

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LIBTAYO safely and effectively. See full prescribing information for LIBTAYO.

**LIBTAYO® (cemiplimab-rwlc) injection, for intravenous use**  
**Initial U.S. Approval: 2018**

### RECENT MAJOR CHANGES

Indications and Usage (1.2)	02/2021
Dosage and Administration (2.2)	11/2020
Warnings and Precautions (5.1, 5.3)	11/2020

### INDICATIONS AND USAGE

LIBTAYO is a programmed death receptor-1 (PD-1) blocking antibody indicated:

#### Cutaneous Squamous Cell Carcinoma (CSCC)

- 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. (1.1)

#### Basal Cell Carcinoma (BCC)

- for the treatment of patients with locally advanced BCC (laBCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate. (1.2)
- for the treatment of patients with metastatic BCC (mBCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate.<sup>1</sup> (1.2)

<sup>1</sup>The mBCC indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for mBCC may be contingent upon verification and description of clinical benefit.

### DOSAGE AND ADMINISTRATION

The recommended dosage of LIBTAYO is 350 mg as an intravenous infusion over 30 minutes every 3 weeks. (2.1)

### DOSAGE FORMS AND STRENGTHS

Injection: 350 mg/7 mL (50 mg/mL) solution in a single-dose vial. (3)

### CONTRAINDICATIONS

None. (4)

### WARNINGS AND PRECAUTIONS

- Immune-Mediated Adverse Reactions (5.1)
  - Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, including the following: immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated dermatologic adverse reactions, immune-mediated nephritis and renal dysfunction, and solid organ transplant rejection.
  - Monitor for early identification and management. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment.
  - Withhold or permanently discontinue LIBTAYO based on the severity of reaction. (2.2)
- Infusion-Related Reactions: Interrupt, slow the rate of infusion, or permanently discontinue based on severity of reaction. (2.2, 5.2)
- Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT): Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after being treated with a PD-1/PD-L1 blocking antibody. (5.3)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use of effective contraception. (5.4, 8.1, 8.3)

### ADVERSE REACTIONS

Most common adverse reactions (incidence  $\geq 20\%$ ) in patients with CSCC or BCC were fatigue, rash, diarrhea, musculoskeletal pain, nausea and pruritus (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Regeneron at 1-877-542-8296 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### USE IN SPECIFIC POPULATIONS

Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 02/2021

## FULL PRESCRIBING INFORMATION: CONTENTS\*

### 1 INDICATIONS AND USAGE

- 1.1 Cutaneous Squamous Cell Carcinoma
- 1.2 Basal Cell Carcinoma

### 2 DOSAGE AND ADMINISTRATION

- 2.1 Recommended Dosage
- 2.2 Dosage Modifications for Adverse Reactions
- 2.3 Preparation and Administration

### 3 DOSAGE FORMS AND STRENGTHS

### 4 CONTRAINDICATIONS

### 5 WARNINGS AND PRECAUTIONS

- 5.1 Severe and Fatal Immune-Mediated Adverse Reactions
- 5.2 Infusion-Related Reactions
- 5.3 Complications of Allogeneic HSCT
- 5.4 Embryo-Fetal Toxicity

### 6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Immunogenicity

### 8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.2 Lactation

### 8.3 Females and Males of Reproductive Potential

### 8.4 Pediatric Use

### 8.5 Geriatric Use

### 11 DESCRIPTION

### 12 CLINICAL PHARMACOLOGY

#### 12.1 Mechanism of Action

#### 12.3 Pharmacokinetics

### 13 NONCLINICAL TOXICOLOGY

#### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

#### 13.2 Animal Toxicology and/or Pharmacology

### 14 CLINICAL STUDIES

#### 14.1 Cutaneous Squamous Cell Carcinoma (CSCC)

#### 14.2 Basal Cell Carcinoma (BCC)

### 16 HOW SUPPLIED/STORAGE AND HANDLING

### 17 PATIENT COUNSELING INFORMATION

\*Sections or subsections omitted from the full prescribing information are not listed.

## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

#### 1.1 Cutaneous Squamous Cell Carcinoma

LIBTAYO is indicated 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.

#### 1.2 Basal Cell Carcinoma

LIBTAYO is indicated for the treatment of patients:

- with locally advanced basal cell carcinoma (laBCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate.
- with metastatic BCC (mBCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate. The mBCC indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for the mBCC indication may be contingent upon verification and description of clinical benefit.

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Recommended Dosage

The recommended dosage of LIBTAYO is 350 mg administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity.

#### 2.2 Dosage Modifications for Adverse Reactions

No dose reduction for LIBTAYO is recommended. In general, withhold LIBTAYO for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue LIBTAYO for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids.

Dosage modifications for LIBTAYO for adverse reactions that require management different from these general guidelines are summarized in Table 1.

**Table 1: Recommended Dosage Modifications for Adverse Reactions**

Adverse Reaction	Severity <sup>a</sup>	Dosage Modifications
<b>Immune-Mediated Adverse Reactions</b> [see <i>Warnings and Precautions (5.1)</i> ]		
Pneumonitis	Grade 2	Withhold <sup>b</sup>
	Grades 3 or 4	Permanently discontinue
Colitis	Grades 2 or 3	Withhold <sup>b</sup>
	Grade 4	Permanently discontinue

<b>Adverse Reaction</b>	<b>Severity<sup>a</sup></b>	<b>Dosage Modifications</b>
Hepatitis with no tumor involvement of the liver	AST or ALT increases to more than 3 and up to 8 times ULN or Total bilirubin increases to more than 1.5 and up to 3 times the ULN	Withhold <sup>b</sup>
	AST or ALT increases to more than 8 times the ULN or Total bilirubin increases to more than 3 times the ULN	Permanently discontinue
Hepatitis with tumor involvement of the liver <sup>c</sup>	Baseline AST or ALT is more than 1 and up to 3 times ULN and increases to more than 5 and up to 10 times ULN or Baseline AST or ALT is more than 3 and up to 5 times ULN and increases to more than 8 and up to 10 times ULN	Withhold <sup>b</sup>
	AST or ALT increases to more than 10 times ULN or Total bilirubin increases to more than 3 times ULN	Permanently discontinue
Endocrinopathies	Grades 3 or 4	Withhold until clinically stable or permanently discontinue depending on severity
Nephritis with Renal Dysfunction	Grade 2 or 3 increased blood creatinine	Withhold <sup>b</sup>
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative Dermatologic Conditions	Suspected SJS, TEN, or DRESS	Withhold <sup>b</sup>
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grade 2, 3 or 4	Permanently discontinue

