Patient has recurrent, advanced, or metastatic disease; AND B. Patient meets ONE of the following (i, ii, or iii): i. Patient meets BOTH of the following (a and b): a. Keytruda is used as first-line or continuation maintenance therapy; AND Note: This is regardless of PD-L1 status. b. The tumor is negative for actionable mutations; OR Note: Examples of actionable mutations include sensitizing epidermal growth factor receptor (EGFR) mutation, anaplastic lymphoma kinase (ALK) fusions, NTRK gene fusion-positive, ROS1, BRAF V600E, MET 14 skipping mutation, RET rearrangement. ii. Patient meets BOTH of the following (a and b): a. Keytruda is used as first-line or subsequent therapy; AND Note: This is regardless of the PD-L1 status. b. The tumor is positive for one of the following mutations [(1), (2), (3), (4), (5), or (6)]: (1) Epidermal growth factor receptor (EGFR) exon 20 mutation; OR (2) KRAS G12C mutation; OR (3) BRAF V600E mutation; OR (4) NTRK1/2/3 gene fusion; OR (5) MET exon 14 skipping mutation; OR (6) RET rearrangement; OR iii. Keytruda is used as subsequent therapy and the patient meets ONE of the following (a, b, or c): a. Patient meets BOTH of the following [(1) and (2)]: (1) The tumor is epidermal growth factor receptor (EGFR) S768I, L861Q, and/or G719X mutation positive; AND

		(2) The patient has received targeted drug therapy for the specific mutation; OR Note: Examples of targeted drug therapy include Gilotrif (afatinib tablet), Tagrisso (osimertinib tablet), erlotinib, Iressa (gefitinib tablet), or Vizimpro (dacomitinib tablet). b. Patient meets BOTH of the following [(1) and (2)]: (1) The tumor is ROS1 rearrangement positive; AND (2) The patient has received targeted drug therapy for the specific mutation; OR Note: Examples of targeted drug therapy include Xalkori (crizotinib capsule), Rozlytrek (entrectinib capsule), or Zykadia (ceritinib tablet). c. Patient meets ALL of the following [(1), (2), and (3)]: (1) Patient has tried systemic therapy; AND Note: Examples of systemic chemotherapy include cisplatin, carboplatin, Alimta (pemetrexed intravenous infusion), Abraxane (paclitaxel albumin-bound intravenous infusion), gemcitabine, paclitaxel. (2) Patient has not progressed on prior therapy with a programmed death-1 (PD-1)/PD-ligand 1 (PD-L1) inhibitor; AND Note: This includes previous therapy with either one of Keytruda, Opdivo (nivolumab intravenous infusion), or Tecentriq (atezolizumab intravenous infusion). (3) If tumor is positive for an actionable mutation, the patient has received targeted drug therapy for the specific mutation; AND Note: Examples of actionable mutations include sensitizing epidermal growth factor receptor (EGFR) mutation, anaplastic lymphoma kinase (ALK) fusions, NTRK gene fusion positive, ROS1, BRAF V600E, MET exon 14 skipping mutation, RET rearrangement." Added Esophageal Cancer indication. Removed Small Cell Lung Cancer Indication and Criteria "Small Cell Lung Cancer (SCLC) † 1. For the treatment of patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy" Squamous Cell Carcinoma of the Head and Neck (SCCHN) Initial Criteria: Removed "1. Used in combination with platinum and FU for the first-line treatment of patients with metastatic or with unresectable, recurrent SCCHN; OR 2. Used as a single agent; AND 1. Patient has unresectable, recurrent, persistent or metastatic disease; AND

		2. Patient has non-nasopharyngeal disease; AND 3. Disease progressed on or after platinum-containing chemotherapy" Added "A. Patient has recurrent, unresectable, or metastatic disease; AND B. Patient meets ONE of the following (i or ii): i. If the medication is used for first-line treatment, patient must meet ONE of the following (a or b): a. Keytruda is used in combination with chemotherapy; OR Note: Examples of chemotherapy are cisplatin, carboplatin, fluorouracil, gemcitabine. B Keytruda is used as a single agent if the tumors are PD-L1-positive (combined positive score ≥ 1), as determined by an approved test. ii. For subsequent therapy, patient has tried at least one platinum-containing chemotherapy regimen; AND Note: Examples of platinum-contain chemotherapy regimens are: cisplatin or carboplatin with Erbitux (cetuximab intravenous infusion), gemcitabine, or 5-fluorouracil (5-FU). " <u>Bladder Cancer/Urothelial Carcinoma Initial Criteria: Removed</u> "1. Must be used as a single agent; AND 2. Patient has one of the following diagnoses: a. Locally advanced or metastatic Urothelial Carcinoma b. Disease recurrence post-cystectomy c. Recurrent or metastatic Primary Carcinoma of the Urethra; AND i. Patient does not have recurrent stage T3-4 disease or palpable inguinal lymph nodes d. Metastatic Upper GU Tract Tumors e. Metastatic Urothelial Carcinoma of the Prostate; AND 3. Used as first-line therapy in cisplatin-ineligible patients; AND a. Patient is carboplatin-ineligible; OR b. Patient has a PD-L1 expression of ≥10%; OR 4. Used as subsequent therapy after previous platinum treatment" Added "A. Patient meets ONE of the following conditions (i, ii, or iii): i. Patient has tried at least one platinum-based chemotherapy; OR Note: Cisplatin and carboplatin are platinum-based chemotherapies. ii. According to the prescriber, patient is not eligible for platinum-based chemotherapy (i.e., with cisplatin and carboplatin); OR Note: This is regardless of PD-L1 status. iii. Patient meets both of the following (a and b):

