UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – Programmed Death Receptor-1) – Keytruda Qlex Utilization Management Medical Policy
- Keytruda Qlex™ (pembrolizumab and berahyaluronidase alfa-pmph subcutaneous injection – Merck)

REVIEW DATE: 09/09/2026

OVERVIEW

Keytruda Qlex, a combination of pembrolizumab, programmed death receptor-1 (PD-1) blocking antibody, and berahyaluronidase alpha, an endoglycosidase, is indicated for the treatment of the following indications:[1]

- **Biliary tract cancer**, in combination with gemcitabine and cisplatin for the treatment of locally advanced unresectable or metastatic disease in adults.
- **Breast cancer, triple-negative**, in adults:
  - In combination with chemotherapy for the treatment of locally recurrent unresectable or metastatic disease in patients whose tumors express programmed death-ligand 1 (PD-L1) [combined positive score {CPS} ≥ 10] as determined by an FDA-approved test.
  - For the treatment of high-risk, early-stage disease in combination with chemotherapy as neoadjuvant treatment and then continued as a single agent as adjuvant treatment after surgery.
  - In combination with Trodelvy® (sacituzumab govitecan-hziy intravenous infusion), as first-line treatment of adult patients with unresectable locally advanced or metastatic disease whose tumors express PD-L1 (CPS ≥ 10) as determined by an FDA-authorized test.
- **Cervical cancer**, in adults:
  - In combination with chemotherapy, with or without bevacizumab, for persistent, recurrent, or metastatic disease in patients whose tumor expresses PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
  - As a single agent, for treatment of recurrent or metastatic disease with disease progression on or after chemotherapy in patients whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
  - In combination with chemoradiotherapy in patients with locally advanced disease involving the lower third of the vagina, with or without extension to pelvic sidewall, or hydronephrosis/non-functioning kidney, or spread to adjacent pelvic organs (FIGO 2014 Stage III-IVA).
- **Cutaneous squamous cell carcinoma,** for treatment of adults with recurrent or metastatic disease, or locally advanced disease that is not curable by surgery or radiation.
- **Endometrial cancer**, in adults:
  - In combination with carboplatin and paclitaxel, followed by single agent therapy for adults with primary advanced or recurrent disease.
  - In combination with Lenvima® (lenvatinib capsules), for the treatment of advanced disease that is mismatch repair proficient (pMMR) as determined by an FDA-approved test or not microsatellite instability high (MSI-H), in patients who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation.
  - As a single agent, for the treatment of advanced disease that is MSI-H or mismatch repair deficient (dMMR) as determined by an FDA-approved test, in patients who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

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- **Esophageal cancer**, treatment of adults with locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) carcinoma (tumors with epicenter 1 to 5 centimeters above the GEJ) that is not amenable to surgical resection or definitive chemoradiation in the following situations:
  - In combination with platinum- and fluoropyrimidine-based chemotherapy in patients whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
  - As a single agent after one or more prior lines of systemic therapy for tumors of squamous cell histology that express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test.
- **Gastric cancer**, in adults:
  - For the first-line treatment of locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (*HER2*)-positive gastric or GEJ adenocarcinoma whose tumors express PD-L1 (CPS ≥ 1), in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy in adults.
  - In combination with fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of adults with locally advanced unresectable or metastatic *HER2*-negative gastric or GEJ adenocarcinoma whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
- **Head and neck squamous cell carcinoma**, in adults:
  - As a single agent for the treatment of recurrent or metastatic disease with disease progression on or after platinum-containing chemotherapy.
  - In combination with platinum and fluorouracil for the first-line treatment of metastatic or unresectable, recurrent disease.
  - As a single agent, for the first line treatment of metastatic or unresectable, recurrent disease in patients whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
  - As a single agent as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy with or without cisplatin and then as single agent, for resectable locally advanced disease in patients whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
- **Hepatocellular carcinoma**, for treatment of adults with hepatocellular carcinoma secondary to hepatitis B who have received prior systemic therapy other than a PD-1/PD-L1 containing regimen.
- **Melanoma**, in the following situations:
  - For the treatment of unresectable or metastatic disease in adults.
  - As adjuvant treatment of Stage IIB, IIC, or III melanoma following complete resection in patients ≥ 12 years of age.
- **Merkel cell carcinoma**, for treatment of recurrent locally advanced or metastatic disease in adult and pediatric patients ≥ 12 years of age.
- **Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) cancer**, for treatment of unresectable or metastatic MSI-H or dMMR solid tumors, as determined by an FDA-approved test, in adult and pediatric patients ≥ 12 years of age that have progressed following prior treatment and who have no satisfactory alternative treatment options.
- **MSI-H or dMMR colorectal cancer,** for the treatment of adults with unresectable or metastatic disease, as determined by an FDA-approved test.
- **Non-small cell lung cancer** (**NSCLC**), in adults:
  - As a single agent for the first-line treatment of tumors that express PD-L1 (tumor proportion score [TPS] ≥ 1%) as determined by an FDA-approved test, with no epidermal growth factor receptor (*EGFR*) or anaplastic lymphoma kinase (*ALK*) genomic tumor aberrations and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or for metastatic disease.
  - As a single agent for the treatment of metastatic disease in patients whose tumors express PD-L1 (TPS ≥ 1%) as determined by an FDA-approved test and with disease progression on or

