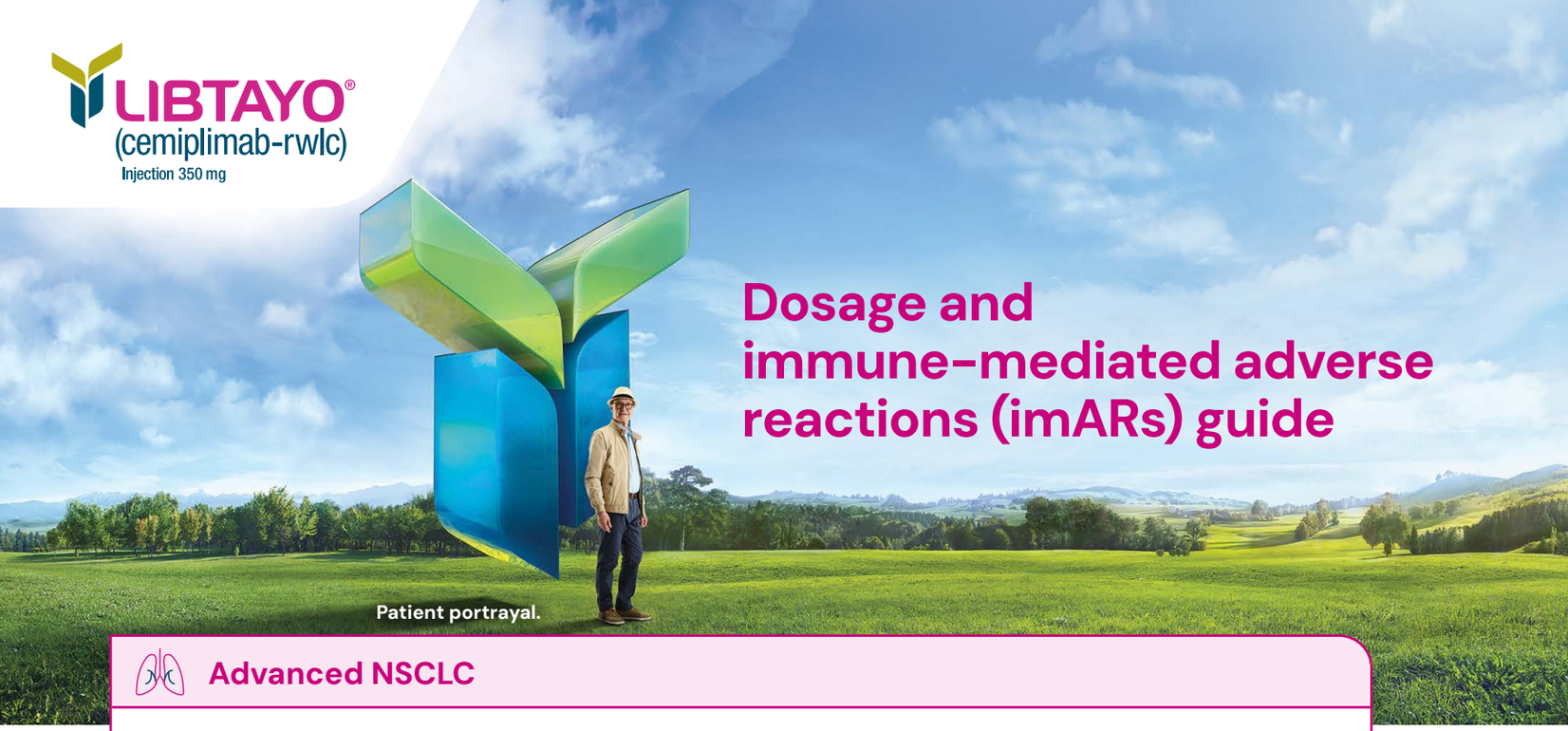
LIBTAYO®
(cemiplimab-rwlc)
Injection 350 mg



Dosage and immune-mediated adverse reactions (imARs) guide

Advanced NSCLC

LIBTAYO in combination with platinum-based chemotherapy

LIBTAYO in combination with platinum-based chemotherapy is indicated for the first-line treatment of adult patients with non–small cell lung cancer (NSCLC) with no EGFR, ALK or ROS1 aberrations and is[1]:

- Locally advanced where patients are not candidates for surgical resection or definitive chemoradiation OR
- Metastatic

LIBTAYO as a single agent

LIBTAYO as a single agent is indicated 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[1]:

- Locally advanced where patients are not candidates for surgical resection or definitive chemoradiation OR
- Metastatic

Advanced CSCC

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]

Advanced BCC

LIBTAYO is indicated for the treatment of patients with locally advanced or metastatic basal cell carcinoma (laBCC or mBCC) who have been previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate.[1]

ALK=anaplastic lymphoma kinase; EGFR=epidermal growth factor receptor; FDA=Food and Drug Administration; PD-L1=programmed death-ligand 1; ROS1=ROS proto-oncogene 1, receptor tyrosine kinase.

Important Safety Information

Warnings and Precautions

Severe and Fatal Immune-Mediated Adverse Reactions

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue at any time after starting treatment. While immune-mediated adverse reactions usually occur during treatment, they can also occur after discontinuation. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously. Early identification and management are essential to ensuring safe use of PD-1/PD-L1–blocking antibodies. The definition of immune-mediated adverse reactions included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. 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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Withhold or permanently discontinue LIBTAYO depending on severity of the adverse reaction (see Section 2 Dosage and Administration in the accompanying Full Prescribing Information). 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.

The incidence and severity of immune-mediated adverse reactions were similar when LIBTAYO was administered as a single agent or in combination with chemotherapy.

