

# Summary of the Risk Management Plan (RMP) for LIBTAYO®

LIBTAYO® (cemiplimab)

Marketing Authorisation Holder : sanofi-aventis (suisse) sa

RMP version 4.0

Date: 04 APR 2023

## **Disclaimer:**

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimize them. The RMP summary of LIBTAYO® is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of LIBTAYO® in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see [www.swissmedicinfo.ch](http://www.swissmedicinfo.ch)) approved and authorized by Swissmedic. Sanofi-aventis (suisse) sa is fully responsible for the accuracy and correctness of the content of this published summary RMP of LIBTAYO®.

## **I.THE MEDICINE AND WHAT IT IS USED FOR**

### **According to Swiss label**

#### Cutaneous squamous cell carcinoma

Libtayo is indicated as monotherapy for the treatment of adult patients with metastatic cutaneous squamous cell carcinoma or locally advanced cutaneous squamous cell carcinoma who are not candidates for curative surgery or curative radiotherapy.

#### Non-small cell lung cancer

Libtayo is indicated as monotherapy for the first-line treatment of adult patients with non-small cell lung cancer (NSCLC) with PD-L1 expression in  $\geq 50\%$  of tumor cells, without EGFR, ALK or ROS1 aberrations, who:

-suffer from locally advanced NSCLC and do not qualify for surgical resection or definitive radiochemotherapy; or

-have metastatic NSCLC

Patients who had smoked fewer than one hundred cigarettes during their lifetime were excluded from the pivotal study.

Libtayo in combination with platinum-based chemotherapy is indicated as first-line treatment for adult patients with NSCLC with squamous histology, independent of that with PD-L1 expression, and for patients with NSCLC with non-squamous histology with PD-L1 expression in at least 1% of tumor cells, without EGFR, ALK, or ROS1 genomic aberrations, who:

-suffer from locally advanced NSCLC and are not eligible for surgical resection or definitive radiochemotherapy; or

-have metastatic NSCLC (see "Clinical Efficacy").

### **According to EU SmPC**

#### Cutaneous squamous cell carcinoma (CSCC)

LIBTAYO® as monotherapy is indicated for the treatment of adult patients with metastatic (mCSCC) or locally advanced CSCC (laCSCC) who are not candidates for curative surgery or curative radiation.

#### Basal Cell Carcinoma (BCC)

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 (HPI).

#### Non-small cell lung cancer (NSCLC)

LIBTAYO as monotherapy is indicated for the first-line treatment of adult patients with non-small

cell lung cancer (NSCLC) expressing PD-L1 (in  $\geq 50\%$  tumour cells), with no EGFR, ALK or ROS1 aberrations, who have:

- locally advanced NSCLC who are not candidates for definitive chemoradiation, or
- metastatic NSCLC

#### Cervical cancer (CC)

LIBTAYO as monotherapy is indicated for the treatment of adult patients with recurrent or metastatic cervical cancer and disease progression on or after platinum-based chemotherapy.

#### Non-small cell lung cancer (NSCLC) in combination therapy

LIBTAYO in combination with platinum-based chemotherapy is indicated for the first-line treatment of adult patients with NSCLC expressing PD-L1 (in  $\geq 1\%$  of tumour cells) with no EGFR, ALK or ROS1 aberrations, who have:

- locally advanced NSCLC who are not candidates for definitive chemoradiation, or
- metastatic NSCLC

## **II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMIZE OR FURTHER CHARACTERIZE THE RISKS**

Important risks of cemiplimab, together with measures to minimise such risks and the proposed studies for learning more about cemiplimab's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals
- Important advice on the medicine's packaging
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly
- The medicine's legal status — the way a medicine is supplied to the patient (eg, with or without prescription) can help to minimise its risks

Together, these measures constitute routine risk minimisation measures.

In the case of cemiplimab, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of cemiplimab is not yet available, it is listed under 'missing information' below.

## II.A List of Important Risks and Missing Information

Important risks of cemiplimab are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of cemiplimab. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (eg, on the long-term use of the medicine).