Adverse Reaction	Severity <sup>a</sup>	Dosage Modifications
Neurological Toxicities	Grade 2	Withhold <sup>b</sup>
	Grades 3 or 4	Permanently discontinue
<b>Other Adverse Reactions</b>		
Infusion-related reactions [ <i>see Warnings and Precautions (5.2)</i> ]	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

ALT=alanine aminotransferase, AST=aspartate aminotransferase, ULN=upper limit of normal, SJS=Stevens-Johnson Syndrome, TEN=toxic epidermal necrolysis, DRESS=Drug Rash with Eosinophilia and Systemic Symptoms

- a. Based on National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0
- b. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.
- c. If AST and ALT are less than or equal to ULN at baseline, withhold or permanently discontinue LIBTAYO based on recommendations for hepatitis with no liver involvement

## 2.3 Preparation and Administration

- Visually inspect for particulate matter and discoloration prior to administration. LIBTAYO is a clear to slightly opalescent, colorless to pale yellow solution that may contain trace amounts of translucent to white particles. Discard the vial if the solution is cloudy, discolored or contains extraneous particulate matter other than trace amounts of translucent to white particles.

### Preparation

- Do not shake.
- Withdraw 7 mL from a vial and dilute with 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP to a final concentration between 1 mg/mL to 20 mg/mL.
- Mix diluted solution by gentle inversion. Do not shake.
- Discard any unused medicinal product or waste material.

### Storage of Infusion Solution

- Store at room temperature up to 25°C (77°F) for no more than 8 hours from the time of preparation to the end of the infusion or at 2°C to 8°C (36°F to 46°F) for no more than 24 hours from the time of preparation to the end of infusion.
- Allow the diluted solution to come to room temperature prior to administration.
- Do not freeze.

### Administration

- Administer by intravenous infusion over 30 minutes through an intravenous line containing a sterile, in-line or add-on 0.2-micron to 5-micron filter.

### 3 DOSAGE FORMS AND STRENGTHS

Injection: 350 mg/7 mL (50 mg/mL), clear to slightly opalescent, colorless to pale yellow solution that may contain trace amounts of translucent to white particles in a single-dose vial.

### 4 CONTRAINDICATIONS

None.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Severe and Fatal Immune-Mediated Adverse Reactions

LIBTAYO is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting PD-1/PD-L1 blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1 blocking antibodies, immune-mediated adverse reactions can also manifest after discontinuation of PD-1/PD-L1 blocking antibodies. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue LIBTAYO depending on severity [*see Dosage and Administration (2.2)*]. In general, if LIBTAYO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids.

Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below.

#### Immune-Mediated Pneumonitis

LIBTAYO can cause immune-mediated pneumonitis. The definition of immune-mediated pneumonitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. In patients treated with other PD-1/PD-L1 blocking

antibodies the incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

Immune-mediated pneumonitis occurred in 3.7% (22/591) of patients receiving LIBTAYO, including fatal (0.3%), Grade 4 (0.3%), Grade 3 (1.0%), and Grade 2 (1.9%) adverse reactions. Pneumonitis led to permanent discontinuation of LIBTAYO in 1.9% of patients and withholding of LIBTAYO in 1.9% of the patients.

Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis resolved in 59% of the 22 patients. Of the 11 patients in whom LIBTAYO was withheld for pneumonitis, 7 reinitiated LIBTAYO after symptom improvement; of these 1/7 (14%) had recurrence of pneumonitis.

### Immune-Mediated Colitis

LIBTAYO can cause immune-mediated colitis. The definition of immune-mediated colitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. The primary component of the immune-mediated colitis was diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1 blocking antibodies. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated colitis occurred in 1.2% (7/591) of patients receiving LIBTAYO, including Grade 3 (0.3%) and Grade 2 (0.7%) adverse reactions. Colitis led to permanent discontinuation of LIBTAYO in 0.2% of patients and withholding of LIBTAYO in 0.7% of patients.

Systemic corticosteroids were required in all patients with colitis. Colitis resolved in 71% of the 7 patients. Of the 4 patients in whom LIBTAYO was withheld for colitis, none reinitiated LIBTAYO.

### Immune-Mediated Hepatitis

LIBTAYO can cause immune-mediated hepatitis. The definition of immune-mediated hepatitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology.

Immune-mediated hepatitis occurred in 1.9% (11/591) of patients receiving LIBTAYO, including fatal (0.2%), Grade 4 (0.2%), and Grade 3 (1.5%) adverse reactions. Hepatitis led to permanent discontinuation of LIBTAYO in 0.8% of patients and withholding of LIBTAYO in 0.8% of patients.

Systemic corticosteroids were required in all patients with hepatitis. Nine percent (9%) of these patients (1/11) required additional immunosuppression with mycophenolate. Hepatitis resolved in 64% of the 11 patients. Of the 5 patients in whom LIBTAYO was withheld for hepatitis, none reinitiated LIBTAYO.

### Immune-Mediated Endocrinopathies

#### *Adrenal Insufficiency*

LIBTAYO can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold LIBTAYO depending on severity [*see Dosage and Administration (2.2)*].

Adrenal insufficiency occurred in 0.5% (3/591) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.3%) adverse reactions. No patient discontinued LIBTAYO due to adrenal insufficiency. LIBTAYO was not withheld in any patient due to adrenal insufficiency.

#### *Hypophysitis*

LIBTAYO can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity [see [Dosage and Administration \(2.2\)](#)].

Hypophysitis occurred in 0.2% (1/591) of patients receiving LIBTAYO, which consisted of 1 patient with Grade 3 hypophysitis.

#### *Thyroid Disorders*

LIBTAYO can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity [see [Dosage and Administration \(2.2\)](#)].

*Thyroiditis:* A single case of Grade 1 thyroiditis was observed in 591 patients receiving LIBTAYO in clinical trials.

*Hyperthyroidism:* Hyperthyroidism occurred in 1.9% (11/591) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.5%) adverse reactions. No patient discontinued treatment due to hyperthyroidism. Hyperthyroidism led to withholding of LIBTAYO in 0.3% of patients.

Systemic corticosteroids were required in 9% (1/11) of patients. Hyperthyroidism resolved in 46% of the 11 patients.

*Hypothyroidism:* Hypothyroidism occurred in 7% (42/591) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (6%) adverse reactions. No patient discontinued due to hypothyroidism. Hypothyroidism led to withholding of LIBTAYO in 0.3% of patients. Systemic corticosteroids were not required in any patient with hypothyroidism. Hypothyroidism resolved in 7% of the 42 patients. The majority of patients with hypothyroidism required long-term thyroid hormone replacement.

