Reference number
1980-A

STANDARD MEDICARE PART B MANAGEMENT

KEYTRUDA (pembrolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Melanoma
   i. Keytruda (pembrolizumab) is indicated for the treatment of patients with unresectable or metastatic melanoma.
   ii. Keytruda is indicated for the adjuvant treatment of adult and pediatric (12 years and older) patients with Stage IIB, IIC, or III melanoma.
2. Non-Small Cell Lung Cancer
   i. Keytruda, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.
   ii. Keytruda, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.
   iii. Keytruda, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 (Tumor Proportion Score [TPS ≥1%]) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is:
      a. stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
      b. metastatic.
   iv. Keytruda, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda.
   v. Keytruda, in combination with platinum-containing chemotherapy, is indicated for the treatment of patients with resectable (tumors ≥4 cm or node positive) NSCLC as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.
   vi. Keytruda, as a single agent, is indicated for adjuvant treatment following resection and platinum-based chemotherapy for adult patients with stage 1B (T2a ≥ 4cm), II, or IIIA NSCLC

3. Head and Neck Cancer Squamous Cell Cancer
   i. Keytruda, in combination with platinum and fluorouracil (FU), is indicated for the first-line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC).
   ii. Keytruda, as a single agent, is indicated for the first line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test.

iii. Keytruda, as a single agent, is indicated for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

4. Classical Hodgkin Lymphoma
   i. Keytruda is indicated for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL).
   ii. Keytruda is indicated for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more prior lines of therapy.

5. Primary Mediastinal Large B-cell Lymphoma
   Keytruda is indicated for the treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphomas (PMBCL), or who have relapsed after 2 or more prior lines of therapy.

   Limitations of Use: Keytruda is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

6. Urothelial Carcinoma
   i. Keytruda, as a single agent, is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma:
      a. who are not eligible for any platinum-containing chemotherapy, or
      b. who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
   ii. Keytruda, as a single agent, is indicated for the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

7. Microsatellite Instability-High or Mismatch Repair Deficient Cancer
   Keytruda is indicated for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options.

   Limitations of Use: The safety and effectiveness of Keytruda in pediatric patients with MSI-H central nervous system cancers have not been established.

8. Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer
   Keytruda is indicated for the treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC).

9. Gastric Cancer

   Keytruda is indicated in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma.

10. Esophageal Cancer
    Keytruda is indicated for the treatment of patients with locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation either:
    i. in combination with platinum- and fluoropyrimidine-based chemotherapy, or

ii. as a single agent after one or more prior lines of systemic therapy for patients with tumors of squamous cell histology whose tumors express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test.

11. Cervical Cancer
    i. Keytruda is indicated in combination with chemotherapy, with or without bevacizumab, for the treatment of patients with persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.
    ii. Keytruda is indicated as a single agent for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumor express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.

12. Hepatocellular Carcinoma
    Keytruda is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

13. Biliary Tract Cancer
    Keytruda, in combination with gemcitabine and cisplatin is indicated for the treatment of patients with locally advanced unresectable or metastatic biliary tract cancer (BTC).

14. Merkel Cell Carcinoma
    Keytruda is indicated for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC).

15. Renal Cell Carcinoma
    i. Keytruda, in combination with axitinib, is indicated for the first-line treatment of patients with advanced renal cell carcinoma (RCC).
    ii. Keytruda, in combination with lenvatinib, for the first-line treatment of adult patients with advanced RCC.
    iii. Keytruda, for the adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

16. Endometrial Carcinoma
    i. Keytruda, in combination with lenvatinib, is indicated for the treatment of patients with advanced endometrial carcinoma that is not MSI-H or dMMR, who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation.
    ii. Keytruda, as a single agent, is indicated for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR, as determined by an FDA-approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

17. Tumor Mutational Burden-High Cancer
    Keytruda is indicated for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.

    Limitations of use: The safety and effectiveness of Keytruda in pediatric patients with TMB-H central nervous system cancers have not been established.

18. Cutaneous Squamous Cell Carcinoma
    Keytruda is indicated for the treatment of patients with recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced cSCC that is not curable by surgery or radiation.

19. Triple-Negative Breast Cancer
    i. Keytruda is indicated for the treatment of patients with high-risk early-stage TNBC in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery
    ii. Keytruda is indicated in combination with chemotherapy, for the treatment of patients with locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1 [Combined Positive Score (CPS) ≥10] as determined by an FDA approved test.

