MEDISON

We are **Always Ahead** | We **Grow as One** | We **Care**

ספטמבר 2026

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

חברת מדיסון פארמה בע"מ שמחה להודיעכם על אישור משרד הבריאות לתוספת ההתוויה ושינוי במשטר המינון עבור התכשיר:

LIBTAYO **ליבטאיו**

Concentrate for solution for infusion

מרכיב פעיל : Cemiplimab

התוויות מאושרות :

CCutaneous Squamous Cell Carcinoma
LIBTAYO as monotherapy is indicated for the treatment of adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not candidates for curative surgery or curative radiation.
LIBTAYO as monotherapy is indicated for the adjuvant treatment of adult patients with CSCC at high risk of recurrence after surgery and radiation .

Basal Cell Carcinoma
LIBTAYO as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic basal cell carcinoma (laBCC or mBCC) who have progressed on or are intolerant to a hedgehog pathway inhibitor (HHI).

Non-Small Cell Lung Cancer
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 approved test, with no EGFR, ALK or ROS1 aberrations, and is:
• locally advanced where patients are not candidates for surgical resection or definitive chemoradiation or
• metastatic.

LIBTAYO in combination with platinum-based chemotherapy is indicated for the first-line treatment of adult patients with non-small cell lung cancer (NSCLC) expressing PD-L1 (in ≥ 1% of tumour cells), with no EGFR, ALK or ROS1 aberrations and is:
• locally advanced where patients are not candidates for surgical resection or definitive chemoradiation or
• metastatic.

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להלן העדכונים בהתוויה ובמשטר המינון בעלון לרופא (מסומנים באדום):

4.1 Therapeutic indications

[…]

LIBTAYO as monotherapy is indicated for the adjuvant treatment of adult patients with CSCC at high risk of recurrence after surgery and radiation (see section 5.1 for selection criteria).

4.2 Posology and method of administration

[…]

Locally advanced or metastatic CSCC, BCC, NSCLC

[…]

Adjuvant treatment of high-risk CSCC

The recommended dose of cemiplimab administered as an intravenous infusion over 30 minutes is:

- 350 mg every 3 weeks for 12 weeks followed by 700 mg every 6 weeks, or
- 350 mg every 3 weeks.

Treatment may be continued until disease recurrence, unacceptable toxicity, or up to 48 weeks of total therapy.

[…]

Table 1:Recommended treatment modifications

[…]

Adverse reaction[a]	**Severity**[b]	**Dose modification**	**Additional intervention**
Other immune-mediated adverse reactions(including but not limited to paraneoplastic encephalomyelitis, meningitis, myositis, solid organ transplant rejection, graft-vs-host disease, Guillain-Barre syndrome, central nervous system inflammation, chronic inflammatory demyelinating polyradiculoneuropathy, encephalitis, myasthenia gravis, neuropathy peripheral, myocarditis, pericarditis, immune thrombocytopenic purpura, vasculitis, arthralgia, arthritis, muscular weakness, myalgia, polymyalgia rheumatica, Sjogren's syndrome, keratitis, stomatitis, thyroiditis and haemophagocytic	Grade 2 or 3 based on type of reaction	Withhold LIBTAYO	Initiate symptomatic management including initial dose of 1 to 2 mg/kg/day prednisone or equivalent as clinically indicated followed by a taper
		Resume LIBTAYO if other immune-mediated adverse reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	– Grade 3 based on type of reaction or Grade 4 (excluding endocrinopathies) – Grade 3 or 4 neurologic toxicity – Grade 3 or 4 myocarditis or pericarditis – Confirmed haemophagocytic lymphohistiocytosis – Recurrent Grade 3 immune-mediated adverse reaction	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day as clinically indicated prednisone or equivalent followed by a taper

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lymphohistiocytosis)	– Persistent Grade 2 or 3 immune-mediated adverse reactions lasting 12 weeks or longer (excluding endocrinopathies) Inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks		

להלן העדכונים בעלון לרופא המהווים החמרות (מסומנים באדום):

4.8 Undesirable effects

[…]

Cemiplimab in the adjuvant CSCC setting

The safety of cemiplimab as monotherapy in the adjuvant treatment of patients with CSCC at high risk of recurrence was evaluated in 205 patients in the C-POST study. The median duration of exposure was 47.9 weeks (range: 3 weeks to 52 weeks) in the cemiplimab group.

The safety profile of cemiplimab in the adjuvant setting in the C-POST study is consistent with the known safety profile for cemiplimab monotherapy in advanced cancers. The incidence of immune-mediated adverse reactions of cemiplimab as monotherapy in the C-POST study was 22.9% compared to 20.8% in the monotherapy population with advanced solid malignancies.

