Mass General Brigham
Health Plan

Oncology Immunotherapies
Keytruda (pembrolizumab)
Effective 07/01/2025

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
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 ALL of the following criteria are met:

Merkel Cell Carcinoma
1. Diagnosis of metastatic Merkel cell carcinoma
2. Prescriber is an oncologist
3. Appropriate dosing *(weight required)*

Cervical Cancer
1. Diagnosis of cervical cancer
2. Prescriber is an oncologist
3. Appropriate dosing
4. **ONE** of the following:
    a. **BOTH** of the following:
        i. Requested agent will be used in combination with chemoradiotherapy
        ii. Member has FIGO 2014 Stage III-IVA cervical cancer
    b. **BOTH** of the following:

i. Requested agent will be used in combination with chemotherapy, with or without bevacizumab
ii. Tumor expresses PD-L1 (CPS ≥1)

c. **ALL** of the following:
i. Disease progression following **ONE** systemic chemotherapy regimen
ii. Requested agent will be used as monotherapy
iii. Tumor expresses PD-L1 (CPS ≥1)

Advanced Endometrial Carcinoma

1. Diagnosis of advanced endometrial carcinoma
2. Prescriber is an oncologist
3. Appropriate dosing
4. Member is ≥18 years of age
5. Inadequate response or adverse reaction to **ONE** prior line of systemic therapy, or contraindication to **ALL** systemic therapies
6. Member is not a candidate for surgery or radiation
7. **ONE** of the following:
    a. For advanced endometrial carcinoma that is not MSI-H or dMMR, requested agent will be used in combination with Lenvima (lenvatinib)
    b. For advanced endometrial carcinoma that is MSI-H or dMMR, requested agent will be used as monotherapy

Primary Advanced or Recurrent Endometrial Carcinoma

1. Diagnosis of primary advanced or recurrent endometrial carcinoma
2. Prescriber is an oncologist
3. Appropriate dosing
4. Member is ≥18 years of age
5. ONE of the following:
    a. 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
    b. 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

Advanced Renal Cell Carcinoma (RCC)

1. Diagnosis of advanced renal cell carcinoma
2. Prescriber is an oncologist
3. Appropriate dosing
4. **ONE** of the following:
    a. Tumor is clear cell histology and **ONE** of the following:
        i. Requested agent will be used in combination with Inlyta (axitinib)
        ii. Requested agent will be used in combination with Lenvima (lenvatinib)
        iii. Requested agent will be used as adjuvant treatment following nephrectomy
    b. **BOTH** of the following:

i. Tumor is non-clear cell histology
ii. **ONE** of the following:
    1. Requested agent will be used in combination with Lenvatinib
    2. Requested agent will be used as monotherapy

Stage IIB, IIC or III melanoma

1. Diagnosis of stage IIB, IIC or III melanoma
2. Prescriber is an oncologist
3. Appropriate dosing
4. Requested agent will be used as adjuvant treatment following complete resection

Primary Mediastinal B-Cell Lymphoma (PMBCL)

1. Diagnosis of PMBCL
2. Prescriber is an oncologist
3. Appropriate dosing
4. Inadequate response or adverse reaction to **TWO** systemic chemotherapy regimens or contraindication to the use of **ALL** systemic chemotherapies

Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma (HNSCC)

1. Diagnosis of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC)
2. Prescriber is an oncologist
3. Appropriate dosing
4. **ONE** of the following:
    a. Cancer is non-nasopharyngeal and **ONE** of the following:
        i. Requested agent is used in combination with a platinum agent (cisplatin or carboplatin) and fluorouracil
        ii. Tumor is PD-L1 positive (CPS ≥1)
    b. Inadequate response or adverse reaction to **ONE** platinum-containing regimen, or contraindication to **ALL** platinum-containing regimens

Microsatellite Instability-High/Mismatch Repair Deficient (MSI-H/Dmmr) Solid Tumors or Metastatic Colorectal Cancer (mCRC)

1. Diagnosis of MSI-H/dMMR solid tumors or mCRC
2. Prescriber is an oncologist
3. Appropriate dosing *(weight required)*

Urothelial Carcinoma

1. Diagnosis of locally advanced or metastatic disease urothelial carcinoma
1. Prescriber is an oncologist
2. Appropriate dosing
3. **ONE** of the following:
    a. **BOTH** of the following
        i. Requested agent will be used as monotherapy

ii. Inadequate response or adverse reaction to **ONE**, or contraindication to **ALL** platinum-containing chemotherapy regimens (e.g., regimen containing cisplatin, carboplatin, or oxaliplatin)

b. Requested agent will be used in combination with Padcev

Stage III Non-Small Cell Lung Cancer (NSCLC)

