Mass General Brigham
Health Plan

Oncology Immunotherapies
Keytruda (pembrolizumab)
Effective 01/06/2025

Plan	☒ MassHealth UPPL ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☐ Pharmacy Benefit ☒ Medical Benefit		
Specialty Limitations	N/A		
Contact Information	**Medical and Specialty Medications** All Plans | Phone: 877-519-1908 | Fax: 855-540-3693		
	Non-Specialty Medications All Plans | Phone: 800-711-4555 | Fax: 844-403-1029		
Exceptions	N/A		

Overview

Keytruda (pembrolizumab) is indicated for the following indications:

- Melanoma
  - treatment of patients with unresectable or metastatic melanoma
  - adjuvant treatment of adult and pediatric (12 years and older) patients with Stage IIB, IIC, or III melanoma following complete resection
- Non-Small Cell Lung Cancer
- Malignant Pleural Mesothelioma
- Head and Neck Squamous Cell Cancer
- Classical Hodgkin Lymphoma
- Primary Mediastinal Large B-Cell Lymphoma
- Urothelial Cancer
- Microsatellite Instability-High or Mismatch Repair Deficient Cancer
- Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer
- Gastric Cancer
- Esophageal Cancer
- Cervical Cancer
- Hepatocellular Carcinoma
- Biliary Tract Cancer
- Merkel Cell Carcinoma
- Renal Cell Carcinoma
- Endometrial Carcinoma
- Tumor Mutational Burden-High Cancer
- Cutaneous Squamous Cell Carcinoma
- Triple-Negative Breast Cancer

- For use at an additional recommended dosage of 400 mg every 6 weeks for classical Hodgkin lymphoma and primary mediastinal large B-cell lymphoma in adults

The FDA-approved indications for the agents included in this guideline are supported by the National Comprehensive Cancer Network (NCCN) guidelines. Please refer to the prescribing information for information on specific indications.

Coverage Guidelines

Authorization may be reviewed on a case by case basis for members who are new to the plan currently receiving treatment with requested medication excluding when the product is obtained as samples or via manufacturer's patient assistance programs.

OR

Authorization may be granted for members when ONE the following criteria are met:

1. Diagnosis of **metastatic Merkel cell carcinoma**
    a. Prescriber is an oncologist
    b. Appropriate dosing *(weight required)*
2. Diagnosis of **cervical cancer**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Tumor expresses PD-L1 (CPS ≥1)
    d. **ONE** of the following:
        i. Requested agent will be used in combination with chemotherapy, with or without bevacizumab
        ii. **BOTH** of the following:
            1. Disease progression following **ONE** systemic chemotherapy regimen
            2. Requested agent will be used as monotherapy
3. Diagnosis of **advanced endometrial carcinoma**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Member is ≥18 years of age
    d. Paid claims or physician attestation of inadequate response or adverse reaction to **ONE** prior line of systemic therapy, or contraindication to **ALL** systemic therapies
    e. Member is not a candidate for surgery or radiation
    f. **ONE** of the following:
        i. For advanced endometrial carcinoma that is not MSI-H or dMMR, requested agent will be used in combination with Lenvima (lenvatinib)
        ii. For advanced endometrial carcinoma that is MSI-H or dMMR, requested agent will be used as monotherapy
4. Diagnosis of **primary advanced or recurrent endometrial carcinoma**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Member is ≥18 years of age
    d. ONE of the following:

i. Requested agent will be used in combination with carboplatin and paclitaxel every three weeks for six doses, followed by monotherapy of Keytruda every six weeks
ii. Requested agent will be used as monotherapy with documentation noting that member has already started/completed the initial combination regimen in-hospital or through another provider