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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 Qlex.
    - In combination with pemetrexed and platinum-based chemotherapy, for the first-line treatment of metastatic nonsquamous NSCLC in patients with no *EGFR* or *ALK* genomic tumor aberrations.
    - In combination with carboplatin and either paclitaxel or paclitaxel protein-bound, for first-line treatment in metastatic squamous NSCLC.
    - In combination with platinum-containing chemotherapy, for the neoadjuvant treatment of resectable (tumors ≥ 4 cm or node positive) NSCLC and then continued as a single agent as adjuvant treatment after surgery.
    - As a single agent, as adjuvant treatment following resection and platinum-based chemotherapy for stage IB, II, or IIIA disease.
- **Ovarian Cancer,** in combination with paclitaxel, with or without bevacizumab, for treatment of platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal carcinoma in adults whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-authorized test, and who have received one or two prior systemic treatment regimens.
- **Pleural mesothelioma, malignant**, in combination with pemetrexed and platinum chemotherapy for the first-line treatment of adults with unresectable advanced or metastatic disease.
- **Renal cell carcinoma**, in adults:
    - In combination with Inlyta® (axitinib tablets) or Lenvima, for the first-line treatment of advanced disease in adults.
    - For adjuvant treatment of disease that is intermediate-high or high risk of recurrence following nephrectomy or following nephrectomy and resection of metastatic lesions.
    - In combination Welireg (belzutifan tablets), for adjuvant treatment of renal cell carcinoma with a clear cell component (ccRCC) at intermediate-high or high risk of recurrence following nephrectomy or following nephrectomy and resection of metastatic lesions in adults.
- **Tumor mutational burden-high (TMB-H) cancer**, for treatment of unresectable or metastatic TMB-H (≥ 10 mutations/megabase) disease, as determined by an FDA-approved test, in adult and pediatric ≥ 12 years of age patients that have progressed following prior treatment and who have no satisfactory alternative treatment options.*****
  Limitation of Use: The safety and effectiveness of Keytruda Qlex in pediatric patients ≥ 12 years of age with TMB-H central nervous system cancers have not been established.
- **Urothelial carcinoma**, in adults:
    - Treatment of locally advanced or metastatic disease in patients who are not eligible for platinum-containing chemotherapy as a single agent.
    - Treatment of locally advanced or metastatic disease in patients who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy as a single agent.
    - Treatment of Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer with carcinoma in situ with or without papillary tumors in patients who are ineligible for or have elected not to undergo cystectomy as a single agent.
    - In combination with Padcev® (enfortumab intravenous infusion), as neoadjuvant treatment and then continued after cystectomy as adjuvant treatment, in adult patients with muscle invasive bladder cancer (MIBC).

* This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

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Guidelines

The use of Keytruda Qlex is recommended across multiple National Comprehensive Cancer Network (NCCN) guidelines and the NCCN Compendium.[2-42] Recommendations with a category of evidence of 2B or higher support the approval criteria outlined below.

Dosing

The recommended dose of Keytruda Qlex is 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; or 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks for patients ≥ 12 years of age who weigh ≥ 40 kg.[1]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Keytruda Qlex. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Keytruda Qlex as well as the monitoring required for adverse events and long-term efficacy, approval requires Keytruda Qlex to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Keytruda Qlex is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Biliary Tract Cancer. Approve for the duration noted if the patient meets ALL of the following (A, B, C, and D):

Note: Biliary tract cancer includes gallbladder cancer, intrahepatic cholangiocarcinoma, and extrahepatic cholangiocarcinoma. If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.