1. Diagnosis of stage III non-small cell lung cancer (NSCLC)
2. Prescriber is an oncologist
3. Appropriate dosing
4. Tumor expresses PD-L1 (TPS ≥1%)
5. Member is not a candidate for surgical resection or definitive chemoradiation
6. Member does NOT have EGFR or ALK genomic tumor aberrations

Tumor Mutational Burden-High (TMB-H) Cancer

1. Diagnosis of tumor mutational burden-high (TMB-H) cancer
2. Prescriber is an oncologist
3. Appropriate dosing
4. Tumor has ≥10 mutations/megabase (mut/Mb)

Unresectable or Metastatic Non-Small Cell Lung Cancer (NSCLC)

1. Diagnosis of unresectable or metastatic NSCLC
2. Prescriber is an oncologist
3. Appropriate dosing
4. **ONE** of the following:
    a. 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)*
    b. 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)*
    c. PD-L1 expression and **ONE** of the following:
        i. **BOTH** of the following:
            1. Inadequate response or adverse reaction to **ONE**, or contraindication to **ALL** platinum-containing regimens s (e.g., regimen containing cisplatin, carboplatin, or oxaliplatin)
            2. Requested agent will be used as monotherapy
        ii. **BOTH** of the following:
            1. Member does NOT have EGFR or ALK genomic tumor aberrations
            2. Requested agent will be used as monotherapy in the first-line setting

Resectable Non-Small Cell Lung Cancer (NSCLC)

1. Diagnosis of resectable NSCLC
2. Prescriber is an oncologist
3. Appropriate dosing

4. Requested agent will be used in the neoadjuvant setting in combination with **ONE** of the following:
    a. carboplatin and paclitaxel
    b. cisplatin and pemetrexed
    c. cisplatin and gemcitabine
    d. cisplatin and paclitaxel
5. Requested agent will be continued as monotherapy as adjuvant treatment after surgery

Stage IB (T2a ≥4 cm), II, or IIIA NSCLC

1. Diagnosis of stage IB (T2a ≥4 cm), II, or IIIA NSCLC
2. Prescriber is an oncologist
3. Appropriate dosing
4. Requested agent will be used as adjuvant treatment following resection and platinum-based chemotherapy (e.g., regimen containing cisplatin, carboplatin, or oxaliplatin)

High-Risk Early Stage Triple-Negative Breast Cancer (TNBC)

1. Diagnosis of high-risk early stage TNBC
2. Prescriber is an oncologist
3. Appropriate dosing
4. Requested agent will be used in combination with chemotherapy *(e.g., carboplatin, paclitaxel, cyclophosphamide, doxorubicin, epirubicin)* and then continued as single agent following surgery

Unresectable Locally Advanced or Metastatic TNBC

1. Diagnosis of unresectable locally advanced or metastatic TNBC
2. Prescriber is an oncologist
3. Appropriate dosing
4. Member is PD-L1 positive (CPS ≥10)
5. Requested agent will be used in combination with ONE of the following:
    a. paclitaxel protein-bound
    b. paclitaxel
    c. gemcitabine and carboplatin

Non-Muscle Invasive Bladder Cancer (NMIBC)

1. Diagnosis of NMIBC
2. Prescriber is an oncologist or urologist
3. Appropriate dosing
4. Inadequate response, adverse reaction, or contraindication to BCG
5. Disease is high-risk with carcinoma in situ

Metastatic Squamous Cell Carcinoma of the Esophagus (ESCC)

1. Diagnosis of metastatic squamous cell carcinoma of the esophagus (ESCC)
2. Prescriber is an oncologist
3. Appropriate dosing
4. Tumor expresses PD-L1 (CPS ≥10)

5. Inadequate response or adverse reaction to **ONE** line of systemic therapy, or contraindication to **ALL** other lines of systemic therapy

Advanced, Recurrent or Metastatic Esophageal or Esophagogastric Junction (EGJ) Cancer

1. Diagnosis of advanced, recurrent or metastatic esophageal or esophagogastric junction (EGJ) cancer
2. Prescriber is an oncologist
3. Appropriate dosing
4. **ONE** of the following:
    a. If previously untreated, requested agent will be used in combination with a fluoropyrimidine- (e.g. fluorouracil or capecitabine) and platinum-containing regimen (e.g., regimen containing cisplatin, carboplatin, or oxaliplatin)
    b. **BOTH** of the following:
        i. Requested agent will be used as monotherapy
        ii. Member had at least ONE prior line of systemic therapy for squamous cell tumor with PD-L1 (CPS ≥10)

*Unresectable or Metastatic HER2-**Positive** Gastric Adenocarcinoma, or Gastroesophageal Junction (GEJ) Adenocarcinoma*