5. Diagnosis of **advanced renal cell carcinoma (RCC)**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. **ONE** of the following:
        i. Tumor is clear cell histology and **ONE** of the following:
            1. Requested agent will be used in combination with Inlyta (axitinib)
            2. Requested agent will be used in combination with Lenvima (lenvatinib)
            3. Requested agent will be used as adjuvant treatment following nephrectomy
        ii. **BOTH** of the following:
            1. Tumor is non-clear cell histology
            2. Paid claims or physician attestation of inadequate response, adverse reaction to **ONE** or contraindication to **BOTH** of the following:
                a. Cabometyx (cabozantinib)
                b. Sutent (sunitinib)
6. Diagnosis of **stage IIB, IIC or III melanoma**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Requested agent will be used as adjuvant treatment following complete resection
7. Diagnosis of **primary mediastinal B-cell lymphoma (PMBCL)**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Physician attestation of inadequate response or adverse reaction to **TWO** systemic chemotherapy regimens or contraindication to the use of **ALL** systemic chemotherapy
8. Diagnosis of **recurrent or metastatic head and neck squamous cell carcinoma (HNSCC)**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. **ONE** of the following:
        i. Cancer is non-nasopharyngeal and **ONE** of the following:
            1. Requested agent is used in combination with a platinum agent (cisplatin or carboplatin) and fluorouracil
            2. Tumor is PD-L1 positive (CPS ≥1)
        ii. Inadequate response or adverse reaction to **ONE** platinum-containing regimen, or contraindication to **ALL** platinum-containing regimens
9. Diagnosis of **microsatellite instability-high/mismatch repair deficient (MSI-H/dMMR) solid tumors <u>or</u> metastatic colorectal cancer (mCRC)**
    a. Prescriber is an oncologist
    b. Appropriate dosing *(weight required)*
10. Diagnosis of **urothelial carcinoma** – Locally advanced or metastatic disease
    a. Prescriber is an oncologist

b. Appropriate dosing
c. **ONE** of the following:
    i. **BOTH** of the following
        1. Requested agent will be used as monotherapy
        2. Inadequate response or adverse reaction to **ONE** platinum-containing regimen, or contraindication to **ALL** platinum-containing chemotherapy regimens
    ii. **BOTH** of the following
        1. Requested agent will be used in combination with Padcev
        2. Contraindication to **ALL** cisplatin-containing chemotherapy

11. Diagnosis of **stage III non-small cell lung cancer (NSCLC)**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Tumor expresses PD-L1 (TPS ≥1%)
    a. Requested agent will be used with carboplatin and either pemetrexed or paclitaxel *(e.g., may be bypassed if member already completed chemotherapy)*
12. Diagnosis of **tumor mutational burden-high (TMB-H) cancer**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Tumor has ≥10 mutations/megabase (mut/Mb)
13. Diagnosis of **unresectable or metastatic NSCLC**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. **ONE** of the following:
        i. Requested agent will be used in combination with pemetrexed and either carboplatin or cisplatin for non-squamous NSCLC in the first-line setting *(e.g., may be bypassed if member already completed chemotherapy)*
        ii. Requested agent will be used in combination with carboplatin and either paclitaxel or albumin-bound paclitaxel for squamous NSCLC in the first-line setting *(e.g., may be bypassed if member already completed chemotherapy)*
        iii. PD-L1 expression and **ONE** of the following:
            1. **BOTH** of the following:
                a. Physician attestation of inadequate response or adverse reaction to **ONE** platinum-containing regimen, or contraindication to **ALL** platinum-containing regimens
                b. Requested agent will be used as monotherapy
            2. **BOTH** of the following:
                a. Member does NOT have EGFR or ALK genomic tumor aberrations
                b. Requested agent will be used as monotherapy in the first-line setting
14. Diagnosis of **resectable Non-Small Cell Lung Cancer (NSCLC)**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Requested agent will be used in the neoadjuvant setting in combination with ONE of the following:
        i. carboplatin and paclitaxel

ii. cisplatin and pemetrexed
iii. cisplatin and gemcitabine
iv. cisplatin and paclitaxel

d. Requested agent will be continued as monotherapy as adjuvant treatment after surgery