A) Patient is ≥ 18 years of age; AND

B) The medication is used in combination with cisplatin or carboplatin and gemcitabine; AND

C) Patient meets ONE of the following (i or ii):

- **i.** Approve for 1 year if the patient has unresectable, resected gross residual, or metastatic disease; OR
- **ii.** Approve for a total of 6 months if the patient meets BOTH of the following (a and b):
  - **a)** Patient has resectable locoregionally advanced gallbladder cancer; AND
  - **b)** The medication is used for neoadjuvant therapy; AND

D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):

A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR

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B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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2. Bladder Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient meets ONE of the following conditions (i, ii, iii, or iv):
  - **i.** Patient has locally advanced or metastatic disease; OR
  - **ii.** The medication is used as subsequent therapy; OR
  - **iii.** The medication is used as neoadjuvant or adjuvant therapy; OR
  - **iv.** Patient meets BOTH of the following (a and b):
    - **a)** Patient has high-risk, non-muscle invasive bladder cancer; AND
    - **b)** Patient is Bacillus Calmette-Guerin (BCG) unresponsive; AND
- **C)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
- **A)** 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
- **B)** 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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3. Breast Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has triple-negative disease; AND
  Note: Triple negative disease is estrogen receptor-negative, progesterone receptor-negative, human epidermal growth factor receptor 2 (*HER2*)-negative.
- **C)** Patient meets ONE of the following (i or ii):
  - **i.** Patient meets BOTH of the following (a and b):
    - **a)** Patient has recurrent unresectable (local or regional) or Stage IV disease; AND
    - **b)** Patient's tumor expression for programmed death-ligand 1 (PD-L1) has a combined positive score (CPS) ≥ 10; OR
  - **ii.** The medication is used for neoadjuvant and/or adjuvant therapy; AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
- **A)** 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
- **B)** 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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4. Cervical Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
- **A)** Patient is ≥ 18 years of age; AND

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B) Patient meets ONE of the following (i or ii):
  i. Patient meets BOTH of the following (a and b):
    a) Patient has recurrent or metastatic disease; AND
    b) Patient's tumor expression for programmed death-ligand 1 (PD-L1) has a combined positive score (CPS) ≥ 1; OR
  ii. Patient has FIGO 2014 stage III to IVA disease or FIGO 2018 stage III to IVA disease; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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5. Colon, Rectal, or Appendiceal Cancer. Approve for the duration noted if the patient meets ALL of the following (A, B, C, and D):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria.
A) Patient is ≥ 18 years of age; AND
B) The disease is polymerase epsilon/delta (POLE/POLD1) mutation positive with ultra-hypermutated phenotype (tumor mutational burden > 50 mutations/megabase); AND
C) Patient meets ONE of the following (i or ii):
  i. Approve for 1 year of the patient meets ONE of the following (a or b):
    a) Patient has locally unresectable or medically inoperable disease; OR
    b) Patient has metastatic, recurrent, or progressive disease; OR
  ii. Approve for 6 months if the medication is used for neoadjuvant therapy; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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6. Cutaneous Squamous Cell Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
A) Patient is ≥ 18 years of age; AND
B) Patient has locally advanced, recurrent, or metastatic disease; AND
C) According to the prescriber, the disease is not curable by surgery or radiation; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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7. Endometrial Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):
  i. Patients has Stage III or Stage IV disease; OR
  ii. Patient has recurrent disease; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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8. Esophageal and Esophagogastric Junction Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):
  i. Patient meets BOTH of the following (a and b):
    a) Patient is medically fit and planned for esophagectomy; AND
    b) Patient's tumor expression for programmed death-ligand 1 (PD-L1) has a combined positive score (CPS) ≥ 1; OR
  ii. Patient has unresectable locally advance, recurrent, or metastatic disease AND meets ONE of the following (a or b):
    a) Patient's tumor expression for programmed death-ligand 1 (PD-L1) has a combined positive score (CPS) ≥ 1; OR
    b) Patient meets BOTH of the following [(1) and (2)]:
      (1) Patient's tumor expression for programmed death-ligand 1 (PD-L1) has a combined positive score (CPS) ≥ 10; AND
      (2) The medication is used as subsequent line therapy; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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9. Gastric Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.

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A) Patient is ≥ 18 years of age; AND
B) Patient has unresectable locally advanced, recurrent, or metastatic disease; AND
C) Patient's tumor expression for programmed death-ligand 1 (PD-L1) has a combined positive score (CPS) ≥ 1; AND
D) The medication is used in combination with chemotherapy; AND
Note: Examples of chemotherapy include cisplatin or oxaliplatin and fluorouracil or capecitabine
E) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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10. Head and Neck Squamous Cell Carcinoma. Approve for 1 year if the patients meets ALL of the following (A, B, and C):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):
i. Patient has non-nasopharyngeal disease; OR
ii. Patient meets BOTH of the following (a and b)
a) Patient has nasopharyngeal disease; AND
b) Patient has recurrent, unresectable, oligometastatic, or metastatic disease; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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11. Hepatocellular Carcinoma. Approve for 1 year if the patient meets BOTH of the following (A and B):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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12. Melanoma. Approve for the duration noted below if the patient meets ALL of the following (A, B, and C):
Note: This includes cutaneous melanoma, brain metastases due to melanoma, and uveal melanoma.
A) Patient is ≥ 12 years of age; AND
B) Patient meets ONE of the following (i or ii):
  i. Approve for 1 year if the patient meets ONE of the following (a or b):
    a) Patient has unresectable or metastatic melanoma; OR
    b) The medication will be used as adjuvant treatment; OR
  ii. Approve for 4 months if medication will be used as neoadjuvant treatment; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