Immune-mediated pneumonitis: LIBTAYO can cause immune-mediated pneumonitis. 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 2.6% (33/1281) of patients receiving LIBTAYO, including Grade 4 (0.3%), Grade 3 (0.6%), and Grade 2 (1.6%). Pneumonitis led to permanent discontinuation in 1.3% of patients and withholding of LIBTAYO in 1.4% of patients. Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis resolved in 61% of the 33 patients. Of the 18 patients in whom LIBTAYO was withheld, 10 reinitiated after symptom improvement; of these, 4/10 (40%) had recurrence of pneumonitis.

Immune-mediated colitis: LIBTAYO can cause immune-mediated colitis. The primary component of 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 immune-mediated colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 2% (25/1281) of patients receiving LIBTAYO, including Grade 3 (0.8%) and Grade 2 (0.9%). Colitis led to permanent discontinuation in 0.4% of patients and withholding of LIBTAYO in 1.2% of patients. Systemic corticosteroids were required in all patients with colitis. Colitis resolved in 56% of the 25 patients. Of the 16 patients in whom LIBTAYO was withheld, 6 reinitiated LIBTAYO after symptom improvement; of these, 4/6 (67%) had recurrence

Immune-mediated hepatitis: LIBTAYO can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 2.4% (31/1281) of patients receiving LIBTAYO, including fatal (<0.1%), Grade 4 (0.3%), Grade 3 (1.6%), and Grade 2 (0.2%). Hepatitis led to permanent discontinuation of LIBTAYO in 1.4% of patients and withholding of LIBTAYO in 0.7% of patients. Systemic corticosteroids were required in all patients with hepatitis. Additional immunosuppression with mycophenolate was required in 13% (4/31) of these patients. Hepatitis resolved in 39% of the 31 patients. Of the 9 patients in whom LIBTAYO was withheld, 5 reinitiated LIBTAYO after symptom improvement; of these, 1/5 (20%) had recurrence.

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. Adrenal insufficiency occurred in 0.5% (6/1281) of patients receiving LIBTAYO, including Grade 3 (0.5%). Adrenal insufficiency led to permanent discontinuation of LIBTAYO in 1 (<0.1%) patient. LIBTAYO was withheld in 1 (<0.1%) patient due to adrenal insufficiency and not reinitiated. Systemic corticosteroids were required in 83% (5/6) patients with adrenal insufficiency; of these, the majority remained on systemic corticosteroids. Adrenal insufficiency had resolved in 17% of the 6 patients
- **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 depending on severity. Hypophysitis occurred in 0.5% (7/1281) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.3%) adverse reactions. Hypophysitis led to permanent discontinuation of LIBTAYO in 1 (<0.1%) patient and withholding of LIBTAYO in 2 (0.2%) patients. Systemic corticosteroids were required in 86% (6/7) of patients with hypophysitis. Hypophysitis resolved in 14% of the 7 patients. Of the 2 patients in whom LIBTAYO was withheld for hypophysitis, none of the patients reinitiated
- **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

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Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

- **Thyroiditis:** Thyroiditis occurred in 0.6% (8/1281) of patients receiving LIBTAYO, including Grade 2 (0.3%) adverse reactions. No patient discontinued LIBTAYO due to thyroiditis. Thyroiditis led to withholding of LIBTAYO in 1 (<0.1%) patient. Systemic corticosteroids were not required in any patient with thyroiditis. Thyroiditis resolved in 13% of the 8 patients. Blood thyroid stimulating hormone increased and blood thyroid stimulating hormone decreased have also been reported
- **Hyperthyroidism:** Hyperthyroidism occurred in 3% (39/1281) of patients receiving LIBTAYO, including Grade 3 (<0.1%) and Grade 2 (0.9%). No patient discontinued treatment and LIBTAYO was withheld in 7 (0.5%) patients due to hyperthyroidism. Systemic corticosteroids were required in 8% (3/39) of patients. Hyperthyroidism resolved in 56% of 39 patients. Of the 7 patients in whom LIBTAYO was withheld for hyperthyroidism, 2 patients reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of hyperthyroidism
- **Hypothyroidism:** Hypothyroidism occurred in 7% (87/1281) of patients receiving LIBTAYO, including Grade 3 (<0.1%) and Grade 2 (6%). Hypothyroidism led to permanent discontinuation of LIBTAYO in 3 (0.2%) patients. Hypothyroidism led to withholding of LIBTAYO in 9 (0.7%) patients. Systemic corticosteroids were required in 1.1% (1/87) of patients with hypothyroidism. Hypothyroidism resolved in 6% of the 87 patients. Majority of the patients with hypothyroidism required long-term thyroid hormone replacement. Of the 9 patients in whom LIBTAYO was withheld for hypothyroidism, 1 reinitiated LIBTAYO after symptom improvement and did not have recurrence of hypothyroidism
- **Type 1 diabetes mellitus, which can present with diabetic ketoacidosis:** Monitor for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold LIBTAYO depending on severity. Type 1 diabetes mellitus occurred in <0.1% (1/1281) of patients (Grade 4). No patient discontinued treatment due to Type 1 diabetes mellitus. Type 1 diabetes mellitus led to withholding of LIBTAYO in 0.1% of patients, treatment was reinitiated after symptom improvement. Patient received long-term insulin therapy

Immune-mediated nephritis with renal dysfunction: LIBTAYO can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.7% (9/1281) of patients receiving LIBTAYO, including fatal (<0.1%), Grade 3 (<0.1%), and Grade 2 (0.5%). Nephritis led to permanent discontinuation in 0.2% of patients and withholding of LIBTAYO in 0.4% of patients. Systemic corticosteroids were required in all patients with nephritis. Nephritis resolved in 78% of the 9 patients. Of the 5 patients in whom LIBTAYO was withheld, 4 reinitiated LIBTAYO after symptom improvement; of these, 1/4 (25%) had recurrence.