List of important risks and missing information:

### Important Identified Risks:

- Immune-mediated adverse reactions (imARs) such as immune-mediated pneumonitis, colitis, hepatitis, endocrinopathies, immune-mediated skin reactions, nephritis, and other imARs
- Infusion-related reactions (IRRs)

### Important Potential Risks:

Lack of effect due to anti-drug antibodies (ADAs)

### Missing Information:

Long-term safety data

## II. B Summary of Important Risks

<b>Important Identified Risk: Immune-mediated Adverse Reactions</b>	
<b>Evidence for Linking the Risk to the Medicine</b>	<p><u>Cemiplimab Monotherapy:</u></p> <p>A total of 249 (20.8%) patients exposed to cemiplimab monotherapy in clinical trials experienced at least 1 imAE, including fatal or grade 5 (0.3%), life-threatening or grade 4 (0.6%), severe or grade 3 (5.6%), and moderate or grade 2 (11.2%). Fifty-six (4.7%) patients discontinued treatment due to imAEs.</p> <p><u>Cemiplimab in Combination Therapy (cemiplimab/chemotherapy):</u></p> <p>A total of 59 (18.9%) patients exposed to cemiplimab in combination therapy in clinical trials and included in the RMP experienced at least 1 imAE. Grade <math>\geq 3</math> imAEs were reported in 9 (2.9%) patients, including one patient (0.3%) with grade 5. Three (1.0%) patients discontinued treatment due to imAEs.</p>

<p><b>Risk Factors and Risk Groups</b></p>	<p>Patients with a history of or ongoing autoimmune disease may be at higher risk of developing imAEs and were excluded from the development programme for cemiplimab. Patients who were previously exposed to idelalisib may be at increased risk of experiencing severe immune-mediated mucocutaneous adverse reactions.</p>
<p><b>Risk Minimisation Measures</b></p>	<p>Routine risk communication messages: SmPC sections 4.4 and 4.8 PL sections 2 and 4</p> <p>Routine risk minimisation activities recommending specific clinical measures to address the risk: SmPC sections 4.2 and 4.4 PL sections 2 and 3</p> <p>Other routine risk minimisation measures beyond the Product Information:</p> <p>Legal status:</p> <p>Cemiplimab is subject to restricted medical prescription, and treatment must be initiated and supervised by physicians experienced in the treatment of cancer.</p> <p>Additional risk minimisation measures:</p> <p>Patient Guide and Alert Card</p>

<b>Important Identified Risk: Infusion-related Reactions</b>	
<p><b>Evidence for Linking the Risk to the Medicine</b></p>	<p><u>Cemiplimab Monotherapy:</u></p> <p>In Study 1423, Study 1540, Study 1620, Study 1624 and Study 1676, IRRs occurred in patients receiving cemiplimab. These have also been observed in patients exposed to other PD-1 inhibitors.</p> <p>Infusion-related reactions occurred in 7.3% (87/1198) of patients receiving cemiplimab including 1 (&lt;0.1%) patient with grade 3 IRRs. Infusion-related reactions led to permanent discontinuation of cemiplimab in 1 (&lt;0.1%) patient. The most common symptoms of infusion-related reaction were nausea, pyrexia, and vomiting. All patients recovered from infusion-related reaction.</p> <p><u>Cemiplimab in Combination Therapy (cemiplimab/chemotherapy):</u></p> <p>Infusion-related reactions occurred in 2.2% (7/312) of patients receiving cemiplimab in combination therapy in clinical trials, all &lt; grade 3. No IRRs led to permanent discontinuation of cemiplimab. The most common symptoms of infusion-related reaction were vomiting and pruritus. All patients recovered from infusion-related reaction.</p>
<p><b>Risk Factors and Risk Groups</b></p>	<p>Even though all patients are potentially at risk of IRRs, patients with documented allergic reactions or acute hypersensitivity reactions attributed to antibody treatments may be at higher risk of developing severe IRRs and were excluded from the development programme for cemiplimab.</p>
<p><b>Risk Minimisation Measures</b></p>	<p>Routine communication messages: SmPC sections 4.4 and 4.8 PL sections 2 and 4</p> <p>Routine risk minimisation activities recommending specific clinical measures to address the risk: SmPC sections 4.2, 4.3, and 4.4. PL sections 2 and 3</p> <p>Other routine risk minimisation measures beyond the Product Information:</p> <p>Legal status: Cemiplimab is subject to restricted medical prescription and treatment must be initiated and supervised by physicians experienced in the treatment of cancer.</p> <p>Additional risk minimisation measures: Patient Guide and Alert Card</p>

