Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Cemiplimab-rwlc (Libtayo®)	MP-RX-FP-54-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Cemiplimab-rwlc (Libtayo®), a programmed death receptor-1 (PD-1) blocking antibody approved by the Food and Drug Administration (FDA) for the treatment of certain patients with Cutaneous Squamous Cell Carcinoma (CSCC), Basal Cell Carcinoma (BCC), and Non-Small Cell Lung Cancer (NSCLC).

Background Information

Cemiplimab-rwlc, marketed under the brand name Libtayo®, is a monoclonal antibody derived from recombinant human immunoglobulin G4 (IgG4). It operates by binding to the programmed death receptor-1 (PD-1), preventing its interaction with PD-ligand 1 (PD-L1) and PD-ligand 2 (PD-L2). This binding effectively hinders T-cell proliferation and the production of cytokines. In preclinical studies involving syngeneic mouse tumor models, the blockade of PD-1 activity was observed to result in reduced tumor growth.

Cutaneous squamous cell carcinoma (CSCC)

In the United States, cutaneous squamous cell carcinoma (CSCC) ranks as the second most commonly occurring type of skin cancer, contributing to approximately 7,000 annual fatalities. The number of newly diagnosed cases is expected to increase each year.

On September 28, 2018, the U.S. Food and Drug Administration (FDA) approved Libtayo (cemiplimab-rwlc) for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not suitable candidates for curative surgery or radiation therapy. The safety and efficacy of Libtayo were assessed through two open-label clinical trials involving a total of 108 patients (75 with metastatic disease and 33 with locally advanced disease). The primary endpoint of the study was the objective response rate (ORR), which gauges the percentage of patients experiencing partial shrinkage or complete disappearance of their tumors after treatment. The results indicated that 47.2% of all patients treated with Libtayo experienced a reduction in tumor size or complete tumor disappearance, with most of these patients maintaining these responses during the data analysis period. Common adverse events (AEs) linked to Libtayo included diarrhea, fatigue, and rash. Libtayo can trigger the immune system to target normal organs and tissues throughout the body, potentially affecting their function. In some cases, these reactions can become severe or life-threatening, and in rare instances, lead to fatalities. These immune-mediated AEs encompass colitis, dermatologic adverse reactions, endocrinopathies, hepatitis, pneumonitis, as well as nephritis and renal dysfunction. Patients should also undergo monitoring for

infusion-related reactions. Additionally, Libtayo has the potential to harm a developing fetus; therefore, women of childbearing age should be advised about the potential risk to the fetus and urged to use effective contraception. Women should also avoid breastfeeding.

Basal cell carcinoma (BCC)

In the United States, basal cell carcinoma (BCC) stands as the most common type of skin cancer, with approximately two million new cases being diagnosed each year. While a vast majority of BCC cases are identified early and effectively treated through surgical and radiation interventions, a small fraction of these tumors can exhibit invasiveness, penetrating deeply into surrounding tissues, a condition referred to as locally advanced BCC. Once the cancer metastasizes, spreading to other parts of the body, it becomes considerably more challenging to manag. Libtayo was approved by the FDA on February 9, 2021 as the first immunotherapy for the treatment of patients who have advanced basal cell carcinoma (BCC). This approval applies specifically to patients who have previously been treated with a hedgehog pathway inhibitor (HHI) or for whom HHI treatment is deemed inappropriate. The decision to approve Libtayo was based on FDA Priority Review and data from a pivotal open-label, multicenter, non-randomized Phase 2 clinical trial that involved 132 patients. Among these participants, 112 individuals with unresectable locally advanced BCC (28 patients) or metastatic BCC (84 patients, including nodal and distant cases) were included in the efficacy analysis. Libtayo was administered intravenously at a dosage of 350 mg every 3 weeks, for a maximum duration of 93 weeks, until disease progression, unacceptable side effects, or completion of the planned treatment. Patients in both cohorts exhibited signs of deterioration on HHI therapy, lacked an objective response after nine months of HHI treatment, or had experienced intolerance to previous HHI therapy. The primary efficacy endpoint was the confirmed objective response rate (ORR), with a significant secondary endpoint being the duration of response (DOR). In patients with locally advanced BCC, the confirmed ORR was 29% (with 6% achieving complete response and 23% achieving partial response). Among patients with metastatic BCC, the ORR was 21% (with no complete responses and 21% partial responses). Median DOR for locally advanced BCC patients was not reached (ranging from 2 to 21 months), and for metastatic BCC patients, it was also not reached (ranging from 9 to 23 months). Ongoing assessment of DOR continues for both patient groups. The safety evaluation encompassed all 132 patients, with 32% of them experiencing serious adverse reactions.

Non-small cell lung cancer (NSCLC)

Lung cancer is a leading cause of cancer-related deaths globally, with approximately 2.2 million new cases diagnosed worldwide and 225,000 new cases in the United States in 2020. The majority of lung cancers fall into the non-small cell lung cancer (NSCLC) category, comprising about 84% of all cases. A significant portion of NSCLC cases are diagnosed in advanced stages, and around 25% to 30% of them are expected to test positive for PD-L1 expression in at least 50% of tumor cells.