Immune-mediated dermatologic adverse reactions: LIBTAYO can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS) has occurred with PD-1/PD-L1–blocking antibodies. Immune-mediated dermatologic adverse reactions occurred in 1.9% (24/1281) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (0.8%). Immune-mediated dermatologic adverse reactions led to permanent discontinuation in 0.2% of patients and withholding of LIBTAYO in 1.3% of patients. Systemic corticosteroids were required in all patients with immune-mediated dermatologic adverse reactions. Immune-mediated dermatologic adverse reactions resolved in 71% of the 24 patients. Of the 17 patients in whom LIBTAYO was withheld for dermatologic adverse reaction, 13 reinitiated LIBTAYO after symptom improvement; of these, 5/13 (38%) had recurrence of the dermatologic adverse reaction. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes.

Other immune-mediated adverse reactions: The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% in 1281 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, and vasculitis. Permanently discontinue for Grades 2, 3, or 4 myocarditis
- **Nervous system:** Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, and 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

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Other immune-mediated adverse reactions (continued)

- **Musculoskeletal and connective tissue:** Myositis/polymyositis/dermatomyositis, rhabdomyolysis, and associated sequelae including renal failure, arthritis, polymyalgia rheumatica
- **Endocrine:** Hypoparathyroidism
- **Other (hematologic/immune):** Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis (HLH), systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection, other transplant (including corneal graft) rejection

Infusion-Related Reactions

Severe or life-threatening infusion-related reactions occurred in 0.2% of patients receiving LIBTAYO as a single agent. Monitor patients for signs and symptoms of infusion-related reactions. Common symptoms of infusion-related reaction include nausea, pyrexia, and vomiting. Interrupt or slow the rate of infusion or permanently discontinue LIBTAYO based on severity of reaction.

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.

Embryo-Fetal Toxicity

LIBTAYO can cause fetal harm when administered to a pregnant woman due to an 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.

Adverse Reactions

LIBTAYO as a single agent: the most common adverse reactions (≥15%) are fatigue, musculoskeletal pain, rash, diarrhea, and anemia

LIBTAYO in combination with platinum-based chemotherapy: the most common adverse reactions (≥15%) are alopecia, musculoskeletal pain, nausea, fatigue, peripheral neuropathy, and decreased appetite

Use in Specific Populations

- **Lactation:** 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
- **Females and males of reproductive potential:** Verify pregnancy status in females of reproductive potential prior to initiating LIBTAYO

Please see accompanying full Prescribing Information.

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Preparation in 3 steps[1]

1. **Visually inspect the vial of LIBTAYO 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
   - Do not shake
2. **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.**
3. **Mix diluted solution by gentle inversion. Do not shake.**

Discard any unused medicinal product or waste material.

Dosage and administration[1]

Recommended dosage

A 350 mg dose

IV infusion over 30 minutes

Every 3 weeks

aNSCLC:	aCSCC and aBCC:
Until disease progression or unacceptable toxicity	Until disease progression, unacceptable toxicity, or up to 24 months

- 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
- No dose reduction for LIBTAYO is recommended
- Recommended dosage modifications for ARs can be found on pages 10–11

Refer to the Prescribing Information for the agents administered in combination with LIBTAYO for recommended dosing information, as appropriate.

ARs=adverse reactions; IV=intravenous.

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Storage and handling[1]

LIBTAYO 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 one single-dose vial of:

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

Summary of imARs with LIBTAYO[1]

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 (imARs). Important imARs listed under Warnings and Precautions of the full Prescribing Information may not include all possible severe and fatal imARs. The incidence and severity of imARs were similar when LIBTAYO was administered as a single agent or in combination with chemotherapy.

imARs

- **May be severe or fatal**
- **Can occur in any organ system or tissue**
- **Can occur at any time after starting treatment with PD-1–blocking/ PD-L1–blocking antibodies**
- **Usually manifest during treatment, but can also manifest after discontinuation of PD-1–blocking/PD-L1–blocking antibodies**
- **Can occur simultaneously when affecting more than 1 body system**

Identification and management

Early identification and management of imARs 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 imARs.

Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment.

In cases of suspected imARs, 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 pages 10 and 11 for the recommended dosage modifications.

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 imARs are not controlled with corticosteroids. See pages 10 and 11 for the recommended dosage modifications and the individual adverse reactions section for further details.

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

imARs=immune-mediated adverse reactions.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

Incidence of imARs with LIBTAYO[1]

The data described in Warnings and Precautions reflect exposure to LIBTAYO as a single agent in 1281 patients in 3 open-label, single-arm, multicohort studies, and 2 open-label randomized multi-center studies. These studies included 384 patients with advanced CSCC (Studies 1540 and 1423), 138 patients with advanced BCC (Study 1620), 355 patients with NSCLC (Study 1624), and 404 patients with other advanced solid tumors.

The incidence and severity of imARs were similar when LIBTAYO was administered as a single agent or in combination with chemotherapy.

Incidence, permanent discontinuation rate, and resolution rate of imARs in uncontrolled clinical studies in patients with solid tumors (N=1281)

imARs	Incidence, %	Discontinuation rate, %	Adverse reactions resolved, %
Pneumonitis	2.6	1.3	61
Colitis	2.0	0.4	56
Hepatitis	2.4	1.4	39
Adrenal insufficiency	0.5	<0.1	17
Hypophysitis	0.5	<0.1	14
Thyroiditis	0.6	0	13
Hyperthyroidism	3.0	0	56
Hypothyroidism	7.0	0.2	6
Type 1 diabetes mellitus	<0.1	0	NR
Nephritis with renal dysfunction	0.7	0.2	78
Dermatologic ARs	1.9	0.2	71
Other imARs*	<1% for each	NR	NR

*See page 30 of this guide for descriptions of other imARs with LIBTAYO or other PD-1–blocking/PD-L1–blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.[1]

NR=not reported in the USPI. Does not necessarily mean the value is 0 and may have occurred in a small percentage of patients.

Recommended dosage modifications for ARs[1]

No dose reduction for LIBTAYO is recommended.

