Corporate Medical Policy

Cemiplimab-rwlc (Libtayo®)

File Name:	cemiplimab_libtayo
Origination:	4/2019
Last CAP Review:	8/2020
Next CAP Review:	8/2021
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Description of Procedure or Service

Cemiplimab-rwlc (Libtayo®) is a recombinant human IgG4 monoclonal antibody that is indicated for the treatment of patients with metastatic or locally advanced cutaneous squamous cell carcinoma (CSCC) who are not candidates for curative surgery or curative radiation.

Cutaneous squamous cell carcinoma (CSCC) is the second most common type of skin cancer. The primary treatment goal of CSCC is complete removal of the tumor with maximal preservation of function and cosmesis. Most patients affected by CSCC have localized disease which can be cured with surgery, although some patients may require adjuvant radiotherapy for tumors with aggressive features, positive surgical margins or operable, regional lymph node involvement.

However, in a small percentage of patients CSCC progresses to locally advanced or metastatic disease which is no longer treatable by surgery or radiation. These patients may be considered for palliative systemic therapy which may include cytotoxic agents or EGFR inhibitors, although the data supporting the efficacy of these treatment options are limited.

Cemiplimab-rwlc (Libtayo) is a human programmed death receptor-1 (PD-1) blocking antibody that was approved by the U.S. Food and Drug Administration (FDA) in September 2018 for the treatment of metastatic or locally advanced CSCC. It works by binding to PD-1 and blocking its interaction with PD-1 ligands 1 and 2 (PD-L1 and PD-L2), which is the interaction responsible for inhibition of T-cell proliferation and cytokine production; thus, releasing the PD-1 pathway-mediated inhibition of immune response, including anti-tumor response.

Related Policies:
PD-1 Inhibitors

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for cemiplimab-rwlc (Libtayo®) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Cemiplimab-rwlc (Libtayo) is covered

Initial Therapy

Cemiplimab-rwlc (Libtayo) is considered medically necessary for the treatment of adult patients (≥18 years old) with cutaneous squamous cell carcinoma (CSCC) when the following criteria are met:

- The patient has metastatic or locally advanced disease; **and**
- The patient is not a candidate for curative surgery or curative radiation; **and**
- The patient has not received treatment with another PD-1 inhibitor; **and**
- Cemiplimab-rwlc will be used as single-agent therapy.

Initial authorization: 6 months

Continuation Therapy

Continuation of treatment with cemiplimab-rwlc (Libtayo) beyond 6 months after initiation of therapy, and every 6 months thereafter, is considered medically necessary for the treatment of cutaneous squamous cell carcinoma (CSCC) when the following criteria are met:

- The patient has been receiving cemiplimab-rwlc treatment previously; **and**
- The patient has not had disease progression or unacceptable toxicity while receiving cemiplimab-rwlc.

Use of cemiplimab-rwlc (Libtayo) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, (see Policy Guidelines); **OR**

- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

When Cemiplimab-rwlc (Libtayo) is not covered

Cemiplimab-rwlc (Libtayo) is considered **investigational** and therefore not covered when the above criteria are not met.

Cemiplimab-rwlc (Libtayo) is considered investigational when used for:

1. Non-cancer indications; **OR**

2. When criteria are not met regarding FDA labeling **OR** strong endorsement/support by nationally recognized compendia, as stated under "When Cemiplimab-rwlc (Libtayo) is covered."

Policy Guidelines

Metastatic disease includes nodal (regional) or distant metastasis or both.

The recommended dose of Libtayo is 350 mg given as an intravenous (IV) infusion over 30 minutes every three weeks until disease progression or unacceptable toxicity.

According to the manufacturer's safety information for Libtayo, the most common adverse reactions (≥20% incidence) include fatigue, rash, and diarrhea.

Evidence Summary

The efficacy of cemiplimab-rwlc (Libtayo) for the treatment of metastatic or locally advanced CSCC in patients who are not candidates for curative surgery or curative radiation was evaluated in two open-label, multicenter, non-randomized, multicohort studies, NCT02383212, a phase 1 study with 26 patients and NCT02760498, a phase 2 study with 82 patients.. Of the 108 patients, 33 had locally advanced disease and 75 had metastatic CSCC (69% with distant metastases and 31% only nodal metastases). Half of the patients had received at least one prior anti-cancer systemic therapy, 96% had received prior cancer-related surgery and 79% had received prior radiotherapy. The primary outcome was overall response rate (ORR), as measured by independent central review and/or Response Evaluation Criteria In Solid Tumors (RECIST). Patients received cemiplimab 3mg/kg intravenously every 2 weeks with response assessment every 8 weeks, for up to 48 weeks in the phase 1 trial and up to 96 weeks in the phase 2 trial. Treatment was given until disease progression, unacceptable toxicity or completion of planned treatment. The efficacy analysis was conducted after all patients had at least 6 months of follow-up. The ORR (95% confidence interval) for the 108 patients was 47.2% (37.5-57.1%). The partial response rate was 43.5% and complete response rate 3.7%. The duration of response ranged from 1 to 15+ months, with 61% of patients having a duration of response of ≥6 months. Adverse events in the phase 2 study included diarrhea, fatigue, nausea, constipation and rash; four patients (7%) discontinued treatment due to an adverse event.

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), "Investigational (Experimental) Services."

Please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *J9119, S0353, S0354*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Regeneron Pharmaceuticals, Inc. Libtayo (cemiplimab-rwlc) injection for intravenous use. Highlights of prescribing information. January 2019. Available at: https://www.regeneron.com/sites/default/files/Libtayo_FPI.pdf. Accessed February 2019.

U.S. Food and Drug Administration. FDA approves first treatment for advanced form of the second most common skin cancer. Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm622044.htm. Accessed February 2019.

Migden MR, Rischin D, Schmults CD, et al. PD-1 blockade with cemiplimab in advanced cutaneous squamous-cell carcinoma. N Engl J Med 2018;379(4):341-51. Available at: https://www.nejm.org/doi/pdf/10.1056/NEJMoa1805131. Accessed March 2019.

Falchook GS, Leidner R, Stankevich E, et al. Responses of metastatic basal cell and cutaneous squamous cell carcinomas to anti-PD1 monoclonal antibody REGN2810. J Immunother Cancer 2016;4:70. Available at: https://jitc.biomedcentral.com/articles/10.1186/s40425-016-0176-3. Accessed March 2019.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Squamous Cell Skin Cancer, version 2.2019. Revised October 23, 2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf. Accessed February 2019.

Medical Director review 4/2019

Specialty Matched Consultant Advisory Panel 8/2019

Specialty Matched Consultant Advisory Panel 8/2020

Policy Implementation/Update Information

4/16/19 New policy developed. Libtayo is considered medically necessary for the treatment of adult patients (≥18 years old) with cutaneous squamous cell carcinoma (CSCC). Added HCPCS codes C9044, J3490, J3590, J9999, S0353, and S0354 to Billing/Coding section. References added. Medical Director review 4/2019. **Policy notification given 4/16/19 for effective date 7/16/19.** (krc)

10/1/19 Specialty Matched Consultant Advisory Panel review 8/21/2019. No change to policy intent. Added HCPCS code J9119 to Billing/Coding section and deleted codes C9044, J3490, J3590, and J9999 effective 10/1/19. (krc)

10/1/20 Specialty Matched Consultant Advisory Panel review 8/19/2020. No change to policy statements. (krc)