On February 22, 2021, the U.S. Food and Drug Administration (FDA) granted approval to Libtayo (cemiplimab-rwlc) as a first-line treatment for patients with advanced NSCLC whose tumors exhibit high PD-L1 expression (tumor proportion score ≥50%), confirmed by an FDA-approved test. This indication was supported by data from

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the EMPOWER-Lung 1 study, an open-label, randomized Phase 3 trial that included 710 patients. Researchers aimed to evaluate Libtayo monotherapy compared to platinum-doublet chemotherapy as the first-line treatment in patients with advanced NSCLC who were positive for PD-L1 in ≥50% of tumor cells and without EGFR, ALK or ROS1 aberrations. Patients were randomized to receive either Libtayo or platinum-doublet chemotherapy. The primary endpoints were overall survival (OS) and progression-free survival (PFS). Libtayo reduced the risk of death by 32% compared to chemotherapy, and in patients with PD-L1 expression ≥50%, the risk of death was reduced by 43%. Libtayo also showed statistically significant improvements in OS and PFS compared to chemotherapy.

On November 8, 2022, the FDA approved Libtayo in combination with platinum-based chemotherapy for adult patients with advanced NSCLC without certain genetic aberrations. This approval was based on data from Study 16113, a randomized, double-blind, phase 3 trial. The study included 466 patients with advanced NSCLC who had not received prior systemic treatment. The primary outcome was overall survival, and the trial concluded early due to achieving the pre-established efficacy criteria. Cemiplimab-rwlc plus chemotherapy demonstrated a significant improvement in overall survival compared to placebo plus chemotherapy, with a median OS of 21.9 months versus 13.0 months, respectively. Other measures such as progression-free survival and overall response rate also favored the cemiplimab-rwlc plus chemotherapy group.

- Biomarkers: NCCN panel recommends that individuals with NSCLC be tested for actionable molecular markers, such as EGFR, ALK, ROS1, BRAF, NTRK, MET and RET mutations, before initiating first line therapy to help guide treatment. If there is insufficient tissue to allow testing for all of these markers, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.

Libtayo carries the fallowing precautions:

1. Immune-Mediated Adverse Reactions: Libtayo can lead to immune-mediated adverse reactions that have the potential to be severe or fatal, affecting various organs and tissues. These adverse reactions encompass immune-mediated pneumonitis, colitis, hepatitis, endocrinopathies, dermatologic issues, nephritis, renal dysfunction, and solid organ transplant rejection. Monitoring for early detection and management is essential. Assess liver enzyme levels, creatinine levels, and thyroid function both before starting treatment and periodically during the course. The decision to withhold or permanently discontinue Libtayo should be based on the severity of the reaction.
2. Infusion-Related Reactions: Infusion-related reactions may occur. Depending on the severity of the reaction, healthcare providers may need to interrupt the infusion, slow down the infusion rate, or consider permanent discontinuation.
3. Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT): Patients who receive allogeneic HSCT either before or after treatment with a PD-1/PD-L1 blocking antibody like Libtayo may experience fatal and other serious complications. This is an important consideration when planning HSCT in such patients.

4. Embryo-Fetal Toxicity: Libtayo has the potential to cause harm to a developing fetus. It is crucial to inform females of reproductive potential about the potential risk to a fetus and recommend the use of effective contraception during treatment.

Definitions and Measures

- ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:
    - 0 = Fully active, able to carry on all pre-disease performance without restriction
    - 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light house work, office work
    - 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
    - 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
    - 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
    - 5 = Dead
- Hegdehog pathway inhibitor: FDA-approved examples include vismodegib (Erivedge) and sonidegib (Odomzo) Locally advanced cancer: Cancer that has spread only to nearby tissues or lymph nodes.
- Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.

Approved Indications

Libtayo is indicated by the FDA for the following conditions:

- For the treatment of patients with metastatic cutaneous squamous cell carcinoma (mCSCC) or locally advanced CSCC (laCSCC) who are not candidates for curative surgery or curative radiation.
- For the treatment of patients with locally advanced or metastatic basal cell carcinoma BCC (laBCC or mBCC) who have been previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate.
- Non-Small Cell Lung Cancer (NSCLC)
    - In combination with platinum-based chemotherapy for the first-line treatment of adult patients with non-small cell lung cancer (NSCLC) with no EGFR, ALK or ROS1 aberrations and is either locally advanced where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.

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- As single agent for the first-line treatment of adult patients with NSCLC whose tumors have high PD-L1 expression [Tumor Proportion Score (TPS) ≥ 50%] as determined by an FDA-approved test, with no EGFR, ALK or ROS1 aberrations, and is either locally advanced where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.