Of the 2 patients in whom LIBTAYO was withheld for hypothyroidism, both reinitiated LIBTAYO after symptom improvement; 1 required ongoing hormone replacement therapy; the other did not experience recurrence of hypothyroidism.

#### *Type 1 Diabetes Mellitus, which can present with diabetic ketoacidosis.*

Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold LIBTAYO depending on severity [see [Dosage and Administration \(2.2\)](#)].

Type 1 diabetes mellitus occurred in 0.7% (4/591) of patients, including Grade 4 (0.5%) and Grade 3 (0.2%) adverse reactions. Type 1 diabetes mellitus led to permanent discontinuation of LIBTAYO in 0.2% of patients and withholding of LIBTAYO in 0.3% of patients.

Of the 2 patients in whom LIBTAYO was withheld for Type 1 diabetes mellitus, both reinitiated LIBTAYO and required insulin treatment.

#### Immune-Mediated Nephritis with Renal Dysfunction

LIBTAYO can cause immune-mediated nephritis. The definition of immune-mediated nephritis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology.

Immune-mediated nephritis occurred in 0.5% (3/591) patients receiving LIBTAYO, including Grade 3 (0.3%) and Grade 2 (0.2%) adverse reactions. Nephritis led to permanent discontinuation of LIBTAYO in 0.2% of patients and withholding of LIBTAYO in 0.3% of patients.

Systemic corticosteroids were required in all patients with nephritis. Nephritis resolved in all 3 patients. Of the 2 patients in whom LIBTAYO was withheld for nephritis, none reinitiated LIBTAYO.

#### Immune-Mediated Dermatologic Adverse Reactions

LIBTAYO can cause immune-mediated rash or dermatitis. The definition of immune-mediated dermatologic adverse reaction included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. Exfoliative dermatitis, including Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and DRESS (Drug Rash with Eosinophilia and Systemic Symptoms), has occurred with PD-1/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold or permanently discontinue LIBTAYO depending on severity [*see Dosage and Administration (2.2)*].

Immune-mediated dermatologic adverse reactions occurred in 2.0% (12/591) of patients receiving LIBTAYO, including Grade 3 (1.0%) and Grade 2 (0.8%) adverse reactions. Dermatologic adverse reactions led to permanent discontinuation of LIBTAYO in 0.3% of patients and withholding of LIBTAYO in 1.4% of patients.

Systemic corticosteroids were required in all patients with immune-mediated dermatologic adverse reactions. Immune-mediated dermatologic adverse reactions resolved in 42% of the 12 patients. Of the 8 patients in whom LIBTAYO was withheld for dermatologic adverse reaction, 5 reinitiated LIBTAYO after symptom improvement; of these 60% (3/5) had recurrence of the dermatologic adverse reaction.

#### Other Immune-Mediated Adverse Reactions

The following clinically significant immune-mediated adverse reactions occurred at an incidence of < 1% in 591 patients who received LIBTAYO or were reported with the use of other PD-1/PD-L1 blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.

*Cardiac/Vascular:* Myocarditis, pericarditis, vasculitis



*Nervous System:* Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome / myasthenia gravis (including exacerbation), Guillain-Barre syndrome, nerve paresis, autoimmune neuropathy

*Ocular:* Uveitis, iritis, and other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

*Gastrointestinal:* Pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis, stomatitis

*Musculoskeletal and Connective Tissue:* Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatica

*Endocrine:* Hypoparathyroidism

*Other (Hematologic/Immune):* Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection

## **5.2 Infusion-Related Reactions**

Severe infusion-related reactions (Grade 3) occurred in 0.2% of patients receiving LIBTAYO. Monitor patients for signs and symptoms of infusion-related reactions.

Interrupt or slow the rate of infusion or permanently discontinue LIBTAYO based on severity of reaction [see [Dosage and Administration \(2.2\)](#)].

## **5.3 Complications of Allogeneic HSCT**

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1 blocking antibody. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1 blocking antibody prior to or after an allogeneic HSCT.

## **5.4 Embryo-Fetal Toxicity**

Based on its mechanism of action, LIBTAYO can cause fetal harm when administered to a pregnant woman. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus resulting in fetal death. Advise women of the potential risk to a fetus. Advise females of reproductive potential to

use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose [see *Use in Specific Populations (8.1, 8.3)*].

## 6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling.

- Severe and Fatal Immune-Mediated Adverse Reactions [see *Warnings and Precautions (5.1)*]
- Infusion-Related Reactions [see *Warnings and Precautions (5.2)*]
- Complications of Allogeneic HSCT [see *Warnings and Precautions (5.3)*]

### 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described in Warnings and Precautions reflect exposure to LIBTAYO in 591 patients in two open-label, single-arm, multicohort studies (Study 1423 and Study 1540), including 131 patients with mCSCC (nodal or distant), 88 patients with locally advanced CSCC, and 372 patients with other advanced solid tumors. LIBTAYO as a single agent or in combination with chemotherapy or radiation was administered intravenously at doses of 1 mg/kg every 2 weeks (n=27), 3 mg/kg every 2 weeks (n=470), 3 mg/kg every 3 weeks (n=12), 10 mg/kg every 2 weeks (n=6), 200 mg every 2 weeks (n=20) or 350 mg every 3 weeks (n=56). Among the 591 patients, 47% were exposed for  $\geq 6$  months and 27% were exposed for  $\geq 12$  months.

#### Cutaneous Squamous Cell Carcinoma (CSCC)

The safety of LIBTAYO was evaluated in 219 patients with advanced CSCC (metastatic or locally advanced disease) in Study 1423 and Study 1540 [see *Clinical Studies (14.1)*]. Of these 219 patients, 131 had mCSCC (nodal or distant) and 88 had laCSCC. Patients received LIBTAYO 1 mg/kg every 2 weeks (n=1), 3 mg/kg every 2 weeks (n=162) or 350 mg every 3 weeks (n=56) as an intravenous infusion until disease progression, unacceptable toxicity, or completion of planned treatment. The median duration of exposure was 38 weeks (2 weeks to 110 weeks).

The safety population characteristics were: median age of 72 years (38 to 96 years), 83% male, 96% white, and European Cooperative Oncology Group (ECOG) performance score (PS) of 0 (44%) and 1 (56%).

Serious adverse reactions occurred in 35% of patients. Serious adverse reactions that occurred in at least 2% of patients were pneumonitis, cellulitis, sepsis, and pneumonia.

