GOLD COAST HEALTH PLAN TOTAL Care ADVANTAGE℠

TOTAL CARE ADVANTAGE PART B CLINICAL GUIDELINES

KEYTRUDA QLEX™ *(pembrolizumab and berahyaluronidase alfa-pmph)* subcutaneous injection

PLEASE NOTE: Standard KEYTRUDA™ (pembrolizumab) IV infusion does NOT require a Prior Authorization.

PA Criteria	Criteria Details
Description	KEYTRUDA QLEX is a combination of pembrolizumab, a programmed death receptor-1 (PD-1)-blocking antibody, and berahyaluronidase alfa, an endoglycosidase.
Covered Uses (FDA approved indication)	KEYTRUDA QLEX is indicated for the treatment of: a. **Melanoma:** adult patients with unresectable or metastatic melanoma; the adjuvant treatment of adult and pediatric patients 12 years and older with Stage IIB, IIC or III melanoma following complete resection. b. **Non-Small Cell Lung Cancer (NSCLC)** i. in combination with pemetrexed and platinum chemotherapy, as first-line treatment of adult patients with metastatic non-squamous NSCLC, with no EGFR or ALK genomic tumor aberrations ii. in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, as first-line treatment of adult patients with metastatic squamous NSCLC iii. as a single agent for the first-line treatment of adult 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: 1. Stage III where patients are not candidates for surgical resection or definitive chemoradiation, or 2. metastatic iv. as a single agent for the treatment of adult 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 QLEX v. for the treatment of adult patients with resectable (tumors ≥4 cm or node positive) NSCLC in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery vi. as a single agent, for adjuvant treatment following resection and platinum-based chemotherapy for adult patients with Stage IB (T2a ≥4 cm), II, or IIIA NSCLC c. **Malignant Pleural Mesothelioma (MPM):** in combination with pemetrexed and platinum chemotherapy, as first-line treatment of adult patients with unresectable advanced or metastatic MPM. d. **Head and Neck Squamous Cell Cancer (HNSCC)** i. for the treatment of adult patients with resectable locally advanced HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test, as a single agent as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy (RT) with or without cisplatin and then as a single agent. ii. in combination with platinum and FU for the first-line treatment of adult patients with metastatic or with unresectable, recurrent HNSCC. iii. as a single agent for the first-line treatment of adult 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. iv. as a single agent for the treatment of adult patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

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e. **Urothelial Cancer**
   i. in combination with enfortumab vedotin, for the treatment of adult patients with locally advanced or metastatic urothelial cancer.
   ii. as a single agent for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who:
      1. are not eligible for any platinum-containing chemotherapy, or
      2. who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
   iii. in combination with enfortumab vedotin, as neoadjuvant treatment and then continued after cystectomy as adjuvant treatment of adult patients with muscle invasive bladder cancer (MIBC) who are ineligible for cisplatin-containing chemotherapy.
   iv. as a single agent for the treatment of adult 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

f. **Microsatellite Instability-High or Mismatch Repair Deficient Cancer:** for the treatment of adult and pediatric patients 12 years of age and older with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.

g. **Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer (CRC):** for the treatment of adult patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC) as determined by an FDA-approved test

h. **Gastric Cancer**
   i. in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.
   ii. 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 gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.

i. **Esophageal Cancer**
   i. for the treatment of adult 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:
      1. in combination with platinum- and fluoropyrimidine-based chemotherapy for patients whose tumors express PD-L1 (CPS ≥1), or
      2. as a single agent after one or more prior lines of systemic therapy for patients with tumors of squamous cell histology that express PD-L1 (CPS ≥10) as determined by an FDA-approved test.

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

k. **Hepatocellular Carcinoma (HCC):** for the treatment of adult patients with HCC secondary to hepatitis B who have received prior systemic therapy other than a PD-1/PD-L1-containing regimen.

l. **Biliary Tract Cancer (BTC):** in combination with gemcitabine and cisplatin, for the treatment of adult patients with locally advanced unresectable or metastatic biliary tract cancer.

m. **Merkel Cell Carcinoma (MCC):** for the treatment of adult and pediatric patients 12 years and older with recurrent locally advanced or metastatic Merkel cell carcinoma.