Adverse events were serious in 17.6% of patients.

Adverse events led to permanent discontinuation of cemiplimab in 9.8% of patients.

[…]

Description of selected adverse reactions

The selected adverse reactions described below are based on safety of cemiplimab in 1281 patients in clinical studies in monotherapy. These selected adverse reactions were consistent when cemiplimab was administered as monotherapy in patients with advanced solid malignancies, as monotherapy in the adjuvant setting, or in combination with chemotherapy.

5.1 Pharmacodynamic properties

[…]

Adjuvant treatment of high-risk CSCC

The efficacy of cemiplimab was evaluated for the adjuvant treatment of patients with CSCC at high risk of recurrence after surgery followed by radiotherapy in the C-POST study, a randomised, doubleblind, multicentre, placebo-controlled phase 3 study. Study participants were at high risk of recurrence due to nodal features (extracapsular extension or ≥ 3 involved lymph nodes) and/or non-nodal features (in-

transit metastases, T4 lesion, perineural invasion, or locally recurrent tumour with ≥ 1 additional adverse feature), and completed adjuvant radiation therapy within 2 to 10 weeks of randomisation.

The study excluded patients with autoimmune disease that required systemic therapy with immunosuppressant agents within 5 years; history of solid organ transplant; prior allogeneic or autologous stem cell transplantation; uncontrolled HIV, hepatitis B or hepatitis C infection, or ECOG PS ≥ 2. Patients with CLL were eligible if they had not required systemic therapy for CLL within 6 months.

In the C-POST study, 415 patients were randomised 1:1 to cemiplimab (N=209) or placebo (N=206). In Part 1, 334 patients were assigned to receive 350 mg cemiplimab (N=171) or placebo (N=163) intravenously every 3 weeks for 12 weeks, followed by 700 mg cemiplimab or placebo intravenously every 6 weeks for an additional 36 weeks, and 81 patients were assigned to receive 350 mg cemiplimab (N=38) or placebo (N=43) intravenously every 3 weeks for up to 48 weeks. Treatment continued until disease recurrence, unacceptable toxicity or up to 48 weeks.

In Part 2 of the study, which was open label and optional, patients who had a disease recurrence at any time during the study and were in the placebo arm had the option to receive subsequent treatment with cemiplimab at 350 mg intravenously every 3 weeks. Patients who had a disease recurrence ≥3 months after completing 48 weeks of planned cemiplimab treatment and were in the cemiplimab arm had the option to receive cemiplimab at 350 mg intravenously every 3 weeks. Patients could be treated for up to 96 weeks in Part 2.

The primary endpoint was disease-free survival (DFS) defined as time from randomisation to the first documented disease recurrence by investigator assessment or death due to any cause. Imaging assessments were performed at the end of each 12-week cycle during the 48 weeks. During the followup period, imaging was conducted every 4 months during the first 2 years of planned follow-up and every 6 months thereafter until recurrence.

The study population characteristics were: median age of 71 years (range: 33 to 95); 83.9% male; 91.1% White, 3.1% Asian; 63.6% had ECOG PS 0 and 36.4% had ECOG PS 1. The location of tumour was head and neck (HN) in 82.7 % and non-HN in 17.3% of patients. The high-risk feature was nodal in 58.3% of patients and exclusively non-nodal in 41.7% of patients.

Efficacy results for C-POST study are shown in Table 4 and Figure 1.

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Table 4: Efficacy results for the C-POST study in high-risk CSCC in the adjuvant setting primary analysis

Efficacy Endpoints[a]	Cemiplimab N = 209	Placebo N = 206
Disease-Free Survival (DFS)		
Number of events, n (%)	24 (11.5%)	65 (31.6%)
Disease recurrences, n (%)	18 (8.6%)	61 (29.6%)
Deaths, n (%)[b]	6 (2.9%)	4 (1.9%)
Median (95% CI) in months[c]	NR (NE, NE)	49.4 (48.5, NE)
Hazard ratio (95% CI)[d]	0.32 (0.20, 0.51)	
p-value[e]	<0.0001	

CI: Confidence interval; NE: Not evaluable; NR: Not reached (Data cutoff-Oct 4, 2024)

a. Median duration of follow-up: cemiplimab: 24.5 months; placebo: 23.8 months

b. Deaths that were counted as DFS events as assessed by investigator; does not include deaths in patients who previously had recurrence

c. Based on Kaplan-Meier method

d. Based on stratified proportional hazards model

e. Based on a two-sided p-value

At the time of the updated analysis (data cutoff Apr 07, 2025), 29 (13.9%) DFS events in the cemiplimab group and 68 (33.0%) DFS events in the placebo group were reported at a median follow-up of 31 months in the cemiplimab group and 30 months in the placebo group (HR 0.35; 95% CI 0.23, 0.55). OS results were not mature at the time of pre-specified primary analysis.