Permanent discontinuation due to an adverse reaction occurred in 8% of patients. Adverse reactions resulting in permanent discontinuation were pneumonitis, cough, pneumonia, encephalitis, aseptic meningitis, hepatitis, arthralgia, muscular weakness, neck pain, soft tissue necrosis, complex regional pain syndrome, lethargy, psoriasis, rash maculopapular, proctitis, and confusional state.

The most common ( $\geq 20\%$ ) adverse reactions were fatigue, rash, diarrhea, musculoskeletal pain, and nausea. The most common Grade 3 or 4 adverse reactions ( $\geq 2\%$ ) were cellulitis, anemia,

hypertension, pneumonia, musculoskeletal pain, fatigue, pneumonitis, sepsis, skin infection, and hypercalcemia. The most common ( $\geq 4\%$ ) Grade 3 or 4 laboratory abnormalities worsening from baseline were lymphopenia, anemia, hyponatremia, and hypophosphatemia.

Table 2 summarizes the adverse reactions that occurred in  $\geq 10\%$  of patients and Table 3 summarizes Grade 3 or 4 laboratory abnormalities worsening from baseline in  $\geq 1\%$  of patients receiving LIBTAYO.

**Table 2: Adverse Reactions in  $\geq 10\%$  of Patients with Advanced CSCC Receiving LIBTAYO in Study 1423 and Study 1540**

Adverse Reactions	LIBTAYO N = 219	
	All Grades %	Grades 3-4 %
<b>General and Administration Site</b>		
Fatigue <sup>a</sup>	34	3
<b>Skin and Subcutaneous Tissue</b>		
Rash <sup>b</sup>	31	1
Pruritus <sup>c</sup>	18	0
<b>Gastrointestinal</b>		
Diarrhea <sup>d</sup>	25	0.5
Nausea	21	0
Constipation	13	0.5
Vomiting	10	0.5
<b>Musculoskeletal and Connective Tissue</b>		
Musculoskeletal pain <sup>e</sup>	24	3
Arthralgia	11	1
<b>Respiratory</b>		
Cough <sup>f</sup>	14	0
<b>Hematology</b>		
Anemia	11	4
<b>Endocrine</b>		
Hypothyroidism	10	0
<b>Metabolism and Nutrition</b>		
Decreased appetite	10	0

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v.4.03

a. Composite term includes fatigue and asthenia

- b. Composite term includes rash, rash maculopapular, erythema, dermatitis, dermatitis bullous, rash generalized, pemphigoid, rash erythematous, rash macular, rash pruritic, drug eruption, psoriasis, and skin reaction
- c. Composite term includes pruritus and pruritus allergic
- d. Composite term includes diarrhea and colitis
- e. Composite term includes back pain, pain in extremity, myalgia, musculoskeletal pain, and neck pain
- f. Composite term includes cough and upper airway cough syndrome

**Table 3: Grade 3 or 4 Laboratory Abnormalities Worsening from Baseline in  $\geq 1\%$  of Patients with Advanced CSCC Receiving LIBTAYO in Study 1423 and Study 1540**

Laboratory Abnormality	Grade 3-4 (%) <sup>a</sup>
<b>Chemistry</b>	
Increased aspartate aminotransferase	2
Increased INR	2
<b>Hematology</b>	
Lymphopenia	9
Anemia	5
<b>Electrolytes</b>	
Hyponatremia	5
Hypophosphatemia	4
Hypercalcemia	2

Toxicity graded per NCI CTCAE v. 4.03

- a. Percentages are based on the number of patients with at least 1 post-baseline value available for that parameter

### Basal Cell Carcinoma (BCC)

The safety of LIBTAYO was evaluated in 132 patients with advanced BCC (mBCC N=48, laBCC N=84) in an open-label, single-arm trial (Study 1620) [see *Clinical Studies (14.2)*]. Patients received LIBTAYO 350 mg every 3 weeks as an intravenous infusion for up to 93 weeks or until disease progression or unacceptable toxicity. The median duration of exposure was 42 weeks (range: 2.1 weeks to 94 weeks).

The safety population characteristics were: median age of 68 years (38 to 90 years), 67% male, 74% White, and ECOG performance score (PS) of 0 (62%) and 1 (38%).

Serious adverse reactions occurred in 32% of patients. Serious adverse reactions that occurred in > 1.5% (at least 2 patients) were urinary tract infection, colitis, acute kidney injury, adrenal insufficiency, anemia, infected neoplasm, and somnolence. Fatal adverse reactions occurred in 1.5% of patients who received LIBTAYO, including acute kidney injury and cachexia.

Permanent discontinuation of LIBTAYO due to an adverse reaction occurred in 13% of patients. Adverse reactions resulting in permanent discontinuation of LIBTAYO in > 1.5% (at least 2 patients) were colitis and general physical health deterioration.

Dosage delays of LIBTAYO due to an adverse reaction occurred in 34% of patients. Adverse reactions which required dosage delay in > 2% of patients (at least 3 patients) included blood creatinine increased, diarrhea, colitis, fatigue, headache, pneumonitis, and urinary tract infection.

The most common adverse reactions reported in at least 15% of patients were fatigue, musculoskeletal pain, diarrhea, rash, pruritus, and upper respiratory tract infection.

The most common Grade 3 or 4 adverse reactions (> 2%) were hypertension, colitis, fatigue, urinary tract infection, pneumonia, increased blood pressure, hypokalemia and visual impairment. The most common (> 3%) laboratory abnormality worsening from baseline to Grade 3 or 4 was hyponatremia.

Table 4 summarizes the adverse reactions that occurred in ≥ 10% of patients and Table 5 summarizes Grade 3 or 4 laboratory abnormalities worsening from baseline in ≥ 1% of patients receiving LIBTAYO.