13. Merkel Cell Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 12 years of age; AND
B) Patient meets ONE of the following (i, ii, iii, or iv):
  i. Patient has primary or recurrent locally advanced disease, if according to the prescriber curative surgery and curative radiation therapy are not feasible; OR
  ii. Patient has primary or recurrent regional disease, if according to the prescriber curative surgery and curative radiation therapy are not feasible; OR
  iii. Patient has in-transit disease; OR
  iv. Patient has metastatic (disseminated) disease; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

14. Mesothelioma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
A) Patient is ≥ 18 years of age; AND
B) Patient has ONE of the following (i, ii, iii, or iv):
  i. Pleural mesothelioma; OR
  ii. Peritoneal mesothelioma; OR
  iii. Pericardial mesothelioma; OR
  iv. Tunica vaginalis testis mesothelioma; AND
C) The medication is used in combination with pemetrexed and either cisplatin or carboplatin; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing: Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR

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B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa as administered subcutaneously not more frequently than once every 6 weeks.

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15. Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors. Approve for 1 year if the patient meets BOTH of the following (A and B):
Note: Examples of solid tumors with MSI-H or dMMR are adrenal gland, appendiceal neoplasms and cancers, biliary tract cancers, breast cancer, cervical cancer, chondrosarcoma, colon or rectal cancer, endometrial carcinoma, esophageal or esophagogastric cancers, Ewing sarcoma, gallbladder carcinoma, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, occult primary (cancer of unknown primary), osteosarcoma, ovarian/fallopian tube/primary peritoneal, pancreatic adenocarcinoma, penile cancer, neuroendocrine tumor, prostate cancer, small bowel adenocarcinoma, vaginal cancer, vulvar cancer.
A) Patient is ≥ 12 years of age; AND
B) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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16. Non-Small Cell Lung Cancer – Neoadjuvant and Adjuvant. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
A) Patient is ≥ 18 years of age; AND
B) The tumor is negative for the following actionable biomarkers: epidermal growth factor receptor (*EGFR*) exon 19 deletion or exon 21 L858R, anaplastic lymphoma kinase (*ALK*), *RET*, and *ROS1*; AND
C) Patient has resectable or completely resected Stage IB, Stage II, or Stage III disease; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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17. Non-Small Cell Lung Cancer – Recurrent, Advanced, or Metastatic Disease. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) The tumor is negative for the following actionable biomarkers: epidermal growth factor receptor *(EGFR)* exon 19 deletion or exon 21 L858R, anaplastic lymphoma kinase *(ALK)*, *RET*, and *ROS1*; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR

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B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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18. Ovarian/Fallopian Tube/Peritoneal Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) Patient has platinum-resistant, persistent, or recurrent disease; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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19. Renal Cell Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):
  i. The tumor has clear cell histology and meets ONE of the following (a or b):
    a) Patient meets BOTH of the following [(1) and (2)]:
      (1) The medication is used as adjuvant therapy; AND
      (2) Patient had a nephrectomy; OR
    b) Patient has relapsed or Stage IV disease and the medication is used in combination with Inlyta (axitinib tablets) or Lenvima (lenvatinib capsules); OR
  ii. Patient has relapsed or Stage IV non-clear cell histology; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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20. Tumor Mutational Burden-High (TMB-H) Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
Note: Examples of solid tumors are adrenal cancer, ampullary adenocarcinoma, breast cancer, cervical cancer, cholangiocarcinoma (intrahepatic and extrahepatic), chondrosarcoma, chordoma, endometrial carcinoma, esophageal carcinoma, esophagogastric junction carcinoma, Ewing sarcoma, gallbladder cancer, gastric cancer, head and neck cancer, neuroendocrine cancer, osteosarcoma, ovarian/fallopian tube/primary peritoneal carcinoma, pancreatic adenocarcinoma, penile cancer, primary occult, prostate cancer, salivary gland tumors, thyroid cancer, uterine sarcoma, vaginal cancer, vulvar cancer.
A) Patient is ≥ 12 years of age; AND
B) Patient is not a surgical candidate or has unresectable or metastatic tumor mutational burden-high (≥ 10 mutations/megabase) solid tumor; AND