		a. Patient has non-muscle invasive bladder cancer; AND b. Patient has tried Bacillus Calmette-Guerin (BCG) or intravesical chemotherapy; AND Note: Examples of agents used as intravesical chemotherapy include mitomycin and gemcitabine." Cervical Cancer: Initial Criteria: Removed "used as a single agent" Microsatellite Instability-High or Mismatch Repair Deficient Solid Tumor: Initial Criteria: removed "2. Used as a single agent; AND 3. Patient's disease must be microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND 4. Pediatric patients must not have a diagnosis of MSI-H central nervous system cancer; AND 5. Patient has one of the following cancers: a. Colorectal Cancer † i. Initial therapy in patients with unresectable or metastatic disease who are not candidates for intensive therapy; OR ii. Used as primary treatment in patients with unresectable or metastatic disease who failed adjuvant treatment with FOLFOX (fluorouracil, leucovorin and oxaliplatin) or CapeOX (capecitabine-oxaliplatin) in the previous 12 months; OR iii. Used for unresectable or metastatic disease that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan † b. Pancreatic Adenocarcinoma ‡ i. Second-line therapy for locally advanced, recurrent, or metastatic disease after progression for patients with good performance status c. Bone Cancer (Ewing Sarcoma, Mesenchymal Chondrosarcoma, Osteosarcoma, Dedifferentiated Chondrosarcoma, or High-Grade Undifferentiated Pleomorphic Sarcoma) ‡ i. Used for unresectable or metastatic disease after progression following prior treatment and patient has no satisfactory alternative treatment options d. Gastric adenocarcinoma OR esophageal/esophagogastric junction adenocarcinoma or squamous cell carcinoma ‡ i. Subsequent therapy for unresectable (or not a candidate) locally advanced, recurrent, or metastatic disease e. Ovarian Cancer (included epithelial ovarian, fallopian tube and primary peritoneal cancers) ‡ i. Used for patients with persistent or recurrent disease; AND ii. Patient is not experiencing an immediate biochemical relapse f. Uterine Cancer (Endometrial Carcinoma) ‡

		i. Used for patients with high risk tumors, or recurrent or metastatic disease, that have progressed following prior cytotoxic chemotherapy g. Penile Cancer ‡ i. Used as subsequent treatment of unresectable or metastatic disease that is progressive and there are no other satisfactory treatment options h. Testicular Cancer ‡ i. Used as third-line therapy or after progression with high-dose chemotherapy i. Hepatobiliary Cancer (Gall bladder cancer; intra-/extra-hepatic cholangiocarcinoma) ‡ i. Used as initial therapy for unresectable or metastatic disease j. Cervical Cancer † i. Used for recurrent or metastatic disease k. Other Solid Tumor (e.g., adrenal gland tumors, etc.) i. Used for unresectable or metastatic disease that progressed following prior treatment and there are no satisfactory alternative treatment options" Added "2. One of the following conditions applies (i, ii, iii, iv, v, vi, vii, or viii): i. Patient has advanced or metastatic ampullary cancer; OR ii. Patient has unresectable or metastatic colon or rectal cancer; OR iii. Patient has unresectable or metastatic gallbladder cancer (including intra- and extra-hepatic cholangiocarcinoma); OR iv. Patient has unresectable or metastatic head and neck squamous cell carcinoma; OR v. Patient has persistent or recurrent ovarian/fallopian tube/primary peritoneal carcinoma; OR vi. Patient has locally advanced or metastatic pancreatic adenocarcinoma; OR vii. Patient has advanced or metastatic small bowel carcinoma; OR viii. Patient meets BOTH of the following (a and b): a) Patient has tried at least one prior systemic therapy for an MSI-H or dMMR solid tumor; AND b) Patient has unresectable or metastatic disease" Removed Malignant Pleural Mesothelioma ‡, Central Nervous System Cancer ‡, T-Cell Lymphoma/Extranodal NK ‡, Anal Carcinoma ‡ Criteria. Hepatocelluar Carcinoma: Initial Criteria: Removed "Patient has previously been treated with Nexavar® (sorafenib)" replaced with "Patient has tried at least one tyrosine kinase inhibitor; AND