**Table 4: Adverse Reactions in ≥ 10% of Patients with Advanced BCC Receiving LIBTAYO in Study 1620**

Adverse Reactions	LIBTAYO N = 132	
	All Grades %	Grades 3-4 %
<b>General disorders and administration site conditions</b>		
Fatigue <sup>a</sup>	49	3.8
<b>Musculoskeletal and connective tissue disorders</b>		
Musculoskeletal pain <sup>b</sup>	33	1.5
<b>Gastrointestinal disorders</b>		
Diarrhea	25	0
Nausea	12	0.8
Constipation	11	0.8
<b>Skin and subcutaneous tissue disorders</b>		
Rash <sup>c</sup>	22	0.8
Pruritus	20	0
<b>Infections and infestations</b>		
Upper respiratory tract infection <sup>d</sup>	15	0
Urinary tract infection	12	2.3
<b>Metabolism and nutrition disorders</b>		
Decreased appetite	14	1.5
<b>Blood and lymphatic system disorders</b>		
Anemia	13	0.8
<b>Nervous system disorders</b>		
Headache	12	1.5
<b>Respiratory, thoracic and mediastinal disorders</b>		
Dyspnea <sup>e</sup>	11	0
<b>Vascular disorders</b>		
Hypertension <sup>f</sup>	11	4.5

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v.4.03

- Composite term includes fatigue, asthenia, and malaise
- Composite term includes arthralgia, back pain, myalgia, pain in extremity, musculoskeletal pain, neck pain, musculoskeletal stiffness, musculoskeletal chest pain, musculoskeletal discomfort, and spinal pain
- Composite term includes rash maculo-papular, rash, dermatitis, dermatitis acneiform, erythema, rash pruritic, dermatitis bullous, dyshidrotic eczema, pemphigoid, rash erythematous, and urticaria

- d. Composite term includes upper respiratory tract infection, nasopharyngitis, rhinitis, sinusitis, pharyngitis, respiratory tract infection, and viral upper respiratory tract infection
- e. Composite term includes dyspnea and dyspnea exertional
- f. Composite term includes hypertension and hypertensive crisis

**Table 5: Grade 3 or 4 Laboratory Abnormalities Worsening from Baseline in  $\geq 1\%$  of Patients with Advanced BCC Receiving LIBTAYO in Study 1620**

Laboratory Abnormality	Grade 3-4 (%) <sup>a</sup>
<b>Electrolytes</b>	
Hyponatremia	3.1
Hypokalemia	1.5
<b>Coagulation</b>	
Activated partial thromboplastin time prolonged	2.3
<b>Hematology</b>	
Lymphocyte count decreased	2.3

Toxicity graded per NCI CTCAE v. 4.03

a. Percentages are based on the number of patients with at least 1 post-baseline value available for that parameter

## 6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to cemiplimab-rwlc in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

Anti-drug antibodies (ADA) were tested in 823 patients who received LIBTAYO. The incidence of cemiplimab-rwlc treatment-emergent ADAs was 2.2% using an electrochemiluminescent (ECL) bridging immunoassay; 0.4% were persistent ADA responses. In the patients who developed anti-cemiplimab-rwlc antibodies, there was no evidence of an altered pharmacokinetic profile of cemiplimab-rwlc.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Risk Summary

Based on its mechanism of action, LIBTAYO can cause fetal harm when administered to a pregnant woman [see *Clinical Pharmacology (12.1)*]. There are no available data on the use of LIBTAYO in pregnant women. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus resulting in fetal death (see *Data*). Human IgG4 immunoglobulins (IgG4) are known to cross the placenta; therefore, LIBTAYO has the potential to be transmitted from the mother to the developing fetus. Advise women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

## Data

### *Animal Data*

Animal reproduction studies have not been conducted with LIBTAYO to evaluate its effect on reproduction and fetal development. A central function of the PD-1/PD-L1 pathway is to preserve pregnancy by maintaining maternal immune tolerance to the fetus. In murine models of pregnancy, blockade of PD-L1 signaling has been shown to disrupt tolerance to the fetus and to result in an increase in fetal loss; therefore, potential risks of administering LIBTAYO during pregnancy include increased rates of abortion or stillbirth. As reported in the literature, there were no malformations related to the blockade of PD-1/PD-L1 signaling in the offspring of these animals; however, immune-mediated disorders occurred in PD-1 and PD-L1 knockout mice. Based on its mechanism of action, fetal exposure to cemiplimab-rwlc may increase the risk of developing immune-mediated disorders or altering the normal immune response.

## **8.2 Lactation**

### Risk Summary

There is no information regarding the presence of cemiplimab-rwlc in human milk, or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO.

## **8.3 Females and Males of Reproductive Potential**

### Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating LIBTAYO [*see Use in Specific Populations (8.1)*].

### Contraception

LIBTAYO can cause fetal harm when administered to a pregnant woman [*see Use in Specific Populations (8.1)*].

### *Females*

Advise females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose.

## **8.4 Pediatric Use**

The safety and effectiveness of LIBTAYO have not been established in pediatric patients.

## **8.5 Geriatric Use**

Of the 219 patients with mCSCC or laCSCC who received LIBTAYO in clinical studies, 34% were 65 years up to 75 years and 41% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

Of the 132 patients with BCC who received LIBTAYO in Study 1620, 27% were 65 years up to 75 years, and 32% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

## 11 DESCRIPTION

Cemiplimab-rwlc is a human programmed death receptor-1 (PD-1) blocking antibody. Cemiplimab-rwlc is a recombinant human IgG4 monoclonal antibody that binds to PD-1 and blocks its interaction with PD-L1 and PD-L2. Cemiplimab-rwlc is produced by recombinant DNA technology in Chinese hamster ovary (CHO) cell suspension culture. Cemiplimab-rwlc has an approximate molecular weight of 146 kDa.

LIBTAYO (cemiplimab-rwlc) injection for intravenous use is a sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution with a pH of 6. The solution may contain trace amounts of translucent to white particles.

Each vial contains 350 mg of cemiplimab-rwlc. Each mL contains cemiplimab-rwlc 50 mg, L-histidine (0.74 mg), L-histidine monohydrochloride monohydrate (1.1 mg), sucrose (50 mg), L-proline (15 mg), Polysorbate 80 (2 mg), and Water for Injection, USP.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Binding of the PD-1 ligands PD-L1 and PD-L2, to the PD-1 receptor found on T cells, inhibits T-cell proliferation and cytokine production. Upregulation of PD-1 ligands occurs in some tumors and signaling through this pathway can contribute to inhibition of active T-cell immune surveillance of tumors.

Cemiplimab-rwlc is a recombinant human immunoglobulin G4 (IgG4) monoclonal antibody that binds to PD-1 and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response. In syngeneic mouse tumor models, blocking PD-1 activity resulted in decreased tumor growth.

### 12.3 Pharmacokinetics

Cemiplimab-rwlc pharmacokinetic data were collected in 1062 patients with various solid tumors in a population pharmacokinetic analysis. The pharmacokinetics of cemiplimab-rwlc were linear and dose proportional in the dose range of 1 mg/kg to 10 mg/kg LIBTAYO administered intravenously every 2 weeks.

At 350 mg every 3 weeks, the mean cemiplimab-rwlc concentrations (coefficient of variation, CV%) at steady-state ranged between a minimum concentration of 61 mg/L (45%) and a maximum concentration of 171 mg/L (28%). Steady-state exposure is achieved after 4 months of treatment.