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C) Patient has progressed on prior therapy; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

Other Uses with Supportive Evidence

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21. Adrenal Gland Tumor. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) Patient has unresectable or metastatic adrenocortical carcinoma; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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22. Anal Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
A) Patient is ≥ 18 years of age; AND
B) Patient has locally recurrent, metastatic, or progressive disease; AND
C) Patient meets ONE of the following (i, ii, or iii):
i. The medication is administered before proceeding to abdominoperineal resection; OR
ii. The medication is used for subsequent therapy; OR
iii. The medication is used in combination with chemotherapy; AND
Note: Examples of chemotherapy include carboplatin and paclitaxel.
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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23. Bone Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 12 years of age; AND
B) Patient has ONE of the following conditions (i, ii, or iii):

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i. Chondrosarcoma; OR
ii. Chordoma; OR
iii. Osteosarcoma; OR

C) Patient has unresectable or metastatic disease; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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24. Gestational Trophoblastic Neoplasia. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient has multi-agent chemotherapy resistant disease; AND
Note: Examples of chemotherapy regimens contain etoposide, cisplatin/carboplatin, paclitaxel, bleomycin, ifosfamide, methotrexate.
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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25. Histiocytic Neoplasms. Approve for 1 year if the patient meets BOTH of the following (A and B):
A) Patient has ONE of the following (i or ii):
i. Patient has malignant histiocytic neoplasms; OR
ii. Patient has relapsed or refractory disease; AND
B) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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26. Pediatric Diffuse High-Grade Glioma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
A) Patient is ≥ 12 years of age; AND
B) Patient has a hypermutant tumor; AND
C) Patient meets ONE of the following (i or ii):
i. The medication is used for adjuvant treatment; OR:
ii. The medication is used for recurrent or progressive disease; AND
D) The medication is prescribed by or in consultation with an oncologist.

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Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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27. Penile Cancer: Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) Patient has recurrent or metastatic disease; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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28. Small Bowel Adenocarcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) The disease is polymerase epsilon/delta 1 (POLE/POLD1) mutation positive with ultra-hypermutated phenotype (tumor mutation burden > 50 mutations/megabase); AND
C) Patients meets ONE of the following (i or ii):
  i. Patient has advanced or metastatic disease; OR
  ii. The medication is used as neoadjuvant therapy for resectable disease; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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29. Small Cell Lung Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) The medication is used as subsequent therapy; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR

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B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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30. Soft Tissue Sarcoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) Patient has ONE of the following (i, ii, iii, iv, v, vi, or vii):
i. Alveolar soft part sarcoma; OR
ii. Myxofibrosarcoma; OR
iii. Undifferentiated pleomorphic sarcoma; OR
iv. Dedifferentiated liposarcoma; OR
v. Cutaneous angiosarcoma; OR
vi. Undifferentiated sarcoma; OR
vii. Rhabdomyosarcoma; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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31. Thymic Carcinoma. Approve for 1 year if the patient meets BOTH of the following (A and B):
A) Patient is ≥ 18 years of age; AND
B) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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32. Thyroid Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) Patient has progressive, symptomatic, or metastatic disease; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
C) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
D) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

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33. Vaginal Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) Patient has recurrent or metastatic disease; AND
C) Patient has programmed death-ligand 1 (PD-L1) positive disease (combined positive score [CPS] ≥ 1); AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