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

o. **Endometrial Carcinoma**
   i. in combination with carboplatin and paclitaxel, followed by KEYTRUDA QLEX as a single agent, for the treatment of adult patients with primary advanced or recurrent endometrial carcinoma.
   ii. in combination with lenvatinib, for the treatment of adult patients with advanced endometrial carcinoma that is mismatch repair proficient (pMMR) or not MSI-H 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
   iii. as a single agent, for the treatment of adult 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.

p. **Tumor Mutational Burden-High (TMB-H) Cancer**
   i. for the treatment of adult and pediatric patients 12 years of age and older 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.
      1. *Limitations of Use:* The safety and effectiveness of KEYTRUDA QLEX in pediatric patients 12 years and older with TMB-H central nervous system cancers have not been established

q. **Cutaneous Squamous Cell Carcinoma (cSCC):** for the treatment of adult patients with recurrent or metastatic cSCC or locally advanced cSCC that is not curable by surgery or radiation.

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	r. **Triple-Negative Breast Cancer (TNBC)** i. for the treatment of adult 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. in combination with chemotherapy, for the treatment of adult patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10) as determined by an FDA approved test
Dosing and Administration	**Dosing Regimen** KEYTRUDA QLEX is for subcutaneous use (inject into thigh or abdomen only). KEYTRUDA QLEX must be administered by a healthcare provider. The recommended dose for adults and pediatric patients 12 years of age and older who weigh greater than 40 kg is: • **Every three-week dosing** (395 mg/4,800 units): Inject 2.4 mL subcutaneously in the abdomen or thigh over one minute. • **Every six-week dosing** (790 mg/9,600 units): Inject 4.8 mL subcutaneously in the abdomen or thigh over two minutes. For RCC, administer KEYTRUDA QLEX as a single agent in the adjuvant setting, or in the advanced setting with either: axitinib 5 mg orally twice daily or lenvatinib 20 mg orally once daily. For Endometrial Carcinoma, administer KEYTRUDA QLEX: • in combination with carboplatin and paclitaxel regardless of MMR or MSI status, or • in combination with lenvatinib 20 mg orally once daily for pMMR or not MSI-H tumors, or • as a single agent for MSI-H or dMMR tumors.
Billing and Coding Information	

	10-digit NDC	11-digit NDC
395 mg pembrolizumab + 4800 units berahyaluronidase alfa	0006-3083-01	00006-3083-01
790 mg pembrolizumab + 9600 units berahyaluronidase alfa	0006-5083-01	00006-5083-01

HCPCS Code	Description
C9399	Unclassified drugs or biologicals
J9999	Not otherwise classified, antineoplastic drug

CPT Procedural Codes	Description
96401	Chemotherapy, anti-neoplastic subcutaneous/IM injection

Product Availability	Single-dose vial • 395 mg pembrolizumab and 4,800 units berahyaluronidase alfa per 2.4 mL (165 mg/2,000 units per mL) • 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa per 4.8 mL (165 mg/2,000 units per mL)