In patients with CSCC, cemiplimab-rwlc steady-state exposure at 350 mg every 3 weeks was comparable to the exposure at 3 mg/kg every 2 weeks.

#### Distribution

The volume of distribution of cemiplimab-rwlc at steady state is 5.3 L (26%).

#### Elimination

Cemiplimab-rwlc clearance (CV%) after the first dose is 0.29 L/day (33%) and decreases over time by 29%, resulting in a steady-state clearance ( $CL_{ss}$ ) (CV%) of 0.20 L/day (40%). The elimination half-life (CV%) at steady state is 20.3 days (29%).



## Specific Populations

The following factors have no clinically important effect on the exposure of cemiplimab-rwlc: age (27 to 96 years), sex, body weight (31 to 172 kg), cancer type, albumin level (20 to 93 g/L), renal function (creatinine clearance determined by Cockcroft-Gault 21 mL/min or greater) and hepatic function (total bilirubin greater than 1.0 times up to 3.0 times the ULN). Race [White (N=931), Black (N=47), Asian (N=21)] appears to have no clinically important effect on the exposure of cemiplimab-rwlc. LIBTAYO has not been studied in patients with severe hepatic impairment.

## **13 NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

No studies have been performed to assess the potential of cemiplimab-rwlc for carcinogenicity or genotoxicity.

In a 3-month repeat-dose toxicology study in sexually mature cynomolgus monkeys, there were no cemiplimab-rwlc-related effects on fertility parameters (menstrual cycle, semen analysis, or testicular measurements) or in male or female reproductive organs at doses up to the highest dose tested, 50 mg/kg/week (approximately 5.5 to 25.5 times the human exposure based on AUC at the clinical dose of 350 mg once every 3 weeks).

### **13.2 Animal Toxicology and/or Pharmacology**

In animal models, inhibition of PD-L1/PD-1 signaling increased the severity of some infections and enhanced inflammatory responses. *M. tuberculosis*-infected PD-1 knockout mice exhibit markedly decreased survival compared with wild-type controls, which correlated with increased bacterial proliferation and inflammatory responses in these animals. PD-L1 and PD-1 knockout mice and mice receiving PD-L1 blocking antibody have also shown decreased survival following infection with lymphocytic choriomeningitis virus.

## **14 CLINICAL STUDIES**

### **14.1 Cutaneous Squamous Cell Carcinoma (CSCC)**

The efficacy of LIBTAYO in 219 patients with metastatic (nodal or distant) cutaneous squamous cell carcinoma (mCSCC) or locally advanced CSCC (laCSCC) who were not candidates for curative surgery or curative radiation was evaluated in two open-label, multi-center, non-randomized, multicohort studies: Study 1423 (NCT02383212) and Study 1540 (NCT02760498). Both studies excluded patients with autoimmune disease that required systemic therapy with immunosuppressant agents within 5 years; history of solid organ transplant; prior treatment with anti-PD-1/PD-L1 blocking antibodies or other immune checkpoint inhibitor therapy; infection with HIV, hepatitis B or hepatitis C; or ECOG PS  $\geq$  2.

Patients received LIBTAYO 3 mg/kg intravenously every 2 weeks for up to 48 weeks in Study 1423 or up to 96 weeks in Study 1540. An additional cohort of patients in Study 1540 received 350 mg every 3 weeks for up to 54 weeks. Treatment continued until progression of disease, unacceptable toxicity, or completion of planned treatment. Tumor response assessments were performed every 8 or 9 weeks. The major efficacy outcome measures were confirmed objective response rate (ORR), defined as complete response (CR) plus partial response (PR) as assessed by independent central review (ICR), and ICR-assessed duration of response (DOR).

For patients with mCSCC without externally visible target lesions, ORR was determined by Response Evaluation Criteria in Solid Tumors (RECIST 1.1). For patients with externally visible target lesions (laCSCC and mCSCC), ORR was determined by a composite endpoint that integrated ICR assessments of radiologic data (RECIST 1.1) and digital medical photography (WHO criteria).

*Study 1540*

Among the 193 patients with advanced CSCC enrolled in Study 1540 who received LIBTAYO at either 3 mg/kg every 2 weeks or 350 mg every three weeks, 115 had mCSCC and 78 had laCSCC. The median age was 72 years (38 to 96 years); 83% were male; 97% were White; 45% had ECOG PS 0 and 55% had ECOG PS 1; 34% received at least one prior anti-cancer systemic therapy; 90% received prior cancer-related surgery; and 68% received prior radiotherapy. Among patients with mCSCC, 77% had distant metastases and 23% had only nodal metastases.

For the responding patients presented in [Table 6](#) below, the median time to response was 1.9 months (range: 1.7 to 9.1 months).

Efficacy results in patients who received 3 mg/kg every 2 weeks are presented in [Table 6](#).

**Table 6: Efficacy Results for Study 1540 in CSCC: 3 mg/kg every 2 weeks**

<b>Efficacy Endpoints<sup>a</sup></b>	<b>Metastatic CSCC LIBTAYO 3 mg/kg every 2 weeks</b>	<b>Locally Advanced CSCC LIBTAYO 3 mg/kg every 2 weeks</b>	<b>Combined CSCC</b>
	<b>N = 59</b>	<b>N = 78</b>	<b>N = 137</b>
<b>Confirmed Objective Response Rate (ORR)</b>			
ORR (95% CI)	49% (36, 63)	44% (32, 55)	46% (37, 55)
Complete response (95% CI) <sup>b</sup>	17% (8, 29)	13% (6, 22)	15% (9, 22)
Partial response (95% CI)	32% (21, 46)	31% (21, 42)	31% (24, 40)
<b>Duration of Response (DOR)</b>			
Median DOR in months (Range)	NR (2.8 – 21.6+)	NR (1.9 – 24.2+)	NR (1.9 – 24.2+)
Patients with observed DOR ≥ 6 months, n (%) <sup>c</sup>	27 (93%)	23 (68%)	50 (79%)
Patients with observed DOR ≥ 12 months, n (%) <sup>c</sup>	22 (76%)	12 (35%)	34 (54%)

CI: confidence interval; NR: Not reached; +: Denotes ongoing at last assessment

- a. Median duration of follow up: mCSCC: 16.5 months; laCSCC: 9.3 months; combined CSCC: 11.1 months
- b. Only includes patients with complete healing of prior cutaneous involvement; laCSCC patients in Study 1540 required biopsy to confirm CR
- c. The numerator includes the number of patients whose observed DOR reached at least the specified times of 6 or 12 months. Patients who did not have the opportunity to reach the specified timepoint were included in the denominator only

#### *Study 1540: 350 mg every 3 weeks*

In an additional cohort in Study 1540, 56 patients received cemiplimab-rwlc at a dose of 350 mg intravenously every 3 weeks for up to 54 weeks. With a median duration of follow-up of 8.0 months, the confirmed ORR was 41% (95% CI: 28, 55), and 65% of responders had a DOR  $\geq$  6 months.