34. Vulvar Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
Note: If the tumor is MSI-H or dMMR, see Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors criteria. If the tumor is mutational burden-high, see Tumor Mutational Burden-High (TMB-H) Cancer criteria.
A) Patient is ≥ 18 years of age; AND
B) Patient has advanced, recurrent, or metastatic disease; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 3 weeks; OR
B) 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa administered subcutaneously not more frequently than once every 6 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Keytruda Qlex is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	09/24/2025
Selected Revision	**Mesothelioma:** Removed the requirement that the patient has unresectable or advanced malignant pleural disease. Added that the patient has one of the following: pleural mesothelioma, peritoneal mesothelioma, pericardial mesothelioma, and tunica vaginalis testis mesothelioma as approval options. **Thymic Carcinoma:** Added as new condition of approval.	10/08/2025
Selected Revision	**Cervical Cancer:** The option that the patient has locally advanced FIGO 2014 stage III to IVA disease was modified to the patient has FIGO 2014 stage III to IVA disease or FIGO 2018 Stage III to IVA disease. **Endometrial Carcinoma:** The medication is used for primary or adjuvant therapy, in combination with carboplatin and paclitaxel, or as a single agent for maintenance therapy was added as an option for approval. Added the medication is used as a single agent for maintenance therapy as an approval option when the patient has recurrent disease. **Melanoma:** The approval duration was modified to approval up to 1 year (total) of treatment if the patient is ≥ 12 years of age and the medication will be used as adjuvant treatment. Added approve for 4 months of treatment if the patient is ≥ 18 years of age and the medication is used as neoadjuvant treatment as new option for approval. **Merkel Cell Carcinoma:** Removed the requirement that the patient has recurrent locally advanced or metastatic disease. Added requirement that the patients meets one of the following: patient has primary or recurrent locally advanced disease, if according to the prescriber curative surgery and curative radiation therapy are not feasible; or patient has primary or recurrent regional disease, if according to the prescriber curative surgery and curative radiation therapy are not feasible; or patient has metastatic (disseminated) disease. **Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors:** The note was modified to include appendiceal neoplasms and cancers and vaginal cancer. **Non-Small Cell Lung Cancer – Neoadjuvant and Adjuvant:** The tumor is negative for the following actionable biomarkers: epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R, anaplastic lymphoma kinase (ALK), RET, and ROS1 was added as a requirement of approval. The patient has resectable stage IB to III disease was modified to the patient has resectable or completely resected stage IB to III disease. **Non-Small Cell Lung Cancer – Recurrent, Advanced, or Metastatic Disease:** The tumor is negative for the following actionable biomarkers: epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R, anaplastic lymphoma kinase (ALK), RET, and ROS1 was added as a requirement of approval. The requirement that the patient meets one of the following: patient has squamous cell disease, and the medication is used in combination with chemotherapy; patient has no EGFR or ALK genomic tumor aberrations and the medication is used in combination with chemotherapy; or the tumor is PD-L1 positive, with tumor proportion score (TPS) ≥ 1%, as determined by an approved test was removed. Added the option of approval that the medication is used as first-line therapy and the tumor is positive for one of the following:	11/19/2025

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	EGFR exon 20 mutations, ERBB2 (HER2) mutations, or NRG1 gene fusion. The medication is used for first-line or subsequent therapy and the tumor is positive for one of the following: BRAF V600E mutation, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation was added as an option for approval. Added the optional of approval that the medication is used as subsequent therapy and meets one of the following: tumor is EGFR S768I, L861Q, and/or G719X mutation positive or the medication is used as a single-agent and meets BOTH of the following: the tumor is PD-L1 positive, with tumor proportion score (TPS) ≥ 1% and the patient has not progressed on prior therapy with a programmed death receptor-1 (PD-1)/PD-L1 inhibitor; a Note was added listing previous therapy with either one of Keytruda (pembrolizumab intravenous infusion), Keytruda Qlex, Opdivo (nivolumab intravenous infusion), Opdivo Qvantig (nivolumab and hyaluronidase-nvhy subcutaneous injection), Libtayo (cemiplimab-rwlc intravenous infusion), Imfinzi (durvalumab intravenous infusion), or Tecentriq (atezolizumab intravenous infusion). Added the option of approval that medication is used as first-line or continuation maintenance therapy and the tumor no actionable mutations; a Note was added listing the following actionable mutations: EFGR exon 19 deletion, EFGR exon 21 L858R, EFGR S768I, EGFR L861Q, EGFR G719X, EGFR exon 20 insertion, ALK rearrangement, ROS1 rearrangement, BRAF V600E, NTRK 1/2/3 gene fusion, METex14 skipping, RET rearrangement, ERBB2 (HER2), and NRG1 gene fusion. **Tumor Mutational Burden-High (TMB-H) Cancer:** The Note was modified to include vaginal cancer. **Urothelial Carcinoma:** Added patient has tried at least one platinum-based chemotherapy and the Note: cisplatin and carboplatin are platinum-based chemotherapy as new option for approval. Added according to the prescriber, patient is not eligible for platinum-based chemotherapy and the Note this is regardless of PD-L1 status. Cisplatin and carboplatin are platinum-based chemotherapy as an approval option. Added as an option for approval that the medication is used as adjuvant therapy." **Appendiceal Cancers:** Added as new condition of approval. **Gestational Trophoblastic Neoplasia:** Added as a new condition of approval. **Penile Cancer:** Added as a new condition of approval. **Vaginal Cancers:** Added as new condition of approval. **Vulvar Cancers:** Added as new condition of approval. **Breast Cancer, Cervical Cancer, Esophageal Cancer, Gastric Cancer, and Head and Neck Squamous Cell Carcinoma:** For all of these conditions of approval, the descriptor as determined by an approved test was removed from the approval option that the patient's tumor expression for programmed death-ligand 1 (PD-L1) has a combined positive score (CPS) ≥ 1.	
Early Annual Revision	**Endometrial Carcinoma:** The option of approval that the medications is used for primary or adjuvant therapy and is used in combination with cisplatin and carboplatin or as a single agent for maintenance therapy was removed. When the patient has recurrent disease, the options of approval that the medication is used in combination with Lenvima (lenvatinib capsules); carboplatin and paclitaxel; or as a single agent for maintenance therapy were removed. The option of approval that the patient has Stage III or Stage IV disease was added. **Esophageal and Esophagogastric Junction Cancer:** patient medically fit and planned for esophagectomy; has tumor expression for programmed death-ligand 1 (PD-L1) has a combined positive score (CPS) ≥ 1; and the medication is used in combination with chemotherapy was added. The option that the medication is used as second-line or subsequent therapy was modified to the medication is used as subsequent therapy. The wording "as determined by an approved test" was removed from the requirement that tumor expression for PD-L1 has a CPS ≥ 1. The option that according to the prescriber, the patient is not a candidate for surgical resection or definitive chemoradiation was modified to according to the prescriber, the patient is not a surgical candidate. The requirement that the medication is used for first-line therapy was added to the patient's tumor expression for PD-L1 CPS ≥ 1. When the medication is used as subsequent therapy and the tumor expression for PD-L1 has a CPS ≥ 10, the requirement was added that the patient has unresectable locally advanced, recurrent, or metastatic disease. **Gastric Cancer:** Options of approval that according to the prescriber, the patient is medically fit for surgery with unresectable disease, or according to the prescriber the patient us not a surgical candidate were added. **Head and Neck Squamous Cell Carcinoma:** The requirement that the patient has recurrent, persistent, unresectable or metastatic disease was removed. The requirement	02/18/2026