20. Adult Classical Hodgkin Lymphoma and Adult Primary Mediastinal Large B-Cell Lymphoma: Additional Dosing Regimen of 400mg Every 6 Weeks
    Keytruda is indicated for use at an additional recommended dosage of 400mg every 6 weeks for classical Hodgkin lymphoma and primary mediastinal large B-cell lymphoma in adults.

B. Compendial Uses[2]
1. Non-small cell lung cancer
2. Head and neck cancer
3. Classical Hodgkin lymphoma
4. Urothelial carcinoma
5. Solid tumors
6. Anaplastic thyroid carcinoma
7. Follicular, Oncocytic (Hurthle cell), or papillary thyroid carcinoma
8. Medullary thyroid carcinoma
9. Colorectal cancer
10. Merkel cell carcinoma
11. Gastric cancer
12. Esophageal cancer and esophagogastric junction cancer
13. Cervical cancer
14. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
15. Uveal melanoma
16. Testicular cancer
17. Endometrial carcinoma
18. Anal carcinoma
19. Central Nervous System (CNS) brain metastases
20. Primary mediastinal large B-cell lymphoma
21. Pancreatic adenocarcinoma
22. Biliary Tract cancers
23. Hepatocellular carcinoma
24. Vulvar cancer
25. Thymic carcinoma
26. Mycosis Fungoides/Sezary syndrome
27. Anaplastic large cell lymphoma (ALCL)
28. Extranodal NK/T-cell lymphoma
29. Gestational trophoblastic neoplasia
31. 30. Neuroendocrine and Adrenal TumorsProstate cancer
32. Occult primary cancer
33. Small bowel adenocarcinoma
34. Breast cancer
35. Bone cancer
36. CLL/SLL
37. Penile cancer
38. Soft tissue sarcoma

39. Uterine sarcoma
40. Ampullary Adenocarcinoma
41. Small cell lung cancer
42. Pediatric Diffuse High-Grade Gliomas
43. Kaposi Sarcoma

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions:

A. Pediatric members with TMB-H central nervous system cancers.
B. Members who have experienced disease progression while on programmed death receptor-1 (PD-1) or PD-L1 inhibitor therapy (other than when used as second-line or subsequent therapy for metastatic or unresectable melanoma in combination with ipilimumab following progression on single agent anti-PD-1 immunotherapy).

III. CRITERIA FOR INITIAL APPROVAL

A. Cutaneous Melanoma

Authorization of 12 months may be granted for the treatment of cutaneous melanoma in either of the following settings:

1. Treatment of unresectable, recurrent or metastatic disease.
2. Adjuvant treatment.

B. Non-small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for NSCLC for either of the following clinical settings:

1. Treatment of recurrent, advanced, or metastatic disease.
2. Neoadjuvant treatment when used in combination with platinum-based chemotherapy, and then continued as single agent adjuvant therapy after surgery.
3. Adjuvant treatment following resection and platinum-based chemotherapy.

C. Head and Neck Cancer

Authorization of 12 months may be granted for treatment of head and neck cancer.

D. Classical Hodgkin Lymphoma (cHL)

Authorization of 12 months may be granted for treatment of classical Hodgkin lymphoma.

E. Urothelial Carcinoma

Authorization of 12 months may be granted for treatment of urothelial carcinoma, including bladder cancer, upper genitourinary tract tumors, urothelial carcinoma of the prostate, and primary carcinoma of the urethra.

F. Solid Tumors

Authorization of 12 months may be granted for treatment of solid tumors in members with unresectable or metastatic disease that has progressed following prior treatment and have no satisfactory alternative treatment options when either of the following criteria is met:

1. The requested medication will be used for microsatellite instability-high or mismatch repair deficient solid tumors.

2. The requested medication will be used for tumor mutational burden-high (≥10 mutations/megabase) solid tumors.

G. Neuroendocrine and Adrenal Tumors
Authorization of 12 months may be granted for treatment of neuroendocrine and adrenal tumors.

H. Anaplastic Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of anaplastic thyroid carcinoma for tumor mutational burden-high (≥10 mutations/megabase) tumors.