Contraindications	KEYTRUDA QLEX is contraindicated in patients with known hypersensitivity to berahyaluronidase alfa, hyaluronidase or to any of its excipients.
Recommended Medical Monitoring	KEYTRUDA QLEX is associated with: a. Immune-mediated adverse reactions b. Hypersensitivity and Administration-related reactions c. Complications of allogeneic HSCT d. Embryo-Fetal toxicity Patients should be monitored for any of these reactions. KEYTRUDA QLEX dose may be delayed, reduced or permanently discontinued based on the severity of adverse reactions. KEYTRUDA QLEX can cause fetal harm when administered to a pregnant woman. Verify pregnancy status in females of reproductive potential prior to initiating KEYTRUDA QLEX treatment. Female patients of reproductive potential should be advised to use effective contraception during treatment with KEYTRUDA QLEX and for four months after the last dose.
Approval Criteria	a. Physician administered subcutaneous injection; in-office or HOPD i. Cannot be self-administered b. FDA approved indication (see *Covered Uses*): c. Melanoma **(must meet all)**: i. Diagnosis of melanoma ii. Prescribed by or in consultation with an oncologist iii. Age ≥ 12 years iv. Member weighs > 40 kg v. Disease is Stage IIB, IIC, III, recurrent, unresectable, or metastatic vi. Prescribed as **one** of the following (a, b, or c): a. A single agent b. In combination with Lenvima® or Yervoy® c. In combination with Mekinist® and Tafinlar® for disease with BRAF V600 activating mutation vii. Request meets one of the following (a or b): a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks (for a maximum of 12 months if adjuvant treatment) b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence). d. Non-Small Cell Lung Cancer **(must meet all)**: i. Diagnosis of NSCLC ii. Prescribed by or in consultation with an oncologist iii. Age ≥ 18 years iv. **One** of the following (a or b): a. Disease is resectable or resected

	b. Disease is recurrent, advanced, or metastatic, and request meets one of the following: 1. Disease mutation status is positive for EGFR exon 20, KRAS G12C, NRTK1/2/3, BRAF V600E, MET exon 14 skipping, RET rearrangement, or ERBB2 (HER2) 2. Disease mutation status is positive for EGFR S768I, L861Q, and/or G719X, and member has received prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib 3. Disease mutation status is positive for EGFR exon 19 deletion or L858R, and member has received prior erlotinib ± (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, dacomitinib, or amivantamab-vmjw + Lazertinib 4. Disease mutation status is positive for ROS1 rearrangement, and member has received prior crizotinib, entrectinib, or repotrecitinib 5. Disease mutation status is positive for ALK rearrangement, and member has received prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib 6. Disease mutation status is negative for actionable biomarkers (EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 [HER2]) v. Keytruda or Keytruda Qlex is prescribed in **one** of the following ways: a. For PD-L1 positive disease (TPS ≥ 1%) b. In combination with a chemotherapy regimen c. In combination with a chemotherapy regimen as neoadjuvant treatment, followed by single-agent adjuvant treatment after surgery for patients with resectable (tumors ≥ 4 cm or node positive) disease d. As single-agent continuation maintenance therapy if previously given first line as part of a chemotherapy regimen e. As single-agent adjuvant treatment following resection and platinum-based chemotherapy (e.g., cisplatin, carboplatin) for adult patients with stage IB (T2a ≥ 4 cm), II, or IIIA disease vi. Member does not have contraindications to PD-1/PD-L1 inhibitor therapy (e.g., Opdivo®, Yervoy, Tecentriq®, Imfinzi®) vii. Request meets **one** of the following (a, b, or c): a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks for a maximum of duration of one of the following (i, ii, or iii): i. Adjuvant therapy: 12 months ii. Neoadjuvant, followed by adjuvant treatment: 12 weeks (neoadjuvant), then 39 weeks (adjuvant treatment) iii. All other requests: 24 months iv. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

e. Malignant Pleural Mesothelioma (MPM) **(must meet all)**:
   i. Diagnosis of MPM
   ii. Prescribed by or in consultation with an oncologist
   iii. Age ≥ 18 years
   iv. Disease is unresectable, advanced, or metastatic
   v. Keytruda or Keytruda Qlex is prescribed in combination with pemetrexed and platinum-containing chemotherapy
   vi. Request meets **one** of the following (a, b, or c):
      a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months
      b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