In general, withhold LIBTAYO for severe (Grade 3) imARs. Permanently discontinue LIBTAYO for life-threatening (Grade 4) imARs, recurrent severe (Grade 3) imARs 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 the table below.

Adverse reactions	Severity*	LIBTAYO dosage modifications
Immune-Mediated Adverse Reactions [see Warnings and Precautions (5.1) in accompanying full Prescribing Information]		
Pneumonitis	Grade 2	Withhold†
	Grade 3 or 4	Permanently discontinue
Colitis	Grade 2 or 3	Withhold†
	Grade 4	Permanently discontinue
Hepatitis with no tumor involvement of the liver	AST or ALT increases to more than 3 and up to 8 times the ULN or total bilirubin increases to more than 1.5 and up to 3 times the ULN	Withhold†
	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‡	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†
	AST or ALT increases to more than 10 times ULN or total bilirubin increases to more than 3 times ULN	Permanently discontinue

*NCI CTCAE, Version 4.0.[1]

†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.[1]

‡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.[1]

ALT=alanine aminotransferase; AST=aspartate aminotransferase; NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events; ULN=upper limit of normal.

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Recommended dosage modifications for ARs[1] (cont'd)

Adverse reactions	Severity*	LIBTAYO dosage modifications
Immune-Mediated Adverse Reactions [see Warnings and Precautions (5.1) in accompanying full Prescribing Information]		
Endocrinopathies	Grade 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†
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative dermatologic conditions	Suspected SJS, TEN, or DRESS	Withhold†
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grade 2, 3, or 4	Permanently discontinue
Neurological toxicities	Grade 2	Withhold†
	Grade 3 or 4	Permanently discontinue
Other Adverse Reactions		
Infusion-related reactions [see Warnings and Precautions (5.2)]	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

*Based on NCI CTCAE, Version 4.0.[1]

†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.[1]

DRESS=drug rash with eosinophilia and systemic symptoms; SJS=Stevens-Johnson syndrome; TEN=toxic epidermal necrolysis.

The 3 Rs of imARs management

LIBTAYO can cause side effects resulting from immune activation. This guide identifies imARs associated with LIBTAYO treatment and will help you:

RECOGNIZE

Recognize the signs and symptoms of specific imARs

REVISE

Revise patients' care based on the severity of the imARs

RESUME

Resume treatment if appropriate

Learn how to identify and manage potential imARs.

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Common Terminology Criteria for Adverse Events (CTCAE)[2]

An objective resource for grading the severity of adverse events

The National Cancer Institute CTCAE Version 4.03 definitions help healthcare practitioners identify the grade, or severity, of reported adverse events. Knowing the grade of an adverse event helps with reporting and with treatment modification decisions.

The CTCAE displays Grade 1 through Grade 5 (fatal) with unique clinical descriptions of severity for each adverse event based on this general guideline:

Grade	Definition
1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
2	Moderate; minimal, local, or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
3	Severe or medically significant, but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL†
4	Life-threatening consequences; urgent intervention indicated
5	Death related to AE

Toxicity was graded per the NCI CTCAE, Version 4.03.[1]

*Instrumental ADLs refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.[2]

†Self-care ADLs refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.[2]

ADLs=activities of daily living; AEs=adverse events.

Immune-mediated pneumonitis

Incidence of immune-mediated pneumonitis by grade[1]

	Pneumonitis (N=1281)
All Grades, %	**2.6**
Grade 2, %	1.6
Grade 3, %	0.6
Grade 4, %	0.3
Fatal, %	NR

NR=not reported in the USPI. Does not necessarily mean the value is 0 and may have occurred in a small percentage of patients.

RECOGNIZE[1]

Monitor for, and remind patients to immediately report, any new or worse signs or symptoms, including:

- Cough
- Chest pain
- Shortness of breath

These are not all of the signs and symptoms of immune system problems related to pneumonitis that can happen with LIBTAYO.

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REVISE[1]

Institute medical management promptly, including specialty consultation as appropriate. Manage with dosage modifications and corticosteroids.

Systemic corticosteroids were required in all patients with pneumonitis.

Recommended management of immune-mediated pneumonitis[12]

Pneumonitis	Grade 1	Grade 2	Grade 3	Grade 4
Definition*	• Asymptomatic • Clinical or diagnostic observations only • Intervention not indicated	• Symptomatic • Medical intervention indicated • Limiting instrumental ADL†	• Severe symptoms • Limiting self-care ADL‡ • Oxygen indicated	• Life-threatening respiratory compromise • Urgent intervention indicated (eg, tracheotomy or intubation)
Dosage modification	None	Withhold LIBTAYO (see Resume section below)	Permanently discontinue	
Additional intervention	None	Withhold or permanently discontinue LIBTAYO depending on severity. 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 pneumonitis is not controlled with corticosteroids.		

*Toxicity was graded per the NCI CTCAE, Version 4.03.[1]
†Instrumental ADLs refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.[2]
‡Self-care ADLs refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.[2]
ADLs=activities of daily living.

RESUME[1]

In patients in whom LIBTAYO was withheld, LIBTAYO can be resumed in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue LIBTAYO 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.

Pneumonitis led to withholding of LIBTAYO in 1.4% of patients. Of the 18 patients in whom LIBTAYO was withheld for pneumonitis, 10 reinitiated LIBTAYO after symptom improvement; of these, 4/10 (40%) had recurrence of pneumonitis.

Immune-mediated colitis

Incidence of immune-mediated colitis by grade[1]

	Colitis (N=1281)
All Grades, %	**2.0**
Grade 2, %	0.9
Grade 3, %	0.8
Grade 4, %	NR
Fatal, %	NR

NR=not reported in the USPI. Does not necessarily mean the value is 0 and may have occurred in a small percentage of patients.

RECOGNIZE[1]

Monitor for, and remind patients to immediately report, any new or worse signs or symptoms, including:

- 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

These are not all of the signs and symptoms of immune system problems related to colitis that can happen with LIBTAYO.

LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

REVISE[1]

Institute medical management promptly, including specialty consultation as appropriate. Manage with dosage modifications and corticosteroids.

Systemic corticosteroids were required in all patients with colitis.

Recommended management of immune-mediated colitis[1,2]

Colitis	Grade 1	Grade 2	Grade 3	Grade 4
Definition*	• Asymptomatic • Clinical or diagnostic observations only • Intervention not indicated	• Abdominal pain • Mucus or blood in stool	• Severe abdominal pain • Change in bowel habits • Medical intervention indicated • Peritoneal signs	• Life-threatening consequences • Urgent intervention indicated
Dosage modification	None	Withhold LIBTAYO (see Resume section below)		Permanently discontinue
Additional intervention	None	Withhold or permanently discontinue LIBTAYO depending on severity. 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 colitis is not controlled with corticosteroids.		

*Toxicity was graded per the NCI CTCAE, Version 4.03.[1]

RESUME[1]

In patients in whom LIBTAYO was withheld, LIBTAYO can be resumed in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue LIBTAYO 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.

Colitis led to withholding of LIBTAYO in 1.2% of patients. Of the 16 patients in whom LIBTAYO was withheld for colitis, 6 reinitiated LIBTAYO after symptom improvement; of these, 4/6 (67%) had recurrence of colitis.

Immune-mediated hepatitis

Incidence of immune-mediated hepatitis by grade[1]

	Hepatitis (N=1281)
All Grades, %	**2.4**
Grade 2, %	0.2
Grade 3, %	1.6
Grade 4, %	0.3
Fatal, %	<0.1

RECOGNIZE[1]

Monitor for, and remind patients to immediately report, any new or worse signs or symptoms, including:

- Yellowing of skin or the whites of eyes
- Severe nausea or vomiting
- Pain on the right side of stomach-area (abdomen)
- Dark urine (tea colored)
- Bleeding or bruising more easily than normal

These are not all of the signs and symptoms of immune system problems related to hepatitis that can happen with LIBTAYO.

Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment.

LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

REVISE[1]

Institute medical management promptly, including specialty consultation as appropriate. Manage with dosage modifications and corticosteroids.

Systemic corticosteroids were required in all patients with hepatitis. Thirteen percent (13%) of these patients (4/31) required additional immunosuppression with mycophenolate.

Recommended management of immune-mediated hepatitis with no tumor involvement of the liver and with tumor involvement of the liver[1]

Hepatitis	Moderate severity	Severe
Hepatitis with no tumor involvement of the liver	• AST or ALT >3 and ≤8 × ULN or total bilirubin increases >1.5 and ≤3 × ULN	• AST or ALT >8 × ULN or total bilirubin >3 × ULN
Dosage modification	Withhold LIBTAYO (see Resume section below)	Permanently discontinue
Hepatitis with tumor involvement of the liver*	• Baseline AST or ALT >1 and ≤3 × ULN and increases to >5 and ≤10 × ULN or baseline AST or ALT >3 and ≤5 × ULN and increases >8 and ≤10 × ULN	• AST or ALT >10 × ULN or total bilirubin increases >3 × ULN
Dosage modification	Withhold LIBTAYO (see Resume section below)	Permanently discontinue
Additional intervention	Withhold or permanently discontinue LIBTAYO depending on severity. 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 hepatitis is not controlled with corticosteroids.	

*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.[1]

RESUME[1]

In patients in whom LIBTAYO was withheld, LIBTAYO can be resumed in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue LIBTAYO 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.

Hepatitis led to withholding of LIBTAYO in 0.7% of patients. Of the 9 patients in whom LIBTAYO was withheld for hepatitis, 5 patients reinitiated LIBTAYO after symptom improvement. Of these, 1/5 (20%) had recurrence of hepatitis.

Immune-mediated endocrinopathies

Immune-mediated adrenal insufficiency, hypophysitis, thyroid disorders, and type 1 diabetes mellitus

Incidence of immune-mediated endocrinopathies by grade[1]

	Adrenal insufficiency (N=1281)	Hypophysitis (N=1281)	Thyroiditis (N=1281)	Hyperthyroidism (N=1281)	Hypothyroidism (N=1281)	Type 1 diabetes mellitus (N=1281)
All Grades, %	**0.5**	**0.5**	**0.6**	**3.0**	**7.0**	**<0.1**
Grade 2, %	NR	0.3	0.3	0.9	6.0	NR
Grade 3, %	0.5	0.2	NR	<0.1	<0.1	NR
Grade 4, %	NR	NR	NR	NR	NR	<0.1
Fatal, %	NR	NR	NR	NR	NR	NR

NR=not reported in the USPI. Does not necessarily mean the value is 0 and may have occurred in a small percentage of patients.

LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

RECOGNIZE[1]

Monitor for, and remind patients to immediately report, any new or worse signs or symptoms, including:

- Headaches 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
- Voice gets deeper
- Dizziness or fainting
- Changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

These are not all of the signs and symptoms of immune system problems related to endocrinopathies that can happen with LIBTAYO.

Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment.

Immune-mediated adrenal insufficiency

REVISE[1]

Institute medical management promptly, including specialty consultation as appropriate. Manage with dosage modifications and hormone replacement therapy as warranted.

Systemic corticosteroids were required in 83% (5/6) of patients with adrenal insufficiency. Of these, the majority remained on systemic corticosteroids.