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	that the patient meets One of the following: if the medication is used in first line treatment and the medication is used in combination with chemotherapy or as a single agent for PD-L1 positive tumors; OR the medication is used as subsequent therapy was removed. The requirement that the patient meets ONE of the following: The patient has non-nasopharyngeal disease or the patient has nasopharyngeal disease and has recurrent, unresectable, oligometastatic, or metastatic disease was added. **Merkel Cell Carcinoma:** In-transit regional disease was added as an option for approval. **Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors:** Testicular cancer was removed for the Note of examples of solid tumors. The requirement that the patient is ≥ 12 years of age was added. **Non-Small Cell Lung Cancer – Neoadjuvant and Adjuvant:** The requirement that the patient has resectable or completely resected stage IB to III disease was modified to the patient has resectable or completely resected Stage IB, Stage II, or Stage III disease. **Ovarian/Fallopian Tube/Peritoneal Cancer:** This was added as a new condition of approval. **Tumor Mutational Burden-High (TMB-H) Cancer:** Testicular cancer was removed for the Note of examples of solid tumors. **Anal Carcinoma:** This was added as a new condition of approval. **Bone Cancer:** This was added as a new condition of approval. **Gestational Trophoblastic Neoplasia:** The requirement that the medication is used as a single agent was removed. **Pediatric Diffuse High-Grade Glioma:** This was added as a new condition of approval **Penile Cancer:** The requirement that the patient meets one of the following: the medication is used in combination with fluorouracil and either cisplatin or carboplatin; or the medication is used as single agent for maintenance therapy was removed. **Small Bowel Adenocarcinoma**: This was added as a new condition of approval. **Soft Tissue Sarcoma:** This was added as a new condition of approval.	
Selected Revision	**Breast Cancer:** The requirement that the patient has triple-negative breast cancer was modified to the patient has triple-negative disease. The same change was made in the corresponding Note. The option that the medication is used in combination with chemotherapy was removed. The option that the patient has locally recurrent unresectable or metastatic disease was modified to the patient has recurrent unresectable (local or regional) or Stage IV disease. **Renal Cell Carcinoma:** The tumor has clear cell histology was added as an option of approval. The option that the patient has advanced disease was modified to the patient has relapsed or Stage IV disease. When the medication is used as adjuvant therapy, the patient had a nephrectomy was added as an option of approval. The patient has relapsed or Stage IV non-clear cell histology was added as an option of approval.	07/01/2026
Early Annual Revision	**Biliary Tract Cancer:** Changed duration of approval from 1 year to for duration noted. The requirement that the patient has locally advanced unresectable or metastatic disease was removed. The requirement that the medication is used in combination with cisplatin and gemcitabine was modified to medication is used in combination with cisplatin or carboplatin and gemcitabine. Added option for approval for 1 year for patients with unresectable, resected gross residual, or metastatic disease and medication is used in combination with cisplatin and gemcitabine. Added option for approval for 6 months if patient has resectable locoregionally advanced gall bladder cancer and the medication is used as neoadjuvant therapy. **Bladder Cancer:** This condition was changed to as listed. Previously listed as Urothelial Carcinoma. The option that the patient has tried at least one platinum-based chemotherapy was modified to the medication is used as subsequent therapy. The corresponding Note with examples of platinum-based chemotherapies was removed. The option that according to the prescriber, the patient is not eligible for platinum-based chemotherapy and the corresponding Note was removed. The option that the medication is used as adjuvant therapy was modified to the medication is used as neoadjuvant or adjuvant therapy. **Cervical Cancer:** The option that the patient has persistent, recurrent, or metastatic disease was modified to the patient has recurrent or metastatic disease. **Colon, Rectal, or Appendiceal Cancer:** This condition was changed to as listed. Previously listed as Appendiceal Cancer. Changed duration of approval from 1 year to for duration noted. An option was added to approve for 1 year if: the patient has locally unresectable or medically inoperable disease OR the patient has metastatic, recurrent, or	09/09/2026