I. Follicular, Oncocytic (Hurthle Cell), or Papillary Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of follicular, oncocytic (Hurthle cell), or papillary thyroid carcinoma for microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR) or tumor mutational burden-high (≥10 mutations/megabase) tumors.

J. Medullary Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of medullary thyroid carcinoma for microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR) or tumor mutational burden-high (≥10 mutations/megabase) tumors.

K. Colorectal Cancer (CRC)
Authorization of 12 months may be granted for treatment of colorectal cancer including appendiceal carcinoma when both of the following criteria are met:
1. Disease is unresectable, advanced, or metastatic.
2. Tumor is microsatellite instability-high or mismatch repair deficient.

L. Merkel Cell Carcinoma (MCC)
Authorization of 12 months may be granted for treatment of Merkel cell carcinoma.

M. Gastric Cancer
Authorization of 12 months may be granted for treatment of gastric cancer in members who are not surgical candidates or who have recurrent, locally advanced, or metastatic disease.

N. Esophageal Cancer and Esophagogastric Junction Cancer
Authorization of 12 months may be granted for treatment of esophageal cancer, including esophagogastric junction (EGJ) cancer, in members who are not surgical candidates or who have recurrent, locally advanced, or metastatic disease.

O. Cervical Cancer
Authorization of 12 months may be granted for treatment of cervical cancer.

P. Epithelial Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer
Authorization of 12 months may be granted for the treatment of epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer.

Q. Uveal Melanoma
Authorization of 12 months may be granted for treatment of uveal melanoma.

R. Testicular Cancer
Authorization of 12 months may be granted for the treatment of testicular cancer.

S. Endometrial Carcinoma
Authorization of 12 months may be granted for the treatment of endometrial carcinoma.

T. Anal Carcinoma
Authorization of 12 months may be granted for the treatment of anal carcinoma.

U. CNS Brain Metastases
Authorization of 12 months may be granted for the treatment of CNS brain metastases in members with melanoma or non-small cell lung cancer (NSCLC).

V. Primary Mediastinal Large B-Cell Lymphoma (PMBCL)
Authorization of 12 months may be granted for the treatment of primary mediastinal large B-cell lymphoma.

W. Pancreatic Adenocarcinoma
Authorization of 12 months may be granted for the treatment of pancreatic adenocarcinoma.

X. Biliary Tract Cancers
Authorization of 12 months may be granted for the treatment of biliary tract cancers, including intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer.

Y. Hepatocellular Carcinoma (HCC)
Authorization of 12 months may be granted for treatment of members with hepatocellular carcinoma.

Z. Vulvar Cancer
Authorization of 12 months may be granted for treatment of vulvar cancer.

AA. Renal Cell Carcinoma (RCC)
Authorization of 12 months may be granted for treatment of renal cell carcinoma.

BB. Thymic Carcinoma
Authorization of 12 months may be granted for treatment of thymic carcinoma.

CC. Mycosis Fungoides/Sezary Syndrome
Authorization of 12 months may be granted for treatment of mycosis fungoides or Sezary syndrome.

DD. Extranodal NK/T-cell lymphoma
Authorization of 12 months may be granted for treatment of extranodal NK/T-cell lymphoma.

EE. Anaplastic large cell lymphoma (ALCL)
Authorization of 12 months may be granted for treatment of anaplastic large cell lymphoma (ALCL).

FF. Gestational Trophoblastic Neoplasia
Authorization of 12 months may be granted for treatment of gestational trophoblastic neoplasia.

GG. Prostate Cancer[2]
Authorization of 12 months may be granted for treatment of prostate cancer.

HH. Cutaneous Squamous Cell Skin Carcinoma (cSCC)
Authorization of 12 months may be granted for treatment of cutaneous squamous cell carcinoma (cSCC) that is not curable by surgery or radiation.

II. Occult Primary
Authorization of 12 months may be granted for treatment of occult primary cancer in members with microsatellite instability-high or mismatch repair deficient tumors or tumor mutational burden-high (TMB-H) (≥10 mutations/megabase (mut/Mb) tumors).

JJ. Small Bowel Adenocarcinoma
Authorization of 12 months may be granted for treatment of small bowel adenocarcinoma, when both of the following criteria are met:
1. Disease is advanced or metastatic.
2. Tumor is microsatellite-instability high or mismatch repair deficient.