Recommended management of immune-mediated adrenal insufficiency[1,2]

Adrenal insufficiency	Grade 1	Grade 2	Grade 3	Grade 4
Definition*	• Asymptomatic • Clinical or diagnostic observations only • Intervention not indicated	• Moderate symptoms • Medical intervention indicated	• Severe symptoms • Hospitalization indicated	• Life-threatening consequences • Urgent intervention indicated
Dosage modification	None	Initiate symptomatic treatment, including hormone replacement as clinically indicated	Withhold until clinically stable or permanently discontinue depending on severity Initiate symptomatic treatment, including hormone replacement as clinically indicated	

*Toxicity was graded per the NCI CTCAE, Version 4.03.[1]

LIBTAYO was withheld in 1 (<0.1%) patient due to adrenal insufficiency.[1]

Adrenal insufficiency resolved in 17% of the 6 patients at the time of data cutoff.[1]

LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

Immune-mediated hypophysitis

REVISE[1]

Institute medical management promptly, including specialty consultation as appropriate. Manage with dosage modifications and hormone replacement therapy as clinically indicated. Systemic corticosteroids were required in 86% (6/7) of patients with hypophysitis.

Recommended management of immune-mediated hypophysitis[1,2]

Hypophysitis	Grade 1	Grade 2	Grade 3	Grade 4
Definition*†	• Asymptomatic or mild symptoms • Clinical or diagnostic observations only • Intervention not indicated	• Moderate symptoms • Minimal, local, or noninvasive intervention indicated • Limiting age-appropriate instrumental ADL‡	• Severe or medically significant, but not immediately life-threatening • Hospitalization or prolongation of existing hospitalization indicated • Disabling • Limiting self-care ADL§	• Life-threatening consequences • Urgent intervention indicated
Dosage modification	None	None	Withhold until clinically stable or permanently discontinue depending on severity	

*Toxicity was graded per the NCI CTCAE, Version 4.03.[1]
†Grade definitions taken from "Endocrine disorders—other, specify."[2]
‡Instrumental ADLs refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.[2]
§Self-care ADLs refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.[2]

Initiate hormone replacement as clinically indicated.[1]

Hypophysitis led to withholding in 2 (0.2%) patients. Hypophysitis resolved in 14% of the 7 patients at the time of data cutoff.[1]

Immune-mediated thyroid disorders

REVISE[1]

Institute medical management promptly, including specialty consultation as appropriate. Manage with dosage modifications and hormone replacement therapy as clinically indicated.

Systemic corticosteroids were not required in any patient with thyroiditis. Systemic corticosteroids were required in 8% (3/39) of patients with hyperthyroidism and in 1.1% (1/87) of patients with hypothyroidism.

Recommended management of immune-mediated thyroid disorders[1,2]

Thyroid disorders	Grade 1	Grade 2	Grade 3	Grade 4
Definition*	• Asymptomatic • Clinical or diagnostic observations only • Intervention not indicated	• Symptomatic • Thyroid replacement (hypothyroidism) or thyroid suppression therapy (hyperthyroidism) indicated • Limiting instrumental ADL†	• Severe symptoms • Limiting self-care ADL‡ • Hospitalization indicated	• Life-threatening consequences • Urgent intervention indicated
Dosage modification	None	None	Withhold until clinically stable or permanently discontinue depending on severity	

*Toxicity was graded per the NCI CTCAE, Version 4.03.[1]

†Instrumental ADLs refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.[2]

‡Self-care ADLs refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.[2]

Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity.[1]

Thyroiditis led to withholding of LIBTAYO in 1 (<0.1%) patient. Thyroiditis resolved in 13% of the 8 patients at the time of data cutoff. Blood thyroid stimulating hormone increased and blood thyroid stimulating hormone decreased have also been reported.[1]

Hyperthyroidism led to withholding of LIBTAYO in 0.5% of patients. Of the 7 patients in whom LIBTAYO was withheld for hyperthyroidism, 2 patients reinitiated LIBTAYO after symptom improvement. Of these, none had recurrence of hyperthyroidism.[1]

Hypothyroidism led to withholding of LIBTAYO in 0.7% of patients. Of the 9 patients in whom LIBTAYO was withheld for hypothyroidism, 1 reinitiated LIBTAYO after symptom improvement and did not have recurrence of hypothyroidism.[1]

Immune-mediated type 1 diabetes mellitus

REVISE[1]

Institute medical management promptly, including specialty consultation as appropriate. Manage with dosage modifications and initiate insulin as clinically indicated.

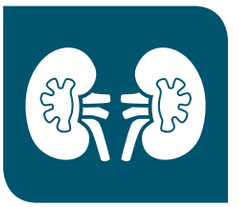
Recommended management of immune-mediated type 1 diabetes mellitus[1,2]

Diabetes mellitus (hyperglycemia)	Grade 1	Grade 2	Grade 3	Grade 4
Definition*	• Fasting glucose value >ULN–160 mg/dL • Fasting glucose value >ULN–8.9 mmol/L	• Fasting glucose value >160–250 mg/dL • Fasting glucose value >8.9–13.9 mmol/L	• >250–500 mg/dL • >13.9–27.8 mmol/L • Hospitalization indicated	• >500 mg/dL • >27.8 mmol/L • Life-threatening consequences
Dosage modification	None	None	Withhold until clinically stable or permanently discontinue depending on severity	

*Toxicity was graded per the NCI CTCAE, Version 4.03.[1]

Initiate treatment with insulin as clinically indicated.

Type 1 diabetes mellitus led to withholding of LIBTAYO in 0.1% of patients. Treatment was reinstated after symptom improvement. Patient received long-term insulin therapy.



Immune-mediated nephritis with renal dysfunction

Incidence of immune-mediated nephritis by grade[1]

	Nephritis (N=1281)
All Grades, %	**0.7**
Grade 2, %	0.5
Grade 3, %	<0.1
Grade 4, %	NR
Fatal, %	<0.1

NR=not reported in the USPI. Does not necessarily mean the value is 0 and may have occurred in a small percentage of patients.

RECOGNIZE[1]

Monitor for, and remind patients to immediately report any new or worse signs or symptoms, including:

- Decrease in amount of urine
- Blood in urine
- Swelling of ankles
- Loss of appetite

These are not all of the signs and symptoms of immune system problems related to nephritis that can happen with LIBTAYO.