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	progressive disease. An option was added to approve for 6 months if the medication is used for neoadjuvant therapy. **Esophageal and Esophagogastric Junction Cancer:** For patients who are medically fit and planned for esophagectomy, the option of approval that the medication is used in combination with chemotherapy and the corresponding Note was removed. For patients who have unresectable locally advanced, recurrent, or metastatic disease, the options for approval that according to the prescriber, the patient is not a surgical candidate; the medication is sued for first-line therapy; and the medication is used in combination with chemotherapy and the corresponding Note were removed. **Gastric Cancer:** The options for approval that according to the prescriber, the patient is medically fit for surgery with unresectable disease or according to the prescriber, the patient is not a surgical candidate were removed. The Note with examples of chemotherapy was modified to examples of chemotherapy include cisplatin or oxaliplatin and fluorouracil or capecitabine. Previously trastuzumab was included in the Note. **Hepatocellular Carcinoma:** The requirements that the disease is secondary to hepatitis B and the medication is used as subsequent-line therapy were removed. **Melanoma:** The age requirements were changed to the patient is ≥ 12 years of age for all options of approval. Previously, patients were required to be ≥ 18 years of age if they had unresectable or metastatic disease or if the medication was used as neoadjuvant treatment. When the medication is used as adjuvant treatment the approval duration was modified to 1 year. Previously approved for up to 1 year (total). **Mesothelioma:** The requirement that the medication is used as first-line therapy was removed. **Non-Small Cell Lung Cancer – Neoadjuvant and Adjuvant:** The duration of approval was modified to approve for 1 year for all conditions. The option to approve for 4 months if the medication is used as neoadjuvant therapy in combination with platinum chemotherapy and the corresponding Note was removed. The option to approve for 1 year (total) if the patient has received adjuvant chemotherapy OR neoadjuvant treatment was removed. **Non-Small Cell Lung Cancer – Recurrent, Advanced, or Metastatic Disease:** The option that the medication is used as first-line therapy and the tumor is positive for ONE of the following mutations: EGFR exon 20 mutation; ERBB2 (HER2) mutation; or NRG1 gene fusion was removed. The option that the medication is used as first-line or subsequent therapy and the tumor is positive for ONE of the following mutations: BRAF V600E mutation; NTRK1/2/3 gene fusion; or MET exon 14 skipping mutation was removed. The options that the medication is used as subsequent therapy and meets ONE of the following: the tumor is EGFR S768I, L861Q, and/or G719X mutation positive; OR the medication us used as single-agent and the tumor is PD-L1 positive, with tumor proportion score (TPS) ≥ 1%; AND the patient has not progressed on prior therapy with a programmed death receptor-1 (PD-1)/PD-L1 inhibitor along with the corresponding Note were removed. The option that the medication is used as first-line or continuation maintenance therapy and has the tumor has no actionable mutations along with the corresponding Note was removed. **Adrenal Gland Tumor:** This was added as a new condition of approval under "Other Uses with Supportive Evidence." **Histiocytic Neoplasms:** This was added as a new condition of approval under "Other Uses with Supportive Evidence." **Pediatric Diffuse High-Grade Glioma:** The requirement that the patient is < 18 years of age was modified to the patient is ≥ 12 years of age. The requirement that the tumor is hypermutant was modified to the patient has a hypermutant tumor. **Small Bowel Adenocarcinoma:** The option that the patient has locally unresectable, medically inoperable, advanced, or metastatic disease was modified to the patient has advanced or metastatic disease. **Small Cell Lung Cancer:** This was added as a new condition of approval under "Other Uses with Supportive Evidence." **Thyroid Carcinoma:** This was added as a new condition of approval under "Other Uses with Supportive Evidence."	

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