KK. Ampullary Adenocarcinoma
Authorization of 12 months may be granted as a single agent for microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR), or tumor mutational burden-high (TMB-H ≥ 10 mut/Mb) ampullary adenocarcinoma.

LL. Breast Cancer
1. Authorization of 12 months may be granted for treatment of triple-negative breast cancer when both of the following criteria are met:
   i. The diagnosis of triple-negative breast cancer is confirmed by the cancer cells testing negative for ALL of the following receptors:
      a. Human epidermal growth factor receptor 2 (HER-2)
      b. Estrogen
      c. Progesterone
   ii. The requested medication will be used in combination with chemotherapy or as a single agent as adjuvant treatment after surgery.
2. Authorization of 12 months may be granted for treatment of breast cancer for recurrent unresectable or metastatic tumors when both of the following criteria are met:
   i. The disease has progressed following prior treatment and the patient has no satisfactory alternative treatment options.
   ii. The tumors are microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR) or tissue tumor mutation burden-high (TMB-H) (≥10 mutations/megabase [mut/Mb]).

MM. Bone Cancer
Authorization of 12 months may be granted for treatment of bone cancer, including chondrosarcoma, chordoma, Ewing Sarcoma, and osteosarcoma.

NN. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
Authorization of 12 months may be granted for treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma.

OO. Penile Cancer
Authorization of 12 months may be granted for treatment of penile cancer.

PP. Soft Tissue Sarcoma
Authorization of 12 months may be granted as a single agent for treatment of the following types of soft tissue sarcoma: alveolar soft part sarcoma (ASPS), myxofibrosarcoma, undifferentiated pleomorphic sarcoma (UPS), cutaneous angiosarcoma, and undifferentiated sarcoma.

QQ. Uterine sarcoma
Authorization of 12 months may be granted for treatment of uterine sarcoma for tumor mutational burden-high (≥10 mutations/megabase) tumors.

RR. Small Cell Lung Cancer
Authorization of 12 months may be granted for treatment of small cell lung cancer.

SS. Pediatric Diffuse High-Grade Gliomas

Authorization of 12 months may be granted for treatment of hypermutant tumor pediatric diffuse high-grade glioma.

TT. Kaposi Sarcoma

Authorization of 12 months may be granted as a single agent for subsequent treatment of relapsed/refractory endemic or classic Kaposi Sarcoma.

IV. CONTINUATION OF THERAPY

A. Adjuvant treatment of melanoma, high-risk early-stage TNBC, renal cell carcinoma, or NSCLC

Authorization for 12 months total therapy may be granted for all members (including new members) who are continuing with the requested medication when all of the following criteria are met:

1. The member is currently receiving therapy with the requested medication.
2. The requested medication is being used as adjuvant treatment for any of the following indications: melanoma, high-risk early-stage TNBC, renal cell carcinoma, or NSCLC.
3. The requested medication has been effective for treating the diagnosis or condition.

B. NSCLC, head and neck cancer, cHL, PMBCL, MSI-H or dMMR Cancers, Gastric Cancer, Esophageal Cancer (including EGJ), Cervical Cancer, urothelial carcinoma, HCC, MCC, RCC, Endometrial carcinoma, cSCC, locally recurrent unresectable or metastatic TNBC, TMB-H Cancer, Biliary Tract Cancer

Authorization for 12 months (up to 24 months of continuous use) may be granted for all members (including new members) who are continuing with the requested medication when all of the following criteria are met:

1. The member is currently receiving therapy with the requested medication.
2. The requested medication is being used to treat NSCLC, head and neck cancer, cHL, PMBCL, MSI-H or dMMR cancers, gastric cancer, esophageal cancer (including EGJ), urothelial carcinoma, cervical cancer, HCC, MCC, RCC, endometrial carcinoma, cSCC, locally recurrent unresectable or metastatic TNBC, TMB-H cancers, and biliary tract cancers.
3. The requested medication has been effective for treating the diagnosis or condition.

C. All Other Indications

Authorization for 12 months may be granted for all members (including new members) who are continuing with the requested medication when all of the following criteria are met:

1. The member is currently receiving therapy with the requested medication.
2. The requested medication is being used to treat any other diagnosis or condition enumerated in Section III.
3. The requested medication has been effective for treating the diagnosis or condition.

V. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Keytruda.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
3. NCCN Guideline: Pediatric central nervous system cancers
4. NCCN Guideline: Prostate cancer
5. NCCN Guideline: Penile cancer

6. NCCN Guideline: Hodgkin lymphoma
7. NCCN Guideline: Thymomas and thymic carcinomas
8. NCCN Guideline: Small cell lung cancer
9. NCCN Guideline: Neuroendocrine and Adrenal Tumors
10. NCCN Guideline: Vulvar cancer
11. NCCN Guideline: Cervical cancer
12. NCCN Guideline: Gestational Trophoblastic Neoplasia
13. NCCN Guideline: Small bowel adenocarcinoma
14. NCCN Guideline: T-cell lymphomas
15. NCCN Guideline: Pediatric Hodgkin lymphoma
16. NCCN Guideline: Squamous cell skin cancer
17. NCCN Guideline: Cutaneous melanoma
18. NCCN Guideline: Kaposi sarcoma
19. NCCN Guideline: Pediatric aggressive mature B-cell lymphomas
20. NCCN Guideline: Bone cancer
21. NCCN Guideline: Testicular cancer
22. NCCN guideline: Merkel cell carcinoma
23. NCCN guideline: Non-small cell lung cancer
24. NCCN guideline: Breast cancer
25. NCCN guideline: Hepatocellular carcinoma
26. NCCN guideline: Soft tissue sarcoma
27. NCCN guideline: Anal carcinoma
28. NCCN guideline: Uveal melanoma
29. NCCN guideline: Gastric cancer
30. NCCN guideline: Esophageal and esophagogastric junction cancers
31. NCCN guideline: Occult primary
32. NCCN guideline: Central nervous system cancer
33. NCCN guideline: Biliary tract cancer
34. NCCN guideline: Thyroid carcinoma
35. NCCN guideline: Ampullary adenocarcinoma
36. NCCN guideline: Bladder cancer
37. NCCN guideline: Colon cancer
38. NCCN guideline: B-cell lymphomas
39. NCCN guideline: Uterine neoplasms
40. NCCN guideline: Primary cutaneous lymphomas
41. NCCN guideline: Rectal cancer
42. NCCN guideline: Chronic lymphocytic leukemia/Small lymphocytic lymphoma
43. NCCN guideline: Ovarian cancer/Fallopian tube cancer/Primary peritoneal cancer
44. NCCN guideline: Pancreatic adenocarcinoma
45. NCCN guideline: Head and neck cancers
46. NCCN guideline: Kidney cancer

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Keytruda are covered in addition to the following:

1. Non-small cell lung cancer
2. Head and neck cancer
3. Classical Hodgkin lymphoma
4. Urothelial carcinoma
5. Solid tumors
6. Adrenocortical carcinoma
7. Anaplastic thyroid carcinoma
8. Follicular, Hurthle cell, or papillary thyroid carcinoma
9. Medullary thyroid carcinoma

10. Colorectal cancer
11. Merkel cell carcinoma
12. Gastric cancer
13. Esophageal cancer and esophagogastric junction cancer
14. Cervical cancer
15. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer
16. Uveal melanoma
17. Testicular cancer
18. Endometrial carcinoma
19. Anal carcinoma
20. Central Nervous System (CNS) brain metastases
21. Primary mediastinal large B-cell lymphoma
22. Pancreatic adenocarcinoma
23. Hepatobiliary cancers
24. Hepatocellular carcinoma
25. Vulvar cancer
26. Thymic carcinoma
27. Mycosis Fungoides/Sezary syndrome
28. Anaplastic large cell lymphoma (ALCL)
29. Extranodal NK/T-cell lymphoma
30. Gestational trophoblastic neoplasia
31. Neuroendocrine and Adrenal Tumors
32. Prostate cancer
33. Occult primary cancer
34. Small bowel adenocarcinoma
35. Breast cancer
36. Bone cancer
37. CLL/SLL
38. Penile cancer
39. Soft tissue sarcoma
40. Uterine sarcoma
41. Ampullary Adenocarcinoma
42. Small cell lung cancer
43. Pediatric Diffuse High-Grade Gliomas
44. Kaposi Sarcoma

VI. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for the compendial uses in section V can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

VII. REFERENCES

1. Keytruda [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; October 2023.
2. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed October 16, 2023.

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