f. Head and Neck Squamous Cell Carcinoma **(must meet all)**:
   i. Diagnosis of HNSCC (locations include paranasal sinuses, larynx, pharynx, lip, oral cavity, salivary glands; may be occult primary – i.e., primary source unknown)
   ii. Prescribed by or in consultation with an oncologist
   iii. Age ≥ 18 years
   iv. Disease is resectable, locally advanced, unresectable, recurrent/persistent, or metastatic
   v. For unresectable, recurrent/persistent, or metastatic disease, prescribed in **one** of the following ways (a, b, c, or d):
      a. Keytruda or Keytruda Qlex: In combination with platinum-containing chemotherapy and either FU, docetaxel, or gemcitabine
      b. Keytruda or Keytruda Qlex: As a first-line single agent and the tumor expresses PD-L1 with a CPS of ≥ 1
      c. Keytruda or Keytruda Qlex: As a single agent for disease that has progressed on or after platinum-containing chemotherapy (e.g., cisplatin, carboplatin)
      d. For nasopharyngeal carcinoma, **one** of the following (a or b):
         i. Failure of Loqtorzi® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced
         ii. Request is for treatment associated with cancer for a state with regulations against step therapy in certain oncology settings
         iii. Request meets **one** of the following:
            a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months
            b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

g. Urothelial Carcinoma **(must meet all)**:
   i. Diagnosis of urothelial carcinoma
   ii. Prescribed by or in consultation with an oncologist or urologist
   iii. Age ≥ 18 years
   iv. Keytruda Qlex is prescribed in **one** of the following ways:
      a. In combination with Padcev®, Inlyta®, or Lenvima® for locally advanced, relapsed, or metastatic disease

b. As a single agent for locally advanced or metastatic disease, and member is ineligible for or has previously received platinum-containing chemotherapy (e.g., cisplatin, carboplatin) or previously received other chemotherapy
c. As a single agent for the treatment of BCG-unresponsive, high-risk, NMIBC with CIS, and member is ineligible for or has elected not to undergo cystectomy
d. As a single agent for adjuvant therapy
e. For MIBC: **Both** of the following (i and ii):
    i. In combination with Padcev® as neoadjuvant treatment and then continued after cystectomy as adjuvant treatment
    ii. Member is ineligible for cisplatin-containing chemotherapy
f. Request meets **one** of the following:
    i. Keytruda Qlex, one of the following
        1. For MIBC, both of the following (1 and 2):
            a. Neoadjuvant: Dose does not exceed 395 mg/4,800 units every three weeks for a maximum of three doses
            b. Adjuvant treatment: Dose does not exceed 395 mg/4,800 units every three weeks for a maximum of 14 doses or 790 mg/9,600 units every six weeks for maximum of seven doses
        2. All other indications: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months
    ii. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence)

h. Microsatellite Instability-High/Mismatch Repair Deficient Cancer **(must meet all)**:
    i. Diagnosis of a solid tumor classified as MSI-H or dMMR (indicative of MMR gene mutation or loss of expression
    ii. Prescribed by or in consultation with an oncologist
    iii. Member meets **both** of the following:
        a. Age ≥ 12 years
        b. Weight > 40 kg
    iv. Keytruda or Keytruda Qlex is prescribed in one of the following ways:
        a. As first-line or subsequent therapy for ampullary adenocarcinoma, CRC, gallbladder cancer, gastric cancer, GEJ cancer, intrahepatic/extrahepatic cholangiocarcinoma, non-nasopharyngeal head, and neck cancer, occult primary tumor, pancreatic adenocarcinoma, or small bowel adenocarcinoma
        b. As subsequent therapy for other solid tumors
    v. Prescribed in one of the following ways:
        a. As a single agent
        b. For gastric or GEJ cancers: as a single agent or in combination with platinum- and fluoropyrimidine-based chemotherapy
    vi. Request meets **one** of the following:
        a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months
        b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