1. Diagnosis of unresectable or metastatic HER2-positive gastric adenocarcinoma, or gastroesophageal junction adenocarcinoma
2. Prescriber is an oncologist
3. Appropriate dosing
4. Requested agent will be used in combination with **ALL** of the following:
    a. trastuzumab
    b. fluoropyrimidine-containing chemotherapy (e.g. fluorouracil or capecitabine)
    c. platinum-containing chemotherapy (e.g., regimen containing cisplatin, carboplatin, or oxaliplatin)

*Unresectable or Metastatic HER2- **Negative** Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma*

1. Diagnosis of unresectable or metastatic HER2- negative gastric or gastroesophageal junction (GEJ) adenocarcinoma
2. Prescriber is an oncologist
3. Appropriate dosing
4. Requested agent will be used in combination with **BOTH** of the following:
    a. fluoropyrimidine- containing regimen (e.g. fluorouracil or capecitabine)
    b. platinum-containing regimen (e.g., regimen containing cisplatin, carboplatin, or oxaliplatin)

Unresectable or Metastatic Melanoma

1. Diagnosis of unresectable or metastatic melanoma
2. Prescriber is an oncologist
3. Appropriate dosing

*Hodgkin lymphoma in **adults***

1. Diagnosis of relapsed or refractory classical Hodgkin lymphoma in adult members

2. Prescriber is a hematologist/oncologist
3. Appropriate dosing
4. Member is ≥ 18 years of age
5. **ONE** of the following:
    a. Member progressed after autologous HSCT with or without brentuximab
    b. Member ineligible for transplant or inadequate response to two or more lines of prior chemotherapy *(see appendix on systemic therapies for Hodgkin lymphoma)*
    c. Member received allogeneic transplant

*Hodgkin lymphoma in **pediatrics***

1. Diagnosis of relapsed or refractory classical Hodgkin lymphoma in pediatric members
2. Prescriber is a hematologist/oncologist
3. Appropriate dosing *(appropriate mg/kg dosing may be accepted without documentation of weight for pediatric members)*
4. Member is < 18 years of age
5. Inadequate response or adverse reaction to **TWO** or more lines of prior chemotherapy *(see appendix on systemic therapies for Hodgkin lymphoma)*

Hepatocellular Carcinoma (HCC)

1. Diagnosis of hepatocellular carcinoma secondary to hepatitis B
2. Prescriber is a hematologist/oncologist
3. Appropriate dosing
4. Inadequate response, adverse reaction to **ONE**, or contraindication to **BOTH** of the following:
    a. Lenvima (lenvatinib)
    b. sorafenib
5. Member has Child-Pugh class A

Metastatic or Locally Advanced Cutaneous Squamous Cell Carcinoma (CSCC)

1. Diagnosis of metastatic or locally advanced cutaneous squamous cell carcinoma
2. Prescriber is an oncologist
3. Appropriate dosing
4. Member is ≥18 years of age
5. Member is not a candidate for surgery and/or radiation therapy *(e.g., metastatic CSCC)*

Locally Advanced or Metastatic Biliary Tract Cancer (BTC)

1. Diagnosis of locally advanced or metastatic biliary tract cancer
2. Prescriber is an oncologist
3. Appropriate dosing
4. Requested agent will be used in combination with **BOTH** of the following:
    a. cisplatin
    b. gemcitabine

Malignant Pleural Mesothelioma (MPM)

1. Diagnosis of unresectable advanced or metastatic malignant pleural mesothelioma (MPM)

2. Prescriber is an oncologist
3. Appropriate dosing
4. Requested agent will be used in combination with pemetrexed and platinum chemotherapy (e.g., regimen containing cisplatin, carboplatin, or oxaliplatin)

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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3. NCCN. Gastric Cancer Version 1.2024; 2024 Mar 7 [cited 2024 Apr 24]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf.
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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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10. NCCN. Uterine Neoplasms. Version 2.2024; 2024 Mar 6 [cited 2024 Aug 30]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf.
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12. NCCN. Biliary Tract Cancers Version 2.2024; 2024 Apr 19 [cited 2024 Apr 24]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf
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
06/11/25 – Reviewed and updated for P&T. Updated formatting and references. Expanded indication for Keytruda in combination with pemetrexed and platinum chemotherapy as first-line treatment of unresectable advanced or metastatic malignant pleural mesothelioma (MPM) was added. Expanded indication for FIGO 2014 stage III-IVA cervical cancer was added. RCC criteria updated based on changes to NCCN guideline removing the trial requirement for Cabometyx (cabozantinib) and sunitinib in nonclear cell histology. Merkel cell carcinoma criteria updated to remove the trial requirement. Criteria for Stage III NSCLC updated to better match FDA labeling. Effective 7/1/25