<b>Additional pharmacovigilance activities</b>	None
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<b>Important Potential Risks: Lack of Effect due to Anti-drug Antibodies</b>	
<b>Evidence for Linking the Risk to the Medicine</b>	<p>In nonclinical studies, the prevalence of immunogenicity/ADA was high; however, continuous exposure was maintained for 80% and 50% of animals throughout the 4-week and 26-week toxicology studies, respectively. As cemiplimab is a human antibody, the presence of ADA following cemiplimab administration to cynomolgus monkeys was expected and not considered predictive of the human ADA response to cemiplimab.</p> <p>In the overall population of patients with solid tumours, immunogenicity was assessed in all patients with solid tumours, including patients with NSCLC in Study 16113 Part 2, after cemiplimab administration as monotherapy (Studies 1423, 1540, 1620, 1624 and 1676) or in combination with radiotherapy and/or chemotherapy (Study 1423) or with chemotherapy (Study 16113 Part 2).</p> <p>The incidence of treatment-emergent ADA in all patients with solid tumours in the ADA analysis set (n=1310) was low (approximately 2.5%), including the subset of patients who received cemiplimab 350 mg Q3W. The ADA titers were generally low (&lt; 1,000). Overall, only 3 patients (0.3%) had a persistent ADA response. No patients were positive for neutralizing antibodies (NABs).</p> <p>The presence of treatment-emergent ADA did not appear to have a clinically meaningful effect on cemiplimab concentrations (Study 1423 Final CSR Appendix 5 [CP Report] Section 4.4, Study 1540 Interim CSR Appendix 5 [CP Report] Section 4.4, Study 1620 Interim CSR Appendix 5 [CP Report] Section 4.3, Study 1624 Primary Analysis CSR Appendix 16.1.15 [CP Report] Section 4.3, Study 1676 Primary Analysis CSR Appendix 16.1.15 [CP Report] Section 4.3 and Study 16113 Part 2 Primary Analysis CSR Appendix 16.1.15 [CP Report] Section 4.3).</p>
<b>Risk Factors and Risk Groups</b>	Risk factors are unknown. Any patient who receives cemiplimab has a potential risk of developing ADAs.

<b>Risk Minimisation Measures</b>	<p>Other routine risk minimisation measures beyond the Product Information:</p> <p>Legal status:</p> <p>Cemiplimab is subject to restricted medical prescription and treatment must be initiated and supervised by physicians experienced in the treatment of cancer.</p>
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## II.C Post-authorisation Development Plan

### II.C.1 Studies which are Conditions of the Marketing Authorisation

The following studies are conditions of the marketing authorisation:

Basal cell carcinoma

**R2810-ONC-1620 (Group 1, mBCC) - A phase 2 study of cemiplimab in patients with advanced BCC who experienced progression of disease on Hedgehog Pathway Inhibitor therapy or were intolerant of prior Hedgehog Pathway Inhibitor therapy.**

Rationale and Study Objectives:

To further confirm clinical efficacy and safety of cemiplimab in mBCC, the MAH should submit the final study report of the clinical study 1620 for mBCC evaluating objective response rate and duration of response of cemiplimab in patients with mBCC who experienced progression of disease on hedgehog pathway inhibitor therapy or were intolerant of prior hedgehog pathway inhibitor therapy.

The primary objective of the study was to estimate the ORR for mBCC (Group 1) or unresectable laBCC (Group 2), according to central review, when treated with cemiplimab monotherapy in patients who had progressed on HHI therapy or were intolerant of prior HHI therapy.

Study Design:

This is an ongoing phase 2, non-randomized, 2-group, multicentre study of cemiplimab at a 350 mg dose administered IV Q3W in patients with advanced BCC who experienced progression of disease on HHI therapy, experienced a response no better than stable disease for at least 9 months or were intolerant of prior HHI therapy.

Study Population:



The study has 2 groups. Group 1 is for patients with metastatic BCC. Group 2 is for adult patients with locally advanced BCC.

#### **II.C.2 Other Studies in Post-authorisation Development Plan**

Not Applicable