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i. Gastric Cancer, Esophageal Cancer, or Gastroesophageal Junction Cancer **(must meet all)**:
   i. Diagnosis of gastric cancer, esophageal cancer, or GEJ cancer
   ii. Prescribed by or in consultation with an oncologist
   iii. Age ≥ 18 years
   iv. **One** of the following:
      a. Disease is unresectable, locally advanced, recurrent, or metastatic
      b. Member is planned for esophagectomy
   v. Member meets **one** of the following:
      a. Keytruda or Keytruda Qlex is prescribed in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, and **both** (i and ii):
         i. HER2-positive gastric or GEJ adenocarcinoma
         ii. Tumor expresses PD-L1 (CPS ≥ 1)
      b. **Both** of the following (i and ii):
         i. Keytruda or Keytruda Qlex is prescribed in combination with platinum- and fluoropyrimidine-based chemotherapy, and **both** (1 and 2):
            1. One of the following (a or b):
               a. HER2-negative gastric or GEJ adenocarcinoma
               b. Esophageal carcinoma or GEJ squamous cell carcinoma
            2. Tumor expresses PD-L1 (CPS ≥ 1)
         ii. **One** of the following (1 or 2):
            1. Failure of Tevimbra® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced
            2. Request is for treatment associated with cancer for a state with regulations against step therapy in certain oncology settings
      c. Keytruda or Keytruda Qlex is prescribed as a single agent after one or more prior lines of systemic therapy for members with tumors of squamous cell GEJ that express PD-L1 (CPS ≥ 10)
      d. Request meets **one** of the following:
         i. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months
         ii. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

j. Cervical Cancer **(must meet all)**:
   i. Diagnosis of cervical cancer
   ii. Prescribed by or in consultation with an oncologist
   iii. Age ≥ 18 years
   iv. Prescribed in **one** of the following ways:
      a. As a single agent, and **all** of the following:
         i. Tumor expresses PD-L1 (CPS ≥ 1)
         ii. Disease is recurrent or metastatic
         iii. Disease has progressed on or after ≥ 1 line of systemic therapy

b. In combination with chemotherapy (e.g., paclitaxel/cisplatin, paclitaxel/carboplatin) with or without bevacizumab, and **both** (i and ii):
   i. Tumor expresses PD-L1 (CPS ≥ 1)
   ii. Disease is persistent, recurrent, or metastatic
c. In combination with Tivdak®, and **all** of the following (i, ii, and iii):
   i. Tumor expresses PD-L1 (CPS ≥ 1) and has not received prior immune-oncology therapy
   ii. Disease is recurrent or metastatic
   iii. Disease has progressed on or after ≥ 1 line of systemic therapy
d. In combination with CRT, and disease is FIGO 2014 Stage III-IVA or FIGO 2018 stage III-IVA
e. Request meets **one** of the following:
   i. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months
   ii. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

k. Hepatocellular Carcinoma **(must meet all)**:
   i. Diagnosis of HCC
   ii. Prescribed by or in consultation with an oncologist
   iii. Age ≥ 18 years
   iv. **One** of the following (a or b):
      a. Prescribed as subsequent-line systemic therapy and member has not previously been treated with immune checkpoint inhibitor therapy (PD-L1/PD-1, e.g., Tecentriq, Opdivo);
      b. Prescribed as first line treatment
   v. Prescribed as a single agent
   vi. Request meets **one** of the following:
      a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months
      b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

l. Biliary Tract Cancer **(must meet all)**:
   i. Diagnosis of BTC
   ii. Prescribed by or in consultation with an oncologist
   iii. Age ≥ 18 years
   iv. **One** of the following (a or b):
      a. Disease is locally advanced unresectable or resected gross residual (R2) disease, or metastatic
      b. Disease is resectable locoregionally advanced and prescribed as neoadjuvant therapy for gallbladder cancer
   v. Prescribed in combination with gemcitabine and cisplatin

	vi. Request meets **one** of the following: a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence). m. Merkel Cell Carcinoma **(must meet all)**: i. Diagnosis of MCC ii. Prescribed by or in consultation with an oncologist iii. Member meets **both** of the following (a and b): a. Age ≥ 12 years b. Weight > 40 kg iv. Disease is recurrent, locally advanced, or metastatic v. Prescribed as a single agent vi. Request meets **one** of the following: a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence). n. Renal Cell Carcinoma **(must meet all)**: i. Diagnosis of RCC ii. Prescribed by or in consultation with an oncologist iii. Age ≥ 18 years iv. Prescribed in **one** of the following ways (a or b): a. Keytruda or Keytruda Qlex: In combination with Inlyta or Lenvima*, and disease is advanced (i.e., relapsed or stage IV) b. Keytruda or Keytruda Qlex: As single-agent adjuvant treatment, and member is at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions v. Request meets **one** of the following: a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months (combination therapy) or 12 months (monotherapy) b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence). o. Endometrial Carcinoma (must meet all): i. Diagnosis of endometrial carcinoma ii. Prescribed by or in consultation with an oncologist iii. Age ≥ 18 years