15. Diagnosis of **stage IB (T2a ≥4 cm), II, or IIIA NSCLC**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Requested agent will be used as adjuvant treatment following resection and platinum-based chemotherapy
16. Diagnosis of **high-risk early stage triple-negative breast cancer (TNBC)**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Requested agent will be used in combination with chemotherapy *(e.g., carboplatin, paclitaxel, cyclophosphamide, doxorubicin, epirubicin)* and then continued as single agent following surgery
17. Diagnosis of **unresectable locally advanced or metastatic TNBC**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Member is PD-L1 positive (CPS ≥10)
    d. Requested agent will be used in combination with ONE of the following:
        i. paclitaxel protein-bound
        ii. paclitaxel
        iii. gemcitabine and carboplatin
18. Diagnosis of **non-muscle invasive bladder cancer (NMIBC)**
    a. Prescriber is an oncologist or urologist
    b. Appropriate dosing
    c. Physician attestation of inadequate response, adverse reaction, or contraindication to BCG
    d. Disease is high-risk with carcinoma in situ
19. Diagnosis of **metastatic squamous cell carcinoma of the esophagus (ESCC)**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Tumor expresses PD-L1 (CPS ≥10)
    d. Physician attestation of inadequate response or adverse reaction to **ONE** line of systemic therapy, or contraindication to **ALL** other lines of systemic therapy
20. Diagnosis of **advanced, recurrent or metastatic esophageal or esophagogastric junction (EGJ) cancer**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. **ONE** of the following:
        i. If previously untreated, requested agent will be used in combination with a fluoropyrimidine- and platinum-containing regimen
        ii. **BOTH** of the following:
            1. Requested agent will be used as monotherapy
            2. Member had at least ONE prior line of systemic therapy for squamous cell tumor with PD-L1 (CPS ≥10)

21. Diagnosis of **unresectable or metastatic HER2-positive gastric adenocarcinoma, or gastroesophageal junction adenocarcinoma**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Requested agent will be used in combination with trastuzumab, fluoropyrimidine-, and platinum-containing chemotherapy
22. Diagnosis of **unresectable or metastatic HER2- negative gastric or gastroesophageal junction (GEJ) adenocarcinoma**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Requested agent will be used in combination with BOTH of the following:
        i. fluoropyrimidine- containing regimen
        ii. platinum-containing regimen
23. Diagnosis of **unresectable or metastatic melanoma**
    a. Prescriber is an oncologist
    b. Appropriate dosing
24. Diagnosis of **Hodgkin lymphoma** in **adult** members
    a. Prescriber is a hematologist/oncologist
    b. Appropriate dosing
    c. Member is ≥ 18 years of age
    d. **ONE** of the following:
        i. Member progressed after autologous HSCT with or without brentuximab
        ii. Member ineligible for transplant or inadequate response to two or more lines of prior chemotherapy *(see appendix on systemic therapies for Hodgkin lymphoma)*
        iii. Member received allogeneic transplant
25. Diagnosis of **Hodgkin lymphoma** in **pediatric** members
    a. Prescriber is a hematologist/oncologist
    b. Appropriate dosing *(appropriate mg/kg dosing may be accepted without documentation of weight for pediatric members)*
    c. Member is < 18 years of age
    d. Inadequate response or adverse reaction to **TWO** or more lines of prior chemotherapy *(see appendix on systemic therapies for Hodgkin lymphoma)*
26. Diagnosis of **hepatocellular carcinoma (HCC)**
    a. Prescriber is a hematologist/oncologist
    b. Appropriate dosing
    c. Physician attestation of inadequate response, adverse reaction, or contraindication to sorafenib
    d. Member has Child-Pugh class A
27. Diagnosis of **metastatic or locally advanced cutaneous squamous cell carcinoma (CSCC)**
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Member is ≥18 years of age
    d. Member is not a candidate for surgery and/or radiation therapy *(e.g., metastatic CSCC)*
28. Diagnosis of **locally advanced or metastatic biliary tract cancer (BTC)**
    a. Prescriber is an oncologist

b. Appropriate dosing
c. Requested agent will be used in combination with **BOTH** of the following:
    i. Cisplatin
    ii. gemcitabine

Continuation of Therapy
Resubmission by prescriber will infer a positive response to therapy.