Other Uses

See Background section above.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J9119	Injection, cemiplimab-rwlc, 1 mg [Libtayo]

ICD-10	Description
C34.90-C34.92	Malignant neoplasm of unspecified part of bronchus or lung
C44.00-C44.99	Other and unspecified malignant neoplasm of skin

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Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Cemiplimab-rwlc (Libtayo®)

A. Criteria For Initial Approval

i. Individual has a diagnosis of unresectable locally advanced, recurrent, or metastatic Basal Cell Carcinoma (BCC) (Label, NCCN 2A); **AND**
   - A. Individual is using as single agent for subsequent therapy; **AND**
   - B. Individual has confirmed disease progression on a hedgehog pathway inhibitor, or ineligible for treatment with a hedgehog pathway inhibitor; **AND**
   - C. Individual has a current ECOG performance status of 0-2; **AND**
   - D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   - E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

ii. Individual has a diagnosis of Cutaneous Squamous Cell Carcinoma (CSCC) (Label, NCCN 2A); **AND**
   - A. One of the following:
     1. Individual is diagnosed with metastatic disease; **OR**
     2. Individual is diagnosed with locally advanced or locally recurrent disease; **OR**
     3. Individual is diagnosed with regional new or regional recurrent disease;

   AND
   - B. Individual is using as single agent; **AND**
   - C. Individual is not a candidate for curative surgery or radiation; **AND**
   - D. Individual has current ECOG performance status of 0-2; **AND**
   - E. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   - F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

iii. Individual has a diagnosis of locally advanced Non-Small Cell Lung Cancer (NSCLC) (Label, NCCN 1); **AND**
   - A. Individual is using as single agent; **AND**
   - B. Individual is not a candidate for surgical resection or chemoradiation; **AND**

C. Individual has a tumor with PD-L1 gene expression with Tumor Proportion Score of greater than or equal to 50% (TPS ≥ 50%); **AND**
D. Individual does not have presence of actionable molecular markers*; **AND**
E. Individual has a current ECOG performance status of 0-2; **AND**
F. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
G. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

iv. Individual has a diagnosis of metastatic Non-Small Cell Lung Cancer (NSCLC) (Label, NCCN 1); **AND**
A. Individual is using as single agent or in combination thearpy; **AND**
B. Individual does not have presence of actionable molecular markers*; **AND**
C. Individual has a current ECOG performance status of 0-2; **AND**
D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

v. Individual has a diagnosis of NSCLC; **AND**
A. One of the following:
1. Individual has recurrent, metastatic or locally advance disease where individual is not a candidate for surgical resection or definitive chemoradiation; **OR**
2. Individual has recurrent, advanced, or metastatic disease; **AND**
B. Individual is using in combination with pemetrexed (NCCN 2A) or platinum-based chemotherapy (Label); **AND**
C. Individual is using for first-line (Label) or maintenance (NCCN 2A) therapy; **AND**
D. Individual does not have presence of actionable molecular markers*; **AND**
E. Individual has a current ECOG performance status of 0-2; **AND**
F. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
G. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

***Note:** Actionable molecular markers include EGFR, ALK, ROS1, BRAF, NTRK, MET and RET mutations. The NCCN panel recommends testing prior to initiating therapy to help guide appropriate treatment. If there is insufficient tissue to allow testing for all of these markers, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes (NCCN 1, 2A).

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Cemiplimab-rwlc (Libtayo®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial

Approval) when there is no evidence of unacceptable toxicity or disease progression while on the current regimen, and the maximum duration of treatment has not been exceeded. The following information should be submitted for reauthorization:

A. A current oncology note documenting the patient's response to treatment showing no progression of disease.
B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

ii. Maximum duration of Therapy:

A. Locally Advanced or Metastatic Basal Cell Carcinoma and Locally Advanced or Metastatic Cutaneous Squamous Cell Carcinoma: Up to 24 months
B. NSCLC: Until disease progression or unacceptable toxicity.

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Libtayo (cemiplimab-rwlc) may not be approved when the above criteria are not met and for all other indications.

Limits or Restrictions

A. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

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Cemiplimab-rwlc (Libtayo®)	Recommended Dosing Schedule	Recommended Duration
Locally Advanced or Metastatic Basal Cell Carcinoma and Locally Advanced or Metastatic Cutaneous Squamous Cell Carcinoma	350 mg i.v. every 3 weeks.	Until disease progression, unacceptable toxicity, or up to 24 months
Non-Small Cell Lung Cancer	350 mg i.v. every 3 weeks.	Until disease progression or unacceptable toxicity.
Exceptions		
None		

Reference Information

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4. Gogishvili M, Melkadze T, Makharadze T, et al. Cemiplimab plus chemotherapy versus chemotherapy alone in non-small cell lung cancer: a randomized, controlled, double-blind phase 3 trial. Nat Med. 2022;28(11):2374-2380.
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7. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
8. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
9. NCCN Clinical Practice Guidelines in Oncology™. © 2021 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on April 5, 2023.
    - Basal Cell Skin Cancer. V1.2023. Revised March 10, 2023.
    - Non-Small Cell Lung Cancer. V2.2023. Revised February 17, 2023.
    - Squamous Cell Skin Cancer. V1.2023. Revised March 10, 2023.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023

Revised: 11/17/2023