	iv. Prescribed in **one** of the following (a or b): a. In combination with Lenvima and **both** of the following (i and ii): i. Disease is pMMR or not MSI-H ii. Progressed following prior systemic therapy (e.g., carboplatin/paclitaxel) b. In combination with carboplatin and paclitaxel and continued as a single agent for maintenance therapy for advanced, recurrent, or Stage III-IV disease v. Request meets **one** of the following: a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence) p. Tumor Mutational Burden-High Cancer **(must meet all)**: i. Diagnosis of a solid tumor classified as TMB-H (i.e., ≥ 10 mutations/megabase [mut/Mb]) ii. Prescribed by or in consultation with an oncologist iii. Member meets **both** of the following (a and b): a. Age ≥ 12 years b. Weight > 40 kg iv. Disease is unresectable or metastatic v. **One** of the following (a or b): a. Disease has progressed following prior treatment b. Prescribed as a first-line therapy for ampullary adenocarcinoma or pancreatic adenocarcinoma vi. Prescribed as a single agent vii. Request meets **one** of the following: a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence) q. Cutaneous Squamous Cell Carcinoma **(must meet all)**: i. Diagnosis of cSCC ii. Prescribed by or in consultation with an oncologist iii. Age ≥ 18 years iv. Member is not a candidate for curative surgery or radiation v. Prescribed as a single agent vi. Request meets **one** of the following: a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of 24 months b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

	r. Triple Negative Breast Cancer **(must meet all)**: i. Diagnosis of TNBC (i.e., estrogen receptor/progesterone receptor [ER/PR] negative and human epidermal growth factor receptor 2 [HER2]-negative) ii. Prescribed by or in consultation with an oncologist iii. Age ≥ 18 years iv. **One** of the following (a, b, or c): a. Disease is high-risk early-stage and prescribed in combination with chemotherapy (e.g., carboplatin, paclitaxel, doxorubicin, cyclophosphamide) as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery b. Disease is locally recurrent unresectable or metastatic, and **both** of the following (i and ii): i. Tumor expresses PD-L1 (CPS ≥ 10) ii. Prescribed in combination with chemotherapy (e.g., paclitaxel, paclitaxel protein-bound, gemcitabine and carboplatin) c. Prescribed as preoperative systemic therapy in combination with carboplatin and docetaxel v. Request meets **one** of the following: a. Keytruda Qlex: Dose does not exceed 395 mg/4,800 units every three weeks or 790 mg/9,600 units every six weeks for a maximum of (i or ii): i. High-risk, early-stage TNBC: 24 weeks as neoadjuvant therapy and 27 weeks as adjuvant therapy ii. Locally recurrent unresectable or metastatic TNBC: 24 months b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence). ***Exclusions*** i. GCHP considers members with any of the following exclusions NOT eligible for Keytruda Qlex: a. Pediatric member 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.
Age Restriction	Dependent on indication; see Clinical Criteria
Coverage Duration	**Initial**: six months. **Reauthorization**: 12 months. Dose will be approved according to the FDA approved labeling or within accepted standards of medical practice.
Other Criteria (LCD, NCD, etc.)	Must follow LCD L37205 – Chemotherapy Drugs and their Adjuncts
Misc Info, Appendix Etc.	None.

STATUS	DATE REVISED	REVIEW DATE	APPROVED/REVIEWED BY	EFFECTIVE DATE
Created	1/16/26	1/16/26	Tamara Chinarian, PharmD, Clinical Pharmacist	N/A
Approved	N/A	2/12/26	Pharmacy & Therapeutics (P&T) Committee	2/12/26