Limitations
1. Initial approvals will be granted for 6 months.
2. Reauthorizations will be granted for 1 year.

References

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7. NCCN. Basal Cell Skin Cancer. Version 3.2024; 2024 Mar 1 [cited 2024 Apr 24]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf.
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13. NCCN. Melanoma: Cutaneous. Version 2.2024; 2024 Apr 3 [cited 2024 Apr 24]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf.
14. NCCN. Head and Neck Cancers. Version 3.2024; 2024 Feb 29 [cited 2024 Apr 24]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf.

Review History

Reviewed and created for P&T. Matched MH UPPL criteria to be in compliance with Masshealth unified formulary requirements. Switched from CVS SGM to custom criteria. Effective 4/1/23.
05/10/23 – Reviewed and updated for P&T. New agent, Imjudo, was added to guideline. The following other updates were made based on expanded indications: Bavencio - Diagnosis update to "Diagnosis of locally advanced or metastatic urothelial carcinoma", Imfinzi -Expanded labeling for BTC, NSCLC, uHCC, Keytruda - criteria update for Unresectable or metastatic NSCLC and Gastric or GEJ adenocarcinoma, Libtayo- criteria update for NSCLC, Opdivo - Expanded indication for Stage IIB, IIC or III melanoma, Tecentriq - Expanded indication for ASPS. Removed the following due to FDA voluntary withdrawal: Tecentriq for locally advanced or metastatic urothelial carcinoma from and Keytruda for 3rd-line setting for gastric cancer (locally advanced or metastatic gastric or gastroesophageal (GEJ) adenocarcinoma whose tumors expressed PD-L1 and had disease progression on or after ≥ 2 prior lines of therapy). References updated. Effective 6/5/23.
07/12/23 – Reviewed and updated for P&T. Add expanded indication for use for Keytruda (pembrolizumab) as a single agent for adjuvant treatment following resection and platinum-based chemotherapy for adults with stage IB (T2a ≥4 cm), II, or IIIA NSCLC. Formatting updates made throughout policy. Jemperli and Opdualag will only be available under MB. Brand preferred and mandatory generic language was added under Limitations. Effective 7/31/23.
09/13/23 – Reviewed and updated for P&T. Expanded indication added to guideline: Padcev in combination with Keytruda® (pembrolizumab) for the treatment of adult patients with locally advanced (la) or metastatic urothelial cancer (mUC) who are not eligible for cisplatin-containing chemotherapy. Minor edits to criteria regarding trial and failure versus contraindication to therapies throughout policy. Effective 10/02/23.
11/15/23 – Reviewed and updated for P&T. Zynyz (relatlimab-dlwr) is added with PA and MB designation. Effective 12/04/23.
04/10/24 – Reviewed and updated for P&T. Criteria updates for Keytruda for the following expanded indications: resectable Non-Small Cell Lung Cancer (NSCLC), unresectable or metastatic HER2- negative gastric or gastroesophageal junction (GEJ) adenocarcinoma, and locally advanced or metastatic biliary tract cancer (BTC). Criteria update for Jemperli for use in combination with carboplatin and paclitaxel, followed by Jemperli as a single agent for the treatment of adult patients with primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR), as determined by an FDA-approved test, or microsatellite instability-high (MSI-H). Effective 5/6/24
12/11/24 – Reviewed and updated for P&T. Separated Keytruda to individual policy for better criteria management. Expanded indications added: in combination with carboplatin and paclitaxel, followed by pembrolizumab as a single agent, for the treatment of adult patients with primary advanced or recurrent endometrial carcinoma (first front-line immunotherapy for advanced endometrial cancer patients regardless of mismatch repair status). Effective 01/06/25