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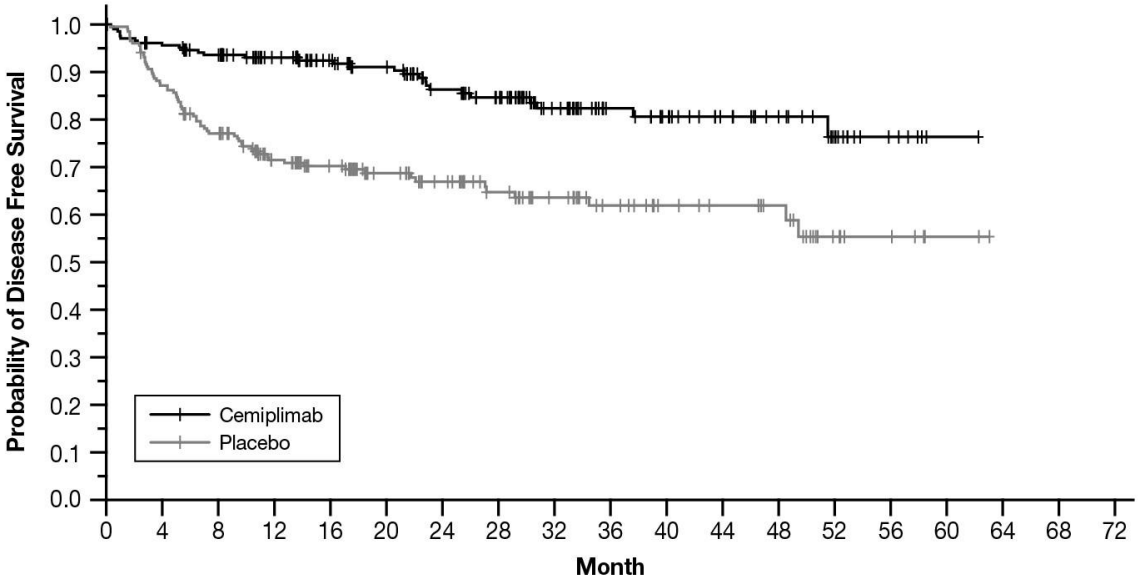
Figure 1: DFS in the C-POST study in high-risk CSCC in the adjuvant setting-updated analysis[a]



Number of Subjects at Risk

Cemiplimab	209	193	184	160	138	125	105	94	67	47	39	30	24	15	6	1	0	0	0
Placebo	206	176	149	116	101	81	70	58	46	35	27	24	20	9	6	2	0	0	0

[a] Based on updated analysis (Data cutoff Apr 07, 2025)

5.2 Pharmacokinetic properties

[…]

In patients with high risk CSCC, the mean simulated concentrations were generated using an updated population PK model and 1000 virtual patients per regimen. In these patients, at 350 mg Q3W for 12 weeks followed by 700 mg Q6W for 36 additional weeks, the mean cemiplimab concentrations at steady-state ranged between a C_{trough} of 52.5 mg/l and a concentration at end of infusion (C_{max}) of 233 mg/l while at 350 mg Q3W for 48 weeks, the mean cemiplimab concentrations at steady-state ranged between a C_{trough} of 66.3 mg/l and a concentration at end of infusion (C_{max}) of 154 mg/l.

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להלן העדכונים בהתוויה ובמשטר המינון בעלון לצרכן (מסומנים באדום):

1. למה מיועדת התרופה?

ליבטאיו משמש לאחר ניתוח להסרת CSCC כדי לסייע במניעת חזרת הסרטן (טיפול משלים).

3. כיצד תשתמש בתרופה?

[...]

<u>מינון</u>

המינון ואופן הטיפול יקבעו על ידי הרופא בלבד. המינון המקובל בדרך כלל הוא מנה של 350 מ"ג אחת ל- 3 שבועות .

כאשר התרופה ניתנת כדי לסייע במניעת חזרת CSCC לאחר ניתוח, הטיפול עשוי להינתן במינון של 350 מ"ג אחת ל-3 שבועות במשך 48 שבועות, או 350 מ"ג אחת ל-3 שבועות במשך 12 שבועות ולאחר מכן 700 מ"ג אחת ל-6 שבועות למשך סך של 48 שבועות.

העלון לרופא והעלון לצרכן נמצאים בקישור, וכן מפורסמים במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום.

בברכה,

מדיסון פארמה בע"מ

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