#### *Study 1423*

Among 26 CSCC patients in Study 1423, 16 had mCSCC and 10 had laCSCC. The median age was 73 years (52 to 88 years); 81% of patients were male; 92% of patients were White; the ECOG PS was 0 (38%) and 1 (62%); 58% of patients had received at least 1 prior anti-cancer systemic therapy; 92% of patients had received prior cancer-related surgery and 81% had received prior radiotherapy. One patient in the mCSCC group was dosed at 1 mg/kg. The rest received 3 mg/kg every 2 weeks.

With a median duration of follow-up of 13.3 months, the confirmed ORR was 50% (95% CI: 30, 70); all responses were PRs. The median time to response was 1.9 months (range: 1.7 to 7.3 months) and 85% of responders had a DOR  $\geq$  6 months.

## **14.2 Basal Cell Carcinoma (BCC)**

The efficacy of LIBTAYO in 112 patients with advanced basal cell carcinoma (BCC) [unresectable locally advanced (laBCC) or metastatic (nodal or distant) (mBCC)] who had progressed on hedgehog pathway inhibitor (HHI) therapy, had not had an objective response after 9 months on HHI therapy, or were intolerant of prior HHI therapy was evaluated in Study 1620 (NCT03132636), an open-label, multi-center, non-randomized study. The study excluded patients with autoimmune disease that required systemic therapy with immunosuppressant agents within 5 years; history of solid organ transplant; prior treatment with anti-PD-1/PD-L1 therapy or other immune checkpoint inhibitor therapy; infection with HIV, hepatitis B or hepatitis C; or ECOG performance score (PS)  $\geq$  2.

Patients received LIBTAYO 350 mg every 3 weeks for up to 93 weeks until disease progression, unacceptable toxicity, or completion of planned treatment. Tumor assessments were performed every 9 weeks for the first 45 weeks of treatment and every 12 weeks thereafter. The major efficacy outcome measures were confirmed objective response rate (ORR) and duration of response (DOR) as assessed by independent central review (ICR). For patients with mBCC without externally visible target lesions, ORR was determined by Response Evaluation Criteria in Solid Tumors (RECIST 1.1). For patients with externally visible target lesions (laBCC and mBCC), ORR was determined by a composite endpoint that integrated ICR assessments of radiologic data (RECIST 1.1) and digital medical photography (WHO criteria).

A total of 112 patients with advanced BCC were included in the efficacy analysis of Study 1620. Of these, 25% had mBCC and 75% had laBCC. In patients with laBCC, the median age was 70 years (42 to 89 years); 67% were male; 68% were White; 61% had ECOG PS 0 and 39% had

ECOG PS 1; 83% had received at least 1 prior cancer-related surgery; and 50% had received prior radiotherapy. In patients with mBCC, the median age was 65.5 years (38 to 90 years); 82% were male; 79% were White; 57% had ECOG PS 0 and 43% had ECOG PS 1; 82% had received at least 1 prior cancer-related surgery; and 61% had received prior radiotherapy. Among patients with mBCC, 32% had distant metastases only, 14% had nodal disease only, and 54% had both distant and nodal disease.

Efficacy results are presented in [Table 7](#). For the responding patients, the median time to response was 3.2 months (range 2.1 to 10.5 months) for the mBCC group and 4.2 months (range 2.1 to 13.4 months) for the laBCC group.

**Table 7: Efficacy Results for Study 1620 in BCC**

Efficacy Endpoints <sup>a</sup>	Metastatic BCC	Locally Advanced BCC
	N = 28	N = 84
<b>Confirmed Objective Response Rate (ORR)</b>		
ORR, n (%) (95% CI)	6 (21%) (8, 41)	24 (29%) (19, 40)
Complete response, n (%)	0	5 (6%)
Partial response, n (%)	6 (21%)	19 (23%)
<b>Duration of Response (DOR)</b>		
Median DOR in months (Range)	NR (9.0 - 23.0+)	NR (2.1 - 21.4+)
Patients with observed DOR ≥ 6 months, n (%)	6 (100%)	19 (79.2%)

CI: confidence interval; NR: Not reached; +: Denotes ongoing at last assessment

a. Median duration of follow up: mBCC 9.5 months; laBCC 15.1 months

## 16 HOW SUPPLIED/STORAGE AND HANDLING

LIBTAYO (cemiplimab-rwlc) injection is a clear to slightly opalescent, colorless to pale yellow solution that may contain trace amounts of translucent to white particles. It is supplied in a carton containing 1 single-dose vial of:

- 350 mg/7 mL (50 mg/mL) (NDC 61755-008-01)

Store in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton. Protect from light. Do not freeze or shake.

## 17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

### Immune-Mediated Adverse Reactions

Advise patients that LIBTAYO can cause immune-mediated adverse reactions including the following [*see Warnings and Precautions (5.1)*]:

- Pneumonitis: Advise patients to contact their healthcare provider immediately for signs or symptoms of pneumonitis, including new or worsening symptoms of cough, chest pain, or shortness of breath.
- Colitis: Advise patients to contact their healthcare provider immediately for signs or symptoms of colitis, including diarrhea, blood or mucus in stools, or severe abdominal pain.
- Hepatitis: Advise patients to contact their healthcare provider immediately for signs or symptoms of hepatitis.
- Endocrinopathies: Advise patients to contact their healthcare provider immediately for signs or symptoms of hypothyroidism, hyperthyroidism, adrenal insufficiency, hypophysitis, or type 1 diabetes mellitus.
- Nephritis: Advise patients to contact their healthcare provider immediately for signs or symptoms of nephritis.
- Dermatologic Adverse Reactions: Advise patients to contact their healthcare provider immediately if they develop a new rash.

#### Infusion-Related Reactions

Advise patients to contact their healthcare provider immediately for signs or symptoms of infusion-related reactions [see *Warnings and Precautions (5.2)*].

#### Complications of Allogeneic HSCT or Solid Organ Transplant Rejection

Advise patients to contact their healthcare provider immediately if they develop signs or symptoms of post-allogeneic HSCT complications or of solid organ transplant rejection [see *Warnings and Precautions (5.1, 5.3)*].

#### Embryo-Fetal Toxicity

Advise females of reproductive potential that LIBTAYO can cause harm to a fetus and to inform their healthcare provider of a known or suspected pregnancy [see *Warnings and Precautions (5.4) and Use in Specific Populations (8.1, 8.3)*].

Advise females of reproductive potential to use effective contraception during treatment and for at least 4 months after the last dose of LIBTAYO [see *Use in Specific Populations (8.3)*].

#### Lactation

Advise female patients not to breastfeed while taking LIBTAYO and for at least 4 months after the last dose [see *Use in Specific Populations (8.2)*].

## **REGENERON**

Manufactured by:

Regeneron Pharmaceuticals, Inc.  
777 Old Saw Mill River Road  
Tarrytown, NY 10591-6707  
U.S. License No. 1760

Marketed by:  
Regeneron Pharmaceuticals, Inc. (Tarrytown, NY 10591) and  
sanofi-aventis U.S. LLC (Bridgewater, NJ 08807)  
©2021 Regeneron Pharmaceuticals, Inc. / sanofi-aventis U.S. LLC.

All rights reserved.

**MEDICATION GUIDE**

LIBTAYO® (Lib-TIE-oh)  
(cemiplimab-rwlc)  
injection

**What is the most important information I should know about LIBTAYO?**

LIBTAYO is a medicine that may treat certain types of skin cancer by working with your immune system. LIBTAYO can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen anytime during treatment or even after your treatment has ended.

**Call or see your healthcare provider right away if you develop any new or worsening signs or symptoms, including:**

**Lung problems.**

- cough
- shortness of breath
- chest pain

**Intestinal problems.**

- diarrhea (loose stools) or more frequent bowel movements than usual
- stools that are black, tarry, sticky, or have blood or mucus
- severe stomach-area (abdomen) pain or tenderness

**Liver problems.**

- yellowing of your skin or the whites of your eyes
- severe nausea or vomiting
- pain on the right side of your stomach-area (abdomen)
- dark urine (tea colored)
- bleeding or bruising more easily than normal

**Hormone gland problems.**

- headache that will not go away or unusual headaches
- eye sensitivity to light
- eye problems
- rapid heartbeat
- increased sweating
- extreme tiredness
- weight gain or weight loss
- feeling more hungry or thirsty than usual
- urinating more often than usual
- hair loss
- feeling cold
- constipation
- your voice gets deeper
- dizziness or fainting
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

**Kidney problems.**

- decrease in your amount of urine
- blood in your urine
- swelling of your ankles
- loss of appetite

**Skin problems.**

- rash
- itching
- skin blistering or peeling
- painful sores or ulcers in mouth or nose, throat, or genital area
- fever or flu-like symptoms
- swollen lymph nodes

**Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with LIBTAYO. Call or see your healthcare provider right away for any new or worsening signs or symptoms which may include:**

- chest pain, irregular heartbeat, shortness of breath or swelling of ankles
- confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs

- double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight
- persistent or severe muscle pain or weakness, muscle cramps
- low red blood cells, bruising

**Infusion reactions that can sometimes be severe.** Signs and symptoms of infusion reactions may include:

- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing
- dizziness
- feel like passing out
- fever
- back or neck pain
- facial swelling

**Rejection of a transplanted organ.** Your healthcare provider should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.

**Complications, including graft-versus-host disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic).** These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with LIBTAYO. Your healthcare provider will monitor you for these complications.

**Getting medical treatment right away may help keep these problems from becoming more serious.** Your healthcare provider will check you for these problems during your treatment with LIBTAYO. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may also need to delay or completely stop treatment with LIBTAYO if you have severe side effects.

### What is LIBTAYO?

LIBTAYO is a prescription medicine used to treat people with:

- a type of skin cancer called cutaneous squamous cell carcinoma (CSCC). LIBTAYO may be used to treat CSCC that has spread or cannot be cured by surgery or radiation.
- a type of skin cancer called basal cell carcinoma (BCC). LIBTAYO may be used when your BCC:
  - cannot be removed by surgery (locally advanced BCC) and you have received treatment with a hedgehog pathway inhibitor (HHI), or if you cannot receive treatment with a HHI.
  - has spread (metastatic BCC) and you have received treatment with a HHI, or if you cannot receive treatment with a HHI.

It is not known if LIBTAYO is safe and effective in children.

**Before you receive LIBTAYO, tell your healthcare provider about all your medical conditions, including if you:**

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- have received an organ transplant
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are pregnant or plan to become pregnant. LIBTAYO can harm your unborn baby.

**Females who are able to become pregnant:**

- Your healthcare provider will give you a pregnancy test before you start treatment with LIBTAYO.
- You should use an effective method of birth control during your treatment and for at least 4 months after the last dose of LIBTAYO. Talk to your healthcare provider about birth control methods that you can use during this time.
- Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with LIBTAYO.
- are breastfeeding or plan to breastfeed. It is not known if LIBTAYO passes into your breast milk. Do not breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO.

**Tell your healthcare provider about all the medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements.



**How will I receive LIBTAYO?**

- Your healthcare provider will give you LIBTAYO into your vein through an intravenous (IV) line over 30 minutes.
- LIBTAYO is usually given every 3 weeks.
- Your healthcare provider will decide how many treatments you will need.
- Your healthcare provider will do blood tests to check you for side effects.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

**What are the possible side effects of LIBTAYO?****LIBTAYO can cause serious side effects, including:**

- See **“What is the most important information I should know about LIBTAYO?”**

The most common side effects of LIBTAYO include tiredness, rash, diarrhea, muscle or bone pain, nausea, and itching. These are not all the possible side effects of LIBTAYO.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**General information about the safe and effective use of LIBTAYO.**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about LIBTAYO, talk with your healthcare provider. You can ask your healthcare provider for information about LIBTAYO that is written for health professionals.

**What are the ingredients of LIBTAYO?**

Active ingredient: cemiplimab-rwlc

Inactive ingredients: L-histidine, L-histidine monohydrochloride monohydrate, sucrose, L-proline, Polysorbate 80, and Water for Injection, USP.

Manufactured by: Regeneron Pharmaceuticals, Inc. 777 Old Saw Mill River Road Tarrytown, NY 10591-6707 U.S. License No. 1760

Marketed by: Regeneron Pharmaceuticals, Inc. (Tarrytown, NY 10591) and sanofi-aventis U.S. LLC (Bridgewater, NJ 08807)

For more information, call 1-877-542-8296

©2021 Regeneron Pharmaceuticals, Inc/sanofi-aventis U.S. LLC.

All rights reserved.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Revised: February 2021