Evaluate creatinine at baseline and periodically during treatment.

LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

REVISE[1]

Institute medical management promptly, including specialty consultation as appropriate. Manage patients with dosage modifications and corticosteroids.

Systemic corticosteroids were required in all patients with nephritis.

Recommended management of immune-mediated nephritis[1,2]

Nephritis with renal dysfunction	Grade 1	Grade 2 increased blood creatinine	Grade 3 increased blood creatinine	Grade 4 increased blood creatinine
Definition*†‡	• Asymptomatic or mild symptoms • Clinical or diagnostic observations only • Intervention not indicated • >1-1.5 × baseline; >ULN-1.5 × ULN‡	• Moderate, local or noninvasive intervention indicated • Limiting instrumental ADL§ • >1.5-3.0 × baseline; >1.5-3.0 × ULN‡	• Severe or medically significant but not immediately life-threatening • Hospitalization or prolongation of existing hospitalization indicated • Disabling • Limiting self-care ADL‖ • >3.0 baseline; >3.0-6.0 × ULN‡	• Life-threatening consequences • Urgent intervention indicated • >6.0 × ULN‡
Dosage modification	None	Withhold LIBTAYO (see Resume section below)	Withhold LIBTAYO (see Resume section below)	Permanently discontinue
Additional intervention	None	Withhold or permanently discontinue LIBTAYO depending on severity. 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 nephritis is not controlled with corticosteroids.		

*Toxicity was graded per the NCI CTCAE, Version 4.03.[1]
†Grade definitions taken from "Renal and urinary disorders—other, specify."[2]
‡Grade definitions taken from "Creatinine increased."[2]
§Instrumental ADLs refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.[2]
‖Self-care ADLs refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.[2]

RESUME[1]

In patients in whom LIBTAYO was withheld, LIBTAYO can be resumed in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue LIBTAYO 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.

Nephritis led to withholding of LIBTAYO in 0.4% of patients. Of the 5 patients in whom LIBTAYO was withheld for nephritis, 4 patients reinitiated LIBTAYO after symptom improvement. Of these, 1/4 (25%) had recurrence of nephritis.

Immune-mediated dermatologic ARs

Immune-mediated rash, dermatitis, Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN)/ drug rash with eosinophilia and systemic symptoms (DRESS)

Incidence of immune-mediated dermatologic ARs by grade[1]

	Dermatologic ARs (N=1281)
All Grades, %	**1.9**
Grade 2, %	0.8
Grade 3, %	0.9
Grade 4, %	NR
Fatal, %	NR

NR=not reported in the USPI. Does not necessarily mean the value is 0 and may have occurred in a small percentage of patients.

Exfoliative dermatitis, including SJS, TEN, and DRESS, has occurred with PD-1/PD-L1–blocking antibodies.[1]

RECOGNIZE[1]

Monitor for, and remind patients to immediately report any new or worse signs or symptoms, including:

- 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

These are not all of the signs and symptoms of immune system problems related to dermatologic ARs that can happen with LIBTAYO.

LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

REVISE[1]

Institute medical management promptly, including specialty consultation as appropriate. Manage patients with dosage modifications and corticosteroids. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes.

Systemic corticosteroids were required in all patients with immune-mediated dermatologic ARs.

Recommended management of immune-mediated dermatologic ARs[1]

Exfoliative dermatologic conditions	Suspected SJS, TEN, or DRESS	Confirmed SJS, TEN, or DRESS
Dosage modification	Withhold (see Resume section below)	Permanently discontinue
Additional intervention	Withhold or permanently discontinue LIBTAYO depending on severity. 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 dermatologic adverse reaction is not controlled with corticosteroids.	

RESUME[1]

In patients in whom LIBTAYO was withheld, LIBTAYO can be resumed in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue LIBTAYO 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.

Dermatologic adverse reactions led to withholding of LIBTAYO in 1.3% of patients. Of the 17 patients in whom LIBTAYO was withheld for dermatologic AR, 13 patients reinitiated LIBTAYO after symptom improvement. Of these, 5/13 (38%) had recurrence of the dermatologic adverse reaction.

Other imARs

Incidence of other imARs[1]

The following clinically significant imARs occurred at an incidence of <1% in 1281 patients who received LIBTAYO or were reported with the use of other PD-1–blocking and 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 imARs, 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/dermatomyositis, 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 thrombocytopenia, solid organ transplant rejection, other transplant (including corneal graft) rejection

RECOGNIZE[1]

Monitor for, and remind patients to immediately report, any new or worse signs or symptoms, including:

- 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

These are not all of the signs and symptoms of immune system problems related to other imARs that can happen with LIBTAYO.

Other imARs can occur in any organ system or tissue. While imARs usually manifest during treatment with PD-1–blocking/PD-L1–blocking antibodies, imARs can also manifest after discontinuation of PD-1–blocking/PD-L1–blocking antibodies. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment.

REVISE[1]

Institute medical management promptly, including specialty consultation as appropriate. Manage with dosage modifications.

Recommended management of other imARs[1]

Myocarditis	Grade 2, 3, or 4
Dosage modification	Permanently discontinue

Neurological toxicities	Grade 2	Grade 3 or 4
Dosage modification	Withhold (see Resume section below)	Permanently discontinue
Additional intervention	Withhold or permanently discontinue LIBTAYO depending on severity. 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 neurological toxicities are not controlled with corticosteroids.	

RESUME[1]

In patients in whom LIBTAYO was withheld, LIBTAYO can be resumed in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue LIBTAYO 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.

Infusion-related reactions

Incidence of severe infusion-related reactions by grade[1]

	Infusion-related reactions (N=1281)
Severe or life-threatening	0.2
Fatal, %	NR

NR=not reported in the USPI. Does not necessarily mean the value is 0 and may have occurred in a small percentage of patients.