		Note: Examples of tyrosine kinase inhibitors include Nexavar (sorafenib tablets), Lenvima (lenvatinib capsules)." Renal Cell Carcinoma (RCC) † Iniital Criteria: Removed "In combination with axitinib, for the first-line treatment of patients with advanced RCC" Added "A. Patient meets ONE of the following (i, ii, or iii): i. Approve if the patient meets ALL of the following (a, b, and c): a. The tumor has clear cell histology; AND b. Patient has relapsed or metastatic disease; AND c. The medication is used in combination with Inlyta (axitinib tablets) or Lenvima (lenvatinib capsules); OR ii. Approve for 1 year if the patient meets ALL of the following (a, b, and c): a. The tumor has non-clear cell histology; AND b. Patient has relapsed or metastatic disease; AND c. The medication is used as single-agent therapy; OR iii. Approve for up to 1 year (total) if patient meets ALL of the following (a, b, c, and d): a. Keytruda is used as adjuvant therapy; AND b. The tumor has clear cell histology; AND c. Patient has advanced disease; AND d. The medication is used as single-agent therapy" Added Endometrial Carcinoma Indication and criteria Tumor Mutational Burden-High: Initial Criteria: Removed "Keytruda is being used as monotherapy" Added: Triple Negative Breast Cancer Indication Updated Length of Authorization: Removed: • cSCC, SCCHN, cHL, NSCLC, Urothelial Carcinoma, MPM, MSI-H/dMMR, PMBCL, Cervical, Anal & Gastric Cancers can be authorized up to a maximum of 24 months of therapy." Added "• Adrenal Gland Tumors, Anal Carcinoma, Bladder Cancer/Urothelial Carcinoma, Cervical Cancer, cHL, CNS Cancer, Cutaneous Melanoma (in combination with ipilimumab), cSCC, Endometrial Carcinoma, Esophageal/GEJ Cancer, Gastric Cancer, HCC, MCC, MSIH/dMMR Cancer, NSCLC (first-line or subsequent therapy), PMBCL, Primary Cutaneous Lymphomas, RCC (first-line or subsequent therapy), SCCHN, SCLC, Thymic Carcinoma, TMB-H Cancer, TNBC (recurrent unresectable or metastatic disease), Uveal Melanoma, and Vulvar Cancer can be authorized up to a maximum of twenty-four (24) months of therapy. • Adjuvant therapy in Cutaneous Melanoma, NSCLC, and RCC can be authorized up to a maximum of twelve (12) months of therapy.

		• Neoadjuvant therapy in TNBC can be authorized up to a maximum of twenty-four (24) weeks of therapy. • Adjuvant therapy in TNBC can be authorized up to a maximum of twenty-seven (27) weeks of therapy." Updated Max Units: removed "cSCC, SCCHN, cHL, NSCLC, Melanoma, Urothelial, Gastric, CNS metastases, PMBCL, Cervical, MSI-H/dMMR Cancer, & TMB-H Cancer: • 200 billable units every 21 days MPM & Uterine Cancer: • 1150 billable units every 14 days Merkel Cell Carcinoma & NK/T-Cell Lymphoma: • 250 billable units every 21 days" Added chart
EmblemHealth & ConnectiCare	08/11/2022	Transferred policy to new template.
EmblemHealth & ConnectiCare	10/23/2020	Updated FDA approval indication for Classical Hodgkin Lymphoma
EmblemHealth & ConnectiCare	7/15/2020	FDA approval indication for MSI-H or mismatch repair deficient colorectal cancer
EmblemHealth & ConnectiCare	6/29/2020	Added indication, criteria, dosing max, icd 10 code for Cutaneous Squamous cell carcinoma
EmblemHealth & ConnectiCare	6/23/2020	Added indication and criteria for Tumor Mutational Burden-High Cancer
EmblemHealth & ConnectiCare	01/1/2020	-Under Guidelines, Melanoma – added for the adjuvant treatment of patients with melanoma with involvement of lymph node(s) following complete resection -Under Guidelines, added Small Cell Lung Cancer (SCLC) indication. For the treatment of patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy -Under Guidelines, Squamous Cell Carcinoma of the Head and Neck (SCCHN), added in combination with platinum and FU for the first-line treatment of patients with metastatic or with unresectable, recurrent SCCHN -Under Guidelines, added Renal Cell Carcinoma indication, in combination with axitinib, for the first-line treatment of patients with advanced RCC

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