RECOGNIZE[1]

Infusion reactions can sometimes be severe. Monitor for, and remind patients to immediately report, any new or worse signs or symptoms, including:

- Nausea
- Vomiting
- Chills or shaking
- Itching or rash
- Flushing
- Shortness of breath or wheezing
- Dizziness
- Feel like passing out
- Fever
- Back or neck pain
- Facial swelling

These are not all of the signs and symptoms of immune system problems related to infusion-related reactions that can happen with LIBTAYO.

LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

REVISE[1]

Manage patients with dosage modifications.

Recommended management of infusion-related reactions[12]

Infusion-related reactions	Grade 1	Grade 2	Grade 3	Grade 4
Definition*	• Mild transient reaction • Infusion interruption not indicated • Intervention not indicated	• Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (eg, antihistamines, NSAIDs, narcotics, IV fluids) • Prophylactic medications indicated for ≤24 h	• Prolonged (eg, not rapidly responsive to symptomatic medication and/or brief interruption of infusion) • Recurrence of symptoms following initial improvement • Hospitalization indicated for clinical sequelae	• Life-threatening consequences • Urgent intervention indicated
Dosage modification	Interrupt or slow rate of infusion		Permanently discontinue	

*Toxicity was graded per the NCI CTCAE, Version 4.03.[1]
NSAIDs=nonsteroidal anti-inflammatory drugs.

Complications of allogeneic HSCT

Allogeneic HSCT before or after treatment with a PD-1/PD-L1–blocking antibody[1]

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. Transplant-related complications include hyperacute GVHD, acute GVHD, chronic GVHD, hepatic 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.

Complications of allogeneic HSCT	
Monitoring	Follow patients closely for evidence of transplant-related complications such as hyperacute GVHD, acute GVHD, chronic GVHD, hepatic VOD, and steroid-requiring febrile syndrome.
Management	Consider the benefit vs risks of treatment with a PD-1/PD-L1–blocking antibody prior to or after an allogeneic HSCT.

GVHD=graft-versus-host disease; HSCT=hematopoietic stem cell transplantation; VOD=veno-occlusive disease.

Advise patients to immediately report signs or symptoms of postallogeneic HSCT complications or of solid organ transplant rejection.[1]

LIBTAYO Surround® Patient Support Program

LIBTAYO Surround can help support patients throughout their treatment journey

LIBTAYO Surround can provide:

- Benefits investigations*
- Prior authorization (PA) and appeal assistance*
- Claims assistance to address questions as you prepare claims and to review the status of claims with your patient's health insurer
- Commercial Copay Program and Patient Assistance Program (PAP)†‡
- Product support*
- Patient Navigators to educate and assist patients once they are prescribed LIBTAYO§

LIBTAYO Surround financial support programs offer patient support that facilitates access to medication when eligible patients need assistance with out-of-pocket costs.

Eligible patients with commercial insurance may pay as little as $0 for LIBTAYO, which includes any product-specific copay, coinsurance, and insurance deductibles—up to $25,000 in assistance per year.‡ Conditions apply. There is no income requirement to qualify for this program.

Billing and coding

- NDC: 61755-008-01 (350 mg/7 mL [50 mg/mL])
- J-code: J9119 Injection, cemiplimab-rwlc, 1 mg

Effective July 1, 2023, the JZ modifier is required for reporting there was no discarded drug.

For more information, call **1.877.LIBTAYO** (1.877.542.8296), select **option 1**, Monday–Friday, 8:00 AM–8:00 PM Eastern Time.

*LIBTAYO Surround provides access and reimbursement support to help your patients receive their medication as quickly as possible. Upon receipt of a LIBTAYO Surround Enrollment Form, a LIBTAYO Surround Reimbursement Specialist may be able to provide several types of assistance.

†Patients who are uninsured, underinsured, or lack coverage may be eligible to receive LIBTAYO at no cost. LIBTAYO Surround can help evaluate patients' eligibility for assistance.

‡Subject to annual maximum copay assistance amount of $25,000. This program is not valid for prescriptions covered by or submitted for reimbursement under Medicare, Medicaid, Veterans Affairs/Department of Defense, TRICARE, or similar federal or state programs. Not a debit card program. The program does not cover or provide support for supplies, procedures, or any physician-related service associated with LIBTAYO. General non–product-specific copays, coinsurance, or insurance deductibles are not covered. This program only applies to patients who are at least 18 years of age, residents of the United States or its territories or possessions, are prescribed LIBTAYO (cemiplimab-rwlc) for an FDA-approved indication, and are insured by a commercial health plan that requires a copayment, coinsurance, and/or deductible amount for LIBTAYO. It is not an insurance benefit. LIBTAYO Surround reserves the right to rescind, terminate, or amend this offer, eligibility, and terms and conditions at any time without notice. Patients, pharmacists, and prescribers cannot seek reimbursement from health insurance or any third party for any part of the benefit received by the patient through this offer. This offer is not conditioned on any past, present, or future purchase, including refills. This offer is non-transferable, limited to one per person, and cannot be combined with any other offer or discount. This program is not valid where prohibited by law, taxed, or restricted. Offer has no cash value. Patients are responsible for any out-of-pocket costs for LIBTAYO that exceed the program assistance limit of $25,000 per year. Program is not valid for cash-paying customers. Additional program conditions may apply.

§Once patients are prescribed LIBTAYO, they have access to our dedicated Patient Navigators. Patient Navigators are available to complement the support provided by patients' healthcare providers.

LIBTAYO®
(cemiplimab-rwlc)
Injection 350 mg

To learn more about LIBTAYO

or to contact a sales representative,
visit **LIBTAYOhcp.com**.

References: 1. LIBTAYO (cemiplimab-rwlc) injection full U.S. prescribing information. Regeneron Pharmaceuticals, Inc. **2.** U.S. Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03. Published May 28, 2009. Updated June 14, 2010